







Genomics R&D Initiative

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Genomics R&D Initiative

ANNUAL PERFORMANCE REPORT 2008-09

The Genomics R&D Initiative is a national program that coordinates federal science departments and agencies in the field of genomics to support key national interests in human health, agriculture and food safety, environment and natural resources management.

HE GENOMICS R&D INITIATIVE IS A ROGRAM THAT COORDINATES FEDE CIENCE DEPARTMENTS AND AGEN









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Executive Summary









The \$19.9 million/yr **Genomics R&D Initiative (GRDI)** sustains intramural genomics research in support of key federal public policy objectives in areas of national interest to strengthen innovation, promote competitiveness, and ensure sustainability for the benefit of all Canadians, under the mandates of NRC (\$6M/yr), Agriculture and Agri-Food Canada (\$6M/yr), Health Canada and the Public Health Agency (\$4M/yr), Natural Resources Canada (\$2M/yr), Environment Canada (\$1M/yr) and Fisheries and Oceans Canada (\$0.9M/yr).

Since the implementation of GRDI in 1999, participating departments and agencies have increased their human resource capacity as well as enhanced the tools, equipment, infrastructure and networks required to undertake genomics R&D and participate in broader, high-impact programs through extensive collaborations with Canadian and international organizations. Investments from the GRDI have allowed public sector scientists to explore promising research avenues towards Canada's economic goals and social wealth and have delivered tangible results that are already helping in many areas important to Canadians. Federal scientists excel in strategically selected areas of genomics research and the GRDI was assessed in its independent formative evaluation as well-managed, effective and efficient. Phase IV of the GRDI ends in March 2011. In a climate of limited resources for government operations, the GRDI forms an integral component of the genomics research program of federal laboratories.

The GRDI has been funded for three-year cycles: Phase I (1999-02), Phase II (2002-05), Phase III (2005-08), and Phase IV (2008-11). Fiscal year 2008-09 was the first year of Phase IV programs. Departments and agencies strategically reviewed their research priorities and held peer-reviewed competitions for the allocation of funds to new projects. The overall GRDI program framework for Phase IV is presented in the following section, entitled **Phase IV GRDI Impact Areas – an Overview**. Fiscal year 2008-09 was also a year of forward-looking discussions for the development of a renewed policy framework for the GRDI to respond to evolving drivers beyond Phase IV.

This Annual Performance Report for 2008-09 follows the Results-based Management and Accountability Framework (RMAF) for the GRDI, which formalizes common measurement criteria according to requirements of the Treasury Board Secretariat. It presents the GRDI program profile and impact areas, its links to departmental objectives and program activity architecture, its relevance to the Federal S&T Strategy, and the research program plans and activities. It then reports on performance for 2008-09 in terms of management, collaborations (Tables 3 and 4), capacity building, research and development (summarized in Annex 3 of Appendix A and illustrated by the summary statistics of outputs in Annexes 2, 4 and 5 of Appendix A), and outreach.

Acronyms

AAFC	Agriculture and Agri-Food Canada	NRC	National Research Council
ABIP	Agricultural Bioproducts Innovation Program	NRCan	Natural Resources Canada
ABL	Aquatic Biotechnology Lab	OECD	Organization for Economic Cooperation
ADM	Assistant Deputy Minister		and Development
ВС	British Columbia	OGD	Other Government Departments
CanSeq	Canadian Canola Genome	PCR	Polymerase Chain Reaction
	Sequencing Initiative	PGIP	Polygalacturonase Inhibitor Proteins
CBN	Cellulosic Biofuel Network	PHAC	Public Health Agency of Canada
CCGI	Canadian Crop Genomics Initiative	QTL	Quantitative Trait Locus
cDNA	complementary DNA	R&D	Research and Development
CFS	Canadian Forest Service	RMAF	Results-based Management
DFO	Fisheries and Oceans Canada		and Accountability Framework
DNA	Deoxyribonucleic Acid	RNA	Ribonucleic Acid
EAB	Emerald Ash Borer	SNP	Single Nucleotide Polymorphism
EC	Environment Canada	S&T	Science and Technology
IPCS	International Programme on Chemical Safety	STAGE	Strategic Technology Applications of Genomics in the Environment
ISAV	Infectious salmon anemia virus	USDA	United States Department of Agriculture
GHI	Genomics and Health Initiative	US EPA	United States Environmental Protection
GRDI	Genomics R&D Initiative		Agency
HC	Health Canada	VTEC	Verotoxigenic Escherichia coli
MPB	Mountain Pine Beetle	WHO	World Health Organization

Phase IV GRDI Impact Areas

The strategic focus of GRDI research is to contribute solutions to issues of key importance to Canadians – protecting and improving human health, developing new treatments for chronic and infectious diseases, protecting the environment, and managing agricultural and natural resources in a way that is sustainable. Focusing on the specific role of federal government research, it supports evidence-based decision making, policy development, formulation of standards and regulations, and facilitates the development of Canadian commercial enterprises.

IMPROVED PUBLIC HEALTH AND WELLNESS

PLANNED RESULTS

Improve knowledge and understanding of human infectious and chronic diseases for public health-related applications including the development of improved or new diagnostic tools.

Realize crop value improvements in cereals, canola and soybean related to seed development and metabolism (oil content, starch quality, anti-nutritional compounds).

IMPACT AREAS

Phase IV GRDI tackles research on issues such as developing new treatments for cancer, heart disease, and a vast range of other acute and chronic diseases; developing vaccines; and understanding how to limit the spread of diseases and potential pandemics. New drugs, nutraceuticals, improved crop yield and nutritional value, and functional foods are the result of genomics-based research towards successful health outcomes.

PLANNED ACTIVITIES

Infectious diseases

- Understand the molecular basis of critical pathogenic and genetic diseases
- Conduct molecular epidemiology of infectious diseases

- Create point-of-care devices for the diagnosis of organisms causing hospital-acquired infections and food and water contamination
- Understand responses to hepatitis C and HIV antiviral treatments
- Clarify the role of vitamin D related to severe influenza infection in seniors
- Develop bacteriophages to prevent common bacterial infections
- Evaluate the role of bacterial pathogens in cystic fibrosis patients

Chronic diseases

- Identify and develop a broad range of targeted therapeutics agents to create the next generation of efficient cancer therapies
- Study interferon-induced hepatic injury
- Identify biomarkers for exposure to mutagenic carcinogens and inhaled contaminants, and effects in cancer, atherosclerosis and asthma development

Food supply

- Decipher the genes that control seed development, carbon partitioning, protein quality, oil quality, starch quality, and the accumulation of anti-nutritional compounds in cereals (wheat, corn), oilseeds (*Brassica*) and legumes (soybean) to improve their productivity and resilience
- Study nutraceutical compounds such as phytosterols, anthramides, and glucans for medical applications

TOWARDS ENVIRONMENTAL SUSTAINABILITY

PLANNED RESULTS

Realize crop value improvements in cereals, canola and soybean related to adaptation to environmental stresses (diseases, pests, drought, cold, and poor soil conditions).

Increase knowledge for forest generation and protection methods, and for addressing environmental impact considerations, through a focused effort on species and traits that are of economic importance to Canada.

Develop and use genomics tools to generate increased understanding of population genetics and structure, as well as of behavioural, physiological and immunological responses to the environment, for the sustainable management of aquatic resources.

Develop genomics applications to understand and remediate environmental contamination and to preserve biodiversity.

IMPACT AREAS

Phase IV GRDI tackles research on issues towards environmental sustainability outcomes such as developing more productive and resistant crops for sustainable agriculture; controlling plant and animal pests and diseases in an environmentally sustainable manner; adapting crops, forests and fish species to respond to climate change related challenges; and protecting endangered species.

PLANNED ACTIVITIES

Agriculture

- Improve the productivity and resilience of Canadian canola crops to meet increasing national and global demands for food and industrial applications (biofuels)
- Develop crops with increased resistance to diseases and insect pests
- Design strategies to engineer increased tolerance to heat, cold and frost in crops

Forestry

- Identify genetic markers for the selection of spruce trees with desired attributes of wood quality and adaptation
- Understand forest host-pathogen genetic interactions to improve sustainable pest control
- Develop and transfer molecular diagnostic tools for the detection and surveillance of forest diseases and pests and phytosanitary certification

Fisheries and aquaculture

- Develop conservation genomics for species of importance to Canada (Atlantic salmon, beluga whales, capelin, Dolly Varden chars)
- Study the migratory fitness of wild salmon
- · Identify redfish species and stock structure
- Study salmon diseases (anemia virus, parasites, louse)

Environment

- Conduct molecular characterization of microbial communities in contaminated soil
- Investigate the toxic effects of environmental contaminants on aquatic microbial communities
- Develop conservation genomics of selected wildlife species (birds, mammals)
- Apply genetic markers to resolve species identification and population structure of aquatic invasive species
- Study emerging infectious diseases in native birds and amphibians

EVIDENCE-BASED DECISION MAKING

PLANNED RESULT

Support federal regulatory decisions under the mandates of participating departments and agencies.

IMPACT AREAS

Phase IV GRDI research is developing: diagnostic tools for the detection, surveillance and management of food-borne and water-borne pathogens (salmonella, *Escherichia coli*), human, aquatic, animal and plant pests and diseases, including quarantine species; detailed characterization of new products (food, pharmaceuticals, medical devices, etc.) to allow their responsible introduction and ongoing monitoring; and forensic tools to monitor fish resources for the sustainable management of fishery openings and access to global markets. Many of the impact areas already described under the above sections also support evidence-based decision making.

PLANNED ACTIVITIES

- Develop monitoring tools for the management of two important fisheries (beluga and salmon)
- Implement the use of genetic information for mixed-stock fishery management
- Understand population genetics and structure of economically important species to guide management decisions
- Develop diagnostic tools for the management of aquatic animal diseases, important for both the wild fisheries and the aquaculture industry
- Develop and use DNA profile for threatened Northern abalone to successfully prosecute poachers in court and facilitate out-of-court settlements
- Validate genomics-based procedures to ensure more accurate data for submission under the Canadian Environmental Protection Act New Substances Notifications Regulations
- Improve 'early warning' signals to industry regulators with DNA-based techniques used to link environmental exposure of specific substances to potential toxic effects

- Provide species identification for improved enforcement of the Wild Animal and Plant Protection and Regulation of International and Interprovincial Trade Act, and the Convention on International Trade in Endangered Species of Wild Fauna and Flora
- Evaluate gene expression changes in human cell lines following exposure to wireless telecommunication signals emitted by cellular phones
- Investigate molecular-level effects of environmental contaminants (priority substances and emerging contaminants) on wild species to improve environmental risk assessment/monitoring
- Detect the presence of genetically modified organisms in aquatic ecosystems
- Detect pathogenic micro-organisms in wastewater

FORMULATION OF POLICIES, STANDARDS AND REGULATIONS

PLANNED RESULTS

Support key federal public policy objectives under the mandates of participating departments and agencies.

Position the Canadian regulatory system for health to enable innovation while minimizing the risks to Canadians through a focused genomics R&D program aimed at strengthening research in priority areas such as genetic information, biotechnology products, human genomics and microbial genomics, related to human, animal and environmental health.

Develop genome-science applications to support regulatory activities in key areas such as environmental risk assessment and management; enforcement and compliance; pollution detection, monitoring and prevention; conservation biology and wildlife genetics; technology forecasting and assessment; and the sustainable development and responsible use of bio-based products and industrial processes.

IMPACT AREAS

Responsible commercial applications that generate wealth for Canadians are enabled by effective regulatory approaches. Phase IV GRDI generates knowledge to support the formulation of policies, standards and regulations related to the responsible introduction and ongoing monitoring of new products such as pharmaceuticals, medical devices, and food commodities; traceability (animals, plants, food, fish); environmental monitoring and remediation; food additives and labelling. Many of the impact areas already described under the above sections also support the formulation of policies, standards and regulations.

PLANNED ACTIVITIES

- Develop a molecular risk assessment strategy for toxin-producing E. Coli
- Understand gene expression patterns linked to dietary fibre and "resistant carbohydrates" to shape a new Health Canada definition for dietary fibre
- Conduct molecular characterization of microbial communities in contaminated soil to validate a new national guidance document under the Canadian Environmental Protection Act
- Integrate systems biology approaches in Health Canada regulatory toxicology assessments
- Develop methods for the evaluation of effluents and chemicals, in collaboration with the British Columbia Ministry of the Environment, to be included in risk assessment processes under the Georgia Basin Action Plan and the Chemical Management Plan

SUPPORT FOR CANADIAN COMMERCIAL ENTERPRISES

PLANNED RESULT

Develop commercially relevant advances in areas of genomics R&D related to human health (e.g. genetic testing, diagnostics, microbial genomics applications, treating and preventing human diseases such as cancer and cardiovascular disease, and pathogen detection).

IMPACT AREAS

Phase IV GRDI scientists collaborate with Canadian companies to support their R&D efforts for the generation of wealth to support Canada's economy.

PLANNED ACTIVITIES

- Commercial development by a private company of antibodies developed by NRC for cancer treatment
- Validation by a commercial partner of Salmonella detection technology developed by PHAC for commercialization to diagnostic laboratories
- Canadian Canola Genome Sequencing Initiative
 Collaborative Research Agreement between NRC,
 AAFC, Genome Alberta and four industry partners
 (Cargill Limited, Dow AgroSciences Canada Inc.,
 KWS SAAT Ag and RAPOOL-Ring GmbH) formalized
 in February 2009

Genomics R&D Initiative (GRDI) - Program Profile

Overview

Genomics is the science that studies DNA sequences and their functions in living organisms. The real potential for genomics to provide benefits lies in its power to enable the study of biological systems in their entirety. This provides the understanding of how genes and their products interact in a given environment and insights into how variation in genes impacts biological outcomes such as productivity, quality, and disease resistance.

Genomics has applications in all areas of life. It provides knowledge to support the development of products and processes to enhance the competitiveness of sectors that are key to the economic wealth of Canadian communities (health, agriculture, forestry, fisheries), to advance sustainable environmental technologies, and to improve the quality of life for Canadians now and in the future. Federal, provincial and municipal governments are major consumers of knowledge and tools derived from these technologies.

The Government of Canada, recognizing its legitimate and necessary role in this area, has been a strong supporter of genomics research for over a decade and has funded federal research through the Genomics R&D Initiative (GRDI) since 1999.

The \$19.9 million/yr GRDI sustains intramural genomics research in support of key federal public policy objectives in areas of national interest to strengthen innovation, promote competitiveness, and ensure sustainability for the benefit of all Canadians, under the mandates of NRC (\$6M/yr), Agriculture and Agri-Food Canada (\$6M/yr), Health Canada and the Public Health Agency (\$4M/yr), Natural Resources Canada (\$2M/yr), Environment Canada (\$1M/yr) and Fisheries and Oceans Canada (\$0.9M/yr). The GRDI has been funded in three-year cycles as shown in Table 1. Phase IV of the GRDI ends in March 2011. In a climate of limited resources for government operations, the GRDI forms and integral component of the genomics research program of federal laboratories.

Table 1: Funding Allocations (\$000)

DEPARTMENT/AGENCY	PHASE I 1999-2002	PHASE II 2002-2005	PHASE III 2005-2008	PHASE IV 2008-2011
Agriculture and Agri-Food Canada	17,000	18,000	18,000	18,000
Environment Canada	3,000	3,000	3,000	3,000
Fisheries and Oceans Canada	2,500	2,700	2,700	2,700
Health Canada / Public Health Agency of Canada	10,000	12,000	12,000	12,000
National Research Council Canada	17,000	18,000	18,000	18,000
Natural Resources Canada	5,000	6,000	6,000	6,000
Medical Research Council ¹	500	-	-	-
Total	55,000	59,700	59,700	59,700

¹ Precursor to the Canadian Institutes of Health Research (CIHR) – one time allocation in fiscal year 1999-2000 to assist in the establishment and support of a Genome Canada Secretariat.

The strategic focus of GRDI research is to contribute solutions to issues of key importance to Canadians – protecting and improving human health, developing new treatments for chronic and infectious diseases, protecting the environment, and managing agricultural and natural resources in a way that is sustainable. Focusing on the specific role of federal government research, it supports evidence-based decision making, policy development, formulation of standards and regulations, and facilitates the development of Canadian commercial enterprises.

Since the implementation of GRDI in 1999, participating departments and agencies have explored research avenues towards Canada's economic goals and social wealth and have delivered tangible results that are already helping in many areas important to Canadians.

To maximize the quality and relevance of research funded under the GRDI, each department uses a competitive program proposal and approval process including scientific peer reviews. Extensive research collaborations in Canada and internationally allow strong

leverage of resources and expertise, and the pursuit of larger-scale multi-disciplinary discovery enterprises (as described in **Tables 2**, **3** and **4**, and Management on page 13).

Governance

An interdepartmental Assistant Deputy Minister (ADM) Coordinating Committee oversees the collective management and coordination of the federal GRDI. The Committee ensures that effective priority setting mechanisms are established within departments, and that government objectives and priorities are addressed. The Committee also ensures that common management principles are implemented and horizontal collaborations between organizations are pursued and undertaken. The committee includes members from each of the organizations receiving funding and guest representatives from Industry Canada and from Genome Canada.

An interdepartmental GRDI Working Group supports the work of the committee. The mandate of the working group is to provide recommendations and advice to the ADM Coordinating Committee regarding strategic priority setting and overall management of the GRDI. The working group also supports evaluation and reporting requirements related to the Initiative.

The National Research Council coordinates interdepartmental activities to manage the GRDI, including the development and implementation of the Resultsbased Management and Accountability Framework, and chairs both the Coordinating Committee and the Working Group.

Formative Evaluation – A Well Managed, Effective, and Efficient Initiative

A formative evaluation of the Genomics R&D Initiative was conducted in 2006 by an independent consultant (Performance Management Network Inc.) concluding to its overall success and relevance to deliver well-managed credible research for policy, regulation and other government decisions. The evaluation confirmed that for the most part, the six government departments had limited capacity to carry out genomics research before the implementation of GRDI, and that GRDI had been successful in increasing that capacity. Departments supported by GRDI funds have managed to increase their human resource capacity as well as enhance the tools, equipment, infrastructure and networks required to undertake genomics R&D

and participate in broader, high-impact programs established through formal and informal collaborations with Canadian and international organizations (governmental, university, non-governmental and private sector organizations). The review also concluded to the legitimate and necessary role for government in genomics R&D, and to the complementing nature of GRDI and other federal or provincial initiatives in this area without overlap or duplication.

A key recommendation of the evaluation was to not only continue support for the Initiative on an ongoing basis, but also to increase its funding base to meet the evolving need for federally performed genomics R&D. Other key recommendations included: that government should identify mechanisms to strengthen the strategic direction for the GRDI to address national priorities, and take steps to ensure that accountability and performance reporting continue as key elements of the initiative. The GRDI ADM Coordinating Committee committed to address the recommendations in a management action plan in accordance with Treasury Board Evaluation Policy and progress is reported annually in the NRC Departmental Performance Report.

Strong Scientific Performance

A bibliometric assessment of research funded by GRDI between 1996 and 2007 was conducted by Science-Metrix in 2009. Its key findings were that: (1) in terms of their scientific impact, GRDI scientists compared favourably with other federal scientists involved in genomics research as well as with Canadian and international peers, publishing papers that were more frequently cited than the Canadian (9%) and world (22%) averages in genomics; (2) the federal government has aligned its research intensity in genomics with those of Canada and of the world since the creation of GRDI in 1999; and (3) the average number of genomics papers produced by GRDI scientists increased during the period of support. Further, genomics accounted for an increased proportion of the federal government's scientific output, rising from 6% in 1996 to 9% in 2007.

Planning for the Future - A Renewed GRDI

There have been numerous developments impacting both the scope and direction of genomics research since the policy authority was provided in 1999 for the GRDI. These include emerging issues in terms of threats to health, safety, food, and energy security, largely related to environmental changes, increasing global trade flow, and human demographics; spectacular

scientific progress in genomics research generating major economic opportunities; a new science policy in Canada provided by the Federal S&T Strategy; the strong role of Genome Canada to support university led large-scale genomics research; recognition of genomics as a strength area for Canada; and conclusions from the formative review of the GRDI that recognized its overall success and relevance and provided recommendations for government action. Most importantly, Canada needs to realign its intramural initiative to address these developments, to prepare for next generation technologies that will revolutionize genomics research, and to ensure that the Canadian genomics program continue to provide Canadians and Canadian business with a competitive advantage. Such a GRDI will constitute an integral component of the federal government's commitment to "promote more effective horizontal" management of cross-cutting issues that touch on government-wide priorities, and application of consistent mechanisms for promoting high accountability in the use of federal S&T resources1,"

Building on the overall success and relevance of the intramural GRDI, incorporating Canada's evolving economic, scientific and policy contexts, and responsively addressing the recommendations received from the Initiative's Formative Review, the federal genomics R&D community is planning a refocused GRDI with strengthened delivery mechanisms around strategic priorities and improved inter-departmental integration to best fulfill the role of federal research towards economic and social goals for Canada. A refocused GRDI will seek to: 1) deliver high impact solutions to identified enduring and emerging issues through horizontal integration and effective partnerships for economic, social, and environmental benefits for Canadians, and 2) support the priorities, policies and mandates of government through concerted high calibre genomics research in areas where federal laboratories have distinct roles and competencies.

The GRDI is one component of a multi-player context for genomics research in Canada. Given Canada's strength in this area and the multiple academic players, genomics research presents a huge opportunity area for government laboratories to leverage their resources and make an impact through their participation in world-class cutting edge collaborative research. A focused well-coordinated GRDI would be able to better align its investments with those of academia, Canadian provinces, and the private sector.

Results-based Management and Accountability Framework

A Results-based Management and Accountability Framework (RMAF) for the GRDI formalizes the commitment of the departments and agencies involved in the Initiative to report on common performance indicators and guides the structure and content of this 2008-09 Annual Performance Report, which covers year 1 or Phase IV funding.

The RMAF logic model reflects the overall objectives of the Initiative organized into four program areas:

Management, Genomics R&D Capacity, Research and Development, and Outreach. The key performance indicators under each of these are:

 Management – Enhanced governance, coordination and partnerships.

- Genomics R&D Capacity Increase and training of Highly Qualified Personnel; advancements in state-of-the-art infrastructure; and increased participation in national and international genomics initiatives.
- Research and Development Access to and sharing of technology and scientific knowledge; application of research results to develop innovative, new or improved methods, products, processes or technologies.
- Outreach Increased awareness and understanding of genomics research results and applications.

An overview of the RMAF is provided in Appendix B, including the Logic Model and related tables of performance indicators.

Canada. 2006. Overcoming barriers to S&T collaboration. Steps towards greater integration.

Links to Departmental Objectives and Program Activity Architecture

Projects funded under the GRDI are focused on departmental mandates and government priorities, and are aligned with the strategies of their respective departments.

The Genomics and Health Initiative (GHI) is the largest horizontal R&D initiative of the National Research Council (NRC). Through its multi-disciplinary approach and research excellence NRC-GHI is supporting goal 2 of the NRC Strategy by making significant contributions to Canadian R&D priorities in health (chronic diseases and agri-food), in energy (biofuels), and for the environment (environmental technologies and bioproducts). GHI also contributes to goal 1 of the NRC Strategy by contributing to the competitiveness of industry by increasing the flow of technologies into high-impact areas of the Canadian economy. Support for these goals is achieved through the funding of research programs that are aligned with key industrial sectors and focused on the translation of scientific and technical knowledge into social and economic development. The initiative enables NRC to deliver on its mandate to translate S&T into value for Canada through partnerships with other government organizations, academia, and industry to provide an integrated approach to S&T initiatives.

Agriculture and Agri-Food Canada (AAFC) provides information, research and technology, programs and policies to support Canada's agriculture, agri-food and agri-based product sectors. The GRDI directly supports two of the department's Strategic Outcomes: A Competitive Sector that Proactively Manages Risk and An Innovative Sector. Funding from the GRDI has enabled AAFC to strengthen the Canadian Crop Genomics Initiative (CCGI) through additional investments in plant genomics and in the formation of multi-disciplinary teams across Canada. Funding from the GRDI has been used to support the advancement of technologies for 1) the development of sustainable food and feed supply from cereals, pulses and oilseeds, and 2) the introduction of crop platforms for the generation of industrial and biofuel products. The CCGI catalyzes the formation of integrated S&T teams within AAFC and in partnership with universities, the private sector, non-governmental organizations and highly regarded international genomic institutes.

The GRDI supports three Health Canada (HC) strategic outcomes: Strengthened Knowledge Base to Address Health and Health Care Priorities: Access to Safe and Effective Health Products and Food Information for Healthy Choices; and Reduced Health and Environmental Risk from Products and Substances, and Safer Living and Working Environments. The contribution of GRDI at HC is to generate knowledge that is vital to the effective regulation of health related products. The Departmental Framework for Biotechnology outlines its biotechnologyrelated roles and responsibilities including providing leadership in policy and regulatory development, informing and engaging the public, ensuring an international position for Canada, and applying the benefits of biotechnology to HC's mandate. Four themes guide research activities of the GRDI: generation, use and societal impacts of human genetic information; health and safety of biotechnology products; human genomic applications and impacts related to diagnostics and disease; and microbial genomic applications and impacts related to diagnostics and disease.

The GRDI supports the strategic outcome of the Public Health Agency of Canada (PHAC) of A Healthier Population by Promoting Health and Preventing Disease and Injury. Two themes guide research activities of the GRDI for PHAC: 1) Public Health Pathogenomics: generating, synthesizing, and moving new knowledge on pathogen genomics and related sciences (proteomics, transcriptomics, metabolomics and bioinformatics) into enhanced infectious disease surveillance, prevention and control programs. New knowledge application takes the form of novel diagnostics, molecular risk assessment tools, vaccines, intervention strategies, and methods for mitigating antimicrobial resistance. 2) Public Health Genomics: generating, synthesizing, and moving new knowledge in human genomics and related sciences (proteomics, transcriptomics, and bioinformatics) aimed at enhancing diagnostic, health promotion and preventative efforts, such as modulation of risk factors for chronic and infectious diseases and/or predictive genetic screening.

The Canadian Forest Service (CFS) of Natural Resources Canada (NRCan) promotes the sustainable development of Canada's forests and the competitiveness of the Canadian forest sector. The GRDI has

developed the foundation for contributing to the NRCan Strategic Outcome Economic Competitiveness and to the Program Activity Innovation from Forests to Market. It contributes to the CFS Intended Outcome: Innovation Is Robust and Adds Economic Value to Each Link of the Forest Sector's Value Chain – from Forest to Market. It is positioned at the leading edge of unique technological platforms for tree and insect tissue culture, molecular diagnostics, population genetics, biological control products and functional genomics. Resulting from this foundation is a critical mass of data, infrastructure, and partnerships that is delivering important practical applications.

Environment Canada (EC) carries out its genomics research through the Strategic Technology Applications of Genomics in the Environment (STAGE) program. Under the aegis of this program, the department has focused funding on projects that examine how genomics tools and methods can be used to support its policy, regulatory decision making, and enforcement mandates. More specifically, projects address the following departmental priorities: *Risk Identification* (e.g. knowledge on the effects of environmental contaminants on the biodiversity and function of microbial communities);

Risk Assessment/Management (e.g. more accurate data for submission and knowledge for assisting regulatory decisions); Conservation Biology and Wildlife Management (e.g. genetic markers for conservation and protection decisions); and Improved Enforcement and Compliance (e.g. sample identification and wildlife forensics). Genomics-derived tools are starting to be applied by end users (regulations, enforcement, conservation strategies etc.). However, not all areas of genomics are at the same stage of maturity and extensive validation of some genomics-based approaches and data are needed before being applied to the enforcement and regulatory mandates of the department.

The National Aquatic Biotechnology and Genomics R&D Program of Fisheries and Oceans Canada (DFO) supports genomics research related to responsibilities for fishery management, monitoring fish habitat, sustaining fisheries and aquaculture, and protecting marine resources. Specific goals for genomics research within four DFO research centres across Canada were developed for aquatic ecosystems and organisms in alignment to the department's mandate and strategic objectives.

Relevance to the Federal S&T Strategy

The federal science policy framework is provided by the 2007 Federal Science and Technology (S&T) Strategy – Mobilizing Science and Technology to Canada's Advantage with its four core principles (promoting world-class excellence; focusing on priorities; encouraging partnerships; enhancing accountability) and its three policy commitments of creating Entrepreneurial, People, and Knowledge Advantages. Canada will achieve a Knowledge Advantage by focusing more of our energies and resources in the priority areas of environmental science and technologies; natural resources and energy; health and related life sciences and technologies; and information and communications technologies.

The S&T Strategy summarizes the role of research pursued inside federal laboratories as upholding regulatory, public policy, and operational mandates in important areas such as health care, food safety, and environmental protection, focusing activities in areas where government is best able to deliver results, and leveraging university and private-sector strengths.

The GRDI is highly relevant to the Federal S&T Strategy, given its strategic focus on supporting government

evidence-based decision making, policy and regulatory development, and the development of Canadian commercial enterprises in the key areas of protecting and improving human health, developing new treatments for chronic and infectious diseases, protecting the environment, and managing agricultural and natural resources in a way that is sustainable.

Programs funded under the GRDI are used to attract, train, and support highly skilled personnel including research scientists, visiting fellows, PhD students, technicians, and policy analysts, providing them access to world-class research infrastructure and networks.

Collaborative relationships are an important part of the GRDI to bring together the unique capabilities, interests, and resources of research partners and stakeholders. They are created among government-based science organizations, universities, industry, and other research institutes, both nationally and internationally, through the sharing of technology platforms and by collaborating in research areas that cut across traditional departmental sectors.

Resources

All departments have levered the GRDI with allocations from their A-base resources and from successful collaborations. **Table 2** provides an overview of resources in 2008-09, showing that leveraged funds represented more than two and a half times the GRDI

investments. Additional in kind leverage included the sharing of technology platforms, materials, and expertise with a variety of partners in research areas that cut across traditional departmental sectors.

Table 2: GRDI and Leveraged Resources (\$000)

DEPARTMENT/AGENCY	GRDI	LEVERAGED	GRDI + LEVERAGED
National Research Council	6,000	16,974	22,974
Agriculture and Agri-Food Canada	6,000	7,200	13,200
Health Canada	1,523	1,000	2,523
Public Health Agency Canada	2,477	4,650	7,127
Natural Resources Canada	2,000	5,249	7,249
Environmental Canada	1,000	1,214	2,214
Fisheries and Oceans Canada	900	2,648	3,548
Total	19,900	38,935	58,835

Research Program Plans and Activities

Projects of the GRDI support innovation and related regulations and policies in the key Canadian economic sectors of forestry, agriculture, fisheries, health, and life sciences. The overall GRDI program framework for Phase IV is presented in the section entitled **Phase IV GRDI Impact Areas**. Highlights of departmental plans and activities for 2008-09 (first year of Phase IV) are provided in the following sections and additional details may be found in **Annex 1** of Appendix A.

The NRC Genomics and Health Initiative (GHI) supports five research programs focusing on canola productivity, treatment of brain tumours, near-patient diagnostic devices, cancer identification and treatment, and diagnostic tools for heart attack patients.

The AAFC Canadian Crop Genomics Initiative focuses on functional genomics of disease and insect resistance, tolerance to stress such as cold and drought, and enhanced quality attributes, in cereals (wheat and corn), oilseeds (*Brassica* and *Arabidopsis*) and legumes (soybeans).

The GRDI activities at HC continue to strengthen the existing scientific knowledge base under the Departmental Framework for Biotechnology of Health Canada which outlines the Department's genomics-related roles and responsibilities including providing leadership in policy and regulation development, informing and engaging the public, ensuring an international position for Canada, and applying the benefits of genomics to HC's mandate.

From the perspective of PHAC, genomics of humans and microbes has the potential to radically alter public health practices in the future, with new approaches for disease surveillance, disease prevention and improvement of health status that can effectively counterbalance health care funding pressures.

The GRDI at NRCan generates in depth scientific knowledge that is critical for the development of tailored solutions to specific forestry issues, such as evolving needs of Canada's forest industry and threats from insects, diseases and climate change, focusing on species and traits that are of economic importance. The following themes are supported: emerging environmental issues such as monitoring and response to pests and pathogens; relationships between genomes to study the genetic profiles and evolution of main pests, host defence mechanisms, host-pathogen interactions; and sustainable forestry and competitiveness towards improvements of tree growth, wood quality, and resistance to biotic and abiotic agents.

Environment Canada has strengthened its internal capacity in eco-toxicogenomics and is using this capacity to explore how best to use genomics to fulfill EC mandates to protect Canadian aquatic systems, terrestrial systems, and wildlife from the harmful effects of existing and emerging environmental stressors (chemical, biological, and physical). Environment Canada investigators participate in broad national and international efforts in eco-toxicogenomics, and are acknowledged for their valuable expertise and scientific contributions.

The DFO continues to focus research on three themes: aquatic resource profiling, aquatic animal health, and aquatic ecosystem health. Increased access to genomics expertise and infrastructure through investments in the Maritimes Region has facilitated new internal and external collaborations. Following DFO's competitive funding allocation process for Phase IV of the GRDI funding, researchers from all of the department's regions are now actively engaged in conducting genomics R&D projects to advance the department's strategic research objectives.

Performance

This 2008-09 Annual Performance Report is presented using the performance indicator categories outlined in the GRDI Results-based Management and Accountability Framework (RMAF), to outline progress on governance, coordination and science partnerships; research capacity; infrastructure; sharing of technology and scientific knowledge; public awareness of genomics; participation in national and international initiatives; and application of research results to develop innovative methods, products, processes or technologies.

Fiscal year 2008-09 was the first year of Phase IV programs. Departments renewed their strategic directions and held competitions for the allocation of funds to new projects. Funding was released with considerable delay, which caused difficulties for the recruitment of highly qualified personnel and the establishment of new projects. Still, cash management decisions within departments and agencies allowed research to proceed without interruption.

Management

Sound management is an important aspect of any government program. The GRDI departments and agencies have established practices to define priorities effectively, support departmental coordination, and select projects to specifically address the identified priorities.

For example at NRC, for a transition year such as 2008-09, the overall GRDI program framework was reviewed based on consultations with the Genomics and Health Initiative Program Coordination Committee (Scientific Leaders and Project Managers) and the

Directors General Committee. A framework for Phase IV was assembled and a peer reviewed competition was launched in December 2006 for the development of programs to be funded under Phase IV. Research teams were encouraged to demonstrate their ability to integrate disciplines in order to drive commercially relevant advances in cutting edge areas of genome and health-sciences. Research programs were required to be aligned with the NRC strategy outlined in the document Science at Work for Canada: A Strategy for the National Research Council 2006-2011. Senior Executives used a formal portfolio approach in the selection of program proposals to establish a balanced portfolio of programs with either short-term commercial potential or longer-term research objectives. Letters of Intent were sent out for external review of quality and relevance against pre-determined evaluation criteria. The proposal evaluation process also included a requirement for each proposal to undergo independent market/strategic positioning studies. Full Proposals were then subject to external scientific peer review. and evaluated against selection criteria favouring integration of research capabilities across NRC institutes, as well as collaboration with external partners in other government departments, academia, and industry. The Expert Panel reviewed all Full Proposals and provided strategic recommendations to NRC Senior Executives who were responsible for final program selection decisions. Other departments and agencies have used similar strategic priority setting and peer reviewed competitive approaches to allocate Phase IV resources.

At the interdepartmental level, steps were taken in 2008-09 to provide a new policy framework for the GRDI at the end of Phase IV (March 2011). A draft proposal was developed under the guidance of the GRDI ADM Coordinating Committee, engaging the Committee in discussions on how to best position the initiative to respond to an evolving economic, scientific and policy context, and take advantage of synergies with other players in the spirit of the Federal S&T Strategy. Acting on this guidance, the interdepartmental Working Group organized 3 days of workshops in November 2008 to plan for the future of the GRDI, attended by 33 representatives from GRDI departments/ agencies and engaging the Canadian Food Inspection and Public Health Agencies and Genome Canada. A Common Functions Advisory Committee, comprised of 25 expert federal scientists, was formed to provide advice on priority elements to be included in the common functions component of the model. Reporting to this Committee, three discussion groups were formed to further elaborate on the identified priority areas: bioinformatics, technology platforms, and biological collections. Another interdepartmental workshop was held in spring 2009 to further develop the shared research priorities of the model and other aspects of the new approach; it was well attended with 46 GRDI participants and a Genome Canada representative. Departments wrote Business Cases to describe the priority areas for genomics research to contribute to their mandates and priorities, and in doing so, engaged their respective stakeholders.

Collaborations

Collaborations are an important part of the GRDI as illustrated by **Tables 3** and **4**. **Table 3** shows GRDI interdepartmental collaborative activities during 2008-09.

Table 3: Interdepartmental GRDI Collaborative Projects

PARTNERS	RESEARCH AREA
AAFC - NRC	Brassica genomics technologies – biorenewable oil for food and fuel
AAFC - NRC	Development of a "Canadian Biofuels Biofertilizer Network"
AAFC - NRC	Canadian Canola Genome Sequencing Initiative
AAFC - NRC	Pre-commercial field trials – gene candidates for plant yield and vigour
NRC - EC	Bioremediation of contaminated soils
NRCan - AAFC	Growth and adaptation in spruce
EC - NRC	Microbial environmental genomics
EC - DFO	Shared equipment and laboratory space
EC - HC	Chemical Management Plan
EC - AAFC	Environmental effects of pharmaceuticals and personal care products on the environment and human health
EC - HC	Nanotechnology research initiative
EC - NRC	Environmental metagenomics, DNA sequencing

Table 4 shows the extent of collaborations with a wide variety of partners, for a total of close to 240 collaborations leveraging expertise and resources. Many projects involve non-governmental researchers from Canadian and international research organizations and universities. For example, AAFC has made a significant contribution to the international *Brassica* genome sequencing effort and has built strong relationships with German scientists in this area. Likewise, their expertise in wheat genomics has led them to work with French scientists and publish in the prestigious journal *Science*.

Table 4: Collaborations by Organization Type

TYPE	NRC	AAFC	нс	PHAC	NRCAN	EC	DFO	TOTALS
Universities (Canadian and International)	13	25	14	23	9	25	15	124
Other International Research Organizations	-	9	4	-	4	3	5	25
Other Canadian Research Institutions	19	-	3	-	4	4	1	31
Private Sector	15	8	3	-	1	1	14	42
Other Public Sector Organizations	-	5	3	-	-	-	7	15
Total	47	47	27	23	18	33	42	237

The non-for-profit organization Genome Canada and its regional centres are supported by the Government of Canada (\$840M since 2000) to advance large-scale genomics research and enhance Canada's international position. This investment was leveraged to more than \$1.7 billion with co-funding from partners. Synergies developed between federal scientists active in the GRDI and academic scientists active under large-scale programs financed by Genome Canada continue to flourish. Federal scientists are playing a key role in the project Designing Oilseeds for Tomorrow's Markets, co-led by the U. of Alberta and the NRC, to develop a canola genotype with improved meal quality for the valuable fish and animal feed market. Relationships built through such projects were central to establishing networks funded through AAFC's Agricultural Bioproducts Innovation Program (ABIP). For example the Cellulosic Biofuel Network (CBN), led by AAFC, is comprised of more than 40 government and university scientists with the common goal of eliminating barriers faced by the Canadian bioethanol industry.

Brassica researchers at AAFC and NRC collaborated in the design and development of a high density expression analysis platform, a microarray that allows approximately 70% of canola genes to be queried simultaneously. The *Canadian Canola Genome Sequencing Initiative* (CanSeq) Collaborative Research Agreement between NRC, AAFC, Genome Alberta and four industry partners (Cargill Limited, Dow Agro-Sciences Canada Inc., KWS SAAT Ag and RAPOOL-Ring GmbH) was formalized in February 2009. This large-scale collaboration ensures strong participation of Canada in a multi-national project aiming at sequencing two chromosomes of the *B. rapa* genome, develop a draft *B. napus* genome sequence and identify genome wide nucleotide variation in *B. napus*.

The NRCan Canadian Forest Service (CFS) is a strong collaborator in the Genome Canada/Genome Quebec project *Arborea II*, which identifies genes linked to the natural variability of growth and wood properties in white spruce, a species of key economic importance. The research is being led by researchers at Université Laval and 30% of the project team members are from the CFS. The CFS is also collaborating in a Genome BC/Genome Alberta project on mountain pine beetle system genomics.

Scientists from PHAC collaborate with researchers and provincial public health and agriculture colleagues across Canada to study the virulence of *Salmonella* exposed to antimicrobials.

Genomics R&D Capacity

As confirmed by the Formative Evaluation completed in 2006, most of the participating departments had limited capacity to carry out genomics research before the implementation of GRDI. Departments supported by GRDI funds are now able to undertake genomics R&D and contribute to broader, high-impact programs established through formal and informal collaborations with Canadian and international organizations.

In 2008-09, the GRDI supported 392 scientific and technical staff, 63 post-doctoral fellows, 106 students (PhD, MSc, BSc, and Co-op), and 13 visiting scientists, for a total of 574 active research and technical personnel. **Annex 2** of Appendix A provides additional detail presented by department.

Departments continued to invest in core infrastructure facilities for DNA sequencing, proteomics and microarrays. Funding was also allocated towards the purchase, maintenance and upgrading of laboratory equipment such as real-time PCR equipment, spectrometers, electrophoresis and hybridization stations.

For example, microarray technology is rapidly evolving and most of the original microarray scanners purchased are now on their 3rd or 4th generation or are obsolete. Upgrades purchased by HC allow considerably improved resolution, now providing over a million spots per microscope slide on the most current spotted microarrays. Funding from GRDI enabled major acquisitions at NRC: a nanoplotter designed for high throughput production and for high density and high precision spot positioning down to picoliter (10 -12 liter) volumes; an FMBIO III Plus scanner for the detection of fluorescent dye-marked samples; a KingFisher Flex 96 for antibody screening and purification; and an ACTA Express Chromatograph for the routine purification of recombinant proteins, used for the purification of three families of lead therapeutics currently under investigation.

Research and Development

Research and Development is the central component of this Initiative, together with activities surrounding the conduct of R&D that are critical to ensuring relevance and impact, such as the transfer of knowledge, techniques and products to research partners and end-users, and the dissemination of research results. As part of the 2008-09 Report on Plans and Priorities, the participating departments established a collective set of planned results to:

- Develop commercially relevant advances in areas of genomics R&D related to human health (e.g. genetic testing, diagnostics, microbial genomic applications, treating and preventing human diseases such as cancer and cardiovascular disease, and pathogen detection);
- Realize crop value improvements in cereals, soybean and canola through improvements in areas related to adaptation to biotic and abiotic stresses (e.g. resistance to disease, tolerance to drought and cold), as well as seed development and metabolism (e.g. related to oil content for biofuels and nutraceutical applications);
- Implement the sustainable management of aquatic resources through the use of genomics tools to: manage fishery openings; generate increased understanding of population genetics and structure; further understanding of behavioural, physiological and immunological responses to the environment; and through the management of aquatic animal diseases;
- Position the Canadian regulatory system for health to enable innovation while minimizing the risks to Canadians through a focused genomics R&D program aimed at strengthening research in priority areas such as genetic information, biotechnology products, human genomics and microbial genomics, related to human, animal and environmental health;
- Improve knowledge and understanding of human infectious and chronic diseases for public healthrelated applications including the development of improved or new diagnostic tools;
- Increase knowledge to support forest generation and protection, and to address environmental impact considerations, through a focused genomics R&D effort on species and traits that are of economic importance to Canada; and
- Develop genome-science applications to support regulatory and enforcement activities in key areas such as environmental risk assessment and management; enforcement and compliance; pollution detection, monitoring and prevention; conservation biology and wildlife genetics; technology forecasting and assessment; and the responsible and sustainable development and use of bio-based products and industrial processes.

The **Phase IV GRDI Impact Areas** section provides the strategic directions and high-impact research areas selected for 2008-11. A detailed account of the results

achieved in 2008-09 against planned results as listed in the 2008-09 Report on Plans and Priorities is provided in **Annex 3**.

An important goal of the GRDI is to ensure that federal research scientists remain influential as part of the world's major scientific players in the rapidly evolving field of genomics. This is achieved through scientific publications and presentations at national and international conferences and workshops, and participation in committees, boards and networks. The following enumerates direct R&D outputs, while **Annex 4** of Appendix A provides additional detail broken down by department/agency:

- 156 publications in refereed journals;
- 107 publications in conference proceedings;
- 147 invited presentations;
- 29 technical reports;
- 17 other publications;
- 146 presentations and posters at national and international conferences;
- 10 book chapters;
- 10 patent applications;
- 2 patents issued;
- 8 material transfer agreements;
- 47 formal collaborative agreements;
- 2 books edited:
- 2 genomics related databases; and
- numerous GenBank deposits (ex. Brassica, wheat, spruce budworm, baculoviruses).

Outreach

While the previous three components are important to ensuring that the right research is done at the right time and that the research results are disseminated within the scientific community, it is also important for genomics to be well understood and accepted by Canadians. Direct and indirect public communications are therefore an important aspect of this initiative; however efforts in this area remained modest in 2008-09. Still, there were 18 media interviews, 11 press releases and several community presentations, citizen engagement activities, demonstrations, tours, and participations in science fairs and in public school events. Additionally, some departments maintain public websites with information related to GRDI research. Additional information detailing department/agency activities is provided in Annex 5 of Appendix A.

Appendix A Supplemental Performance Details

Annex 1 - GRDI Funded Projects by Department

National Research Council Canada

Biochips for the Understanding and Diagnosis of Human Disease

This project aims to develop new tools for understanding the molecular processes underlying critical pathogenic and genetic diseases. The goal is to create small and efficient point-of-care diagnostic devices integrated onto a single silicone chip (biochip) with the capacity to rapidly detect specific pathogenic markers. In particular, this device will focus on diagnosing infectious agents responsible for hospital-acquired infections and threats to food and water safety.

Biorenewable Oil for Food and Fuel

The goal of this project is to apply genomics-based approaches to improve the productivity, yield, oil content and resilience of Canadian canola crops in order to meet increasing national and global demands for this vital crop for both food (oil for cooking) and industrial / non-food applications (biofuels).

Identification of Proteins Targeting the Tumour Microenvironment for Therapeutic Applications

The objective of this project is to tackle the complex treatment of cancer by identifying and developing a broad range of targeted therapeutics agents that can be used to create the next generation of promising and more efficient cancer therapies.

Agriculture and Agri-Food Canada

Biotic Stress

Research in this area is ongoing to develop germplasm and varieties with resistance to economically important diseases and insect pests. Molecular biologists and entomologists are examining and developing a molecular basis for both antibiotic and antixenotic approaches to insect and pathogen resistance.

Abiotic Stress

Parallel gene discovery programs in different systems are pursued to uncover novel and complementary avenues to engineering increased cold tolerance and increased frost resistance. Cold and heat tolerance

and freezing resistance are important characteristics for almost all crops and are of crucial strategic importance to Canada as they have a significant bearing on yield potential and stability.

Quality attributes in cereals (wheat, corn), oilseeds (Brassica/Arabidopsis) and legumes (soybeans)

Research in this area focuses on important aspects of seed quality and aims to decipher the genes that control seed development, carbon partitioning, protein quality, oil quality, starch quality, and the accumulation of anti-nutritional compounds. Compounds of nutraceutical interest under study include phytosterols, anthramides and glucans.

Health Canada

- Development and validation of toxicogenomic tools, and integrated systems biology approaches in regulatory toxicology
- Environmental health applications of toxico-genomics and proteomics. Identification of exposure and effect biomarkers for mutagenic carcinogens in complex environmental matrices
- Application of the p53+/- transgenic mouse for alternative cancer bioassays: genomic characterization of tissues from mice exposed to food borne genotoxic and non-genotoxic carcinogens
- Study of interferon-induced hepatic injury using genomic and proteomic approaches
- Biomarkers of exposure and effects of inhaled contaminants in atherosclerosis and asthma
- Evaluation of possible transcriptional changes in human cell lines following exposure to wireless telecommunication signals (as emitted by cellular phones)
- Nutrigenomics studies to understand the role of genomic determinants of the intestinal epithelial cells and of the microbial flora in the digestion of dietary fibres and carbohydrates

Public Health Agency of Canada

- Host genomics of hepatitis C antiviral treatment response
- A molecular risk assessment strategy for non-O157 Shiga toxin-producing E. Coli
- Development of high-throughput comparative genomic (HTCG) methods for studying the molecular epidemiology of infectious diseases
- Identification and characterization of virus host cell protein-protein interactions
- Influence of genetic variability in innate immunity pathways and micronutrient status on infectious disease outcomes with specific focus on severe influenza infection in seniors and vitamin D status
- Bacteriophages and prevention of common bacterial infections
- MicroRNAs and infectious disease: a novel regulatory mechanism in host-pathogen interaction
- The application of multiplexed, parallel, high throughput, real-time PCR based pathogen detection system for HIV drug resistance testing
- Genetic variability and virulence studies in emerging antimicrobial resistant organisms
- Genomic analysis of "novel" chronic bacterial pathogens in cystic fibrosis patients
- Pyrosequencing and assembly of viral quasispecies

Natural Resources Canada

Genomics/proteomics for identifying commercially desirable tree genes

This area of work aims at developing methods, tools and databases for the discovery of trees possessing commercially desirable attributes and for the conservation of genetic resources. Candidate genes for wood quality, growth and disease resistance are characterized and transferred to tree breeders and the scientific community. Research projects include:

 Discovery of genes controlling wood and fibre traits in white and black spruces and development of genetic markers for the selection of trees with desired attributes

- Functional genomics in spruce
- Genome scan to reveal gene islands underlying productivity and adaptation in spruce
- Isolation and identification of defense genes, and molecular markers associated with disease resistance of *Pinus monticola* to blister rust fungus
- Understanding tree defense response through genomics

Understanding host-pathogen genetic interactions to improve sustainability and productivity

This area of work aims at strengthening basic knowledge of forest pests and their pathogens. Genomics is used to understand pathogen modes of action, host specificity, host-pathogen interactions, ecology, and impact on host populations. The knowledge advances the search for new active ingredients and target sites for the next generation of biopesticides and new and improved biocontrol agents. Innovative molecular technologies for pest diagnostics and identification is also pursued and transferred to end-users in Canada and internationally for surveillance of diseases and pests, and phytosanitary certification. Research projects include:

- Proteomics regulation of virus/larva interactions
- Molecular screening for pathogens of indigenous and introduced coleopteran forest pests
- Comparative genomics of forest defoliators: from DNA to mitigation
- Genomics of fungal tree pathogens
- Emerald ash borer (EAB) sensory genomics: mining for odorant receptors mediating host-finding and mate-finding
- Douglas-fir resistance to root disease and other stress agents

Environment Canada

- Design and optimization of novel DNA microarrays for environmental effects monitoring
- Application of genomics for microbial source tracking and assessing microbial water quality
- Aquatic toxicogenomic of emerging products: nano/biotechnology

- Validation of genomics tools for the prediction of environmental effects: response of fish to contaminated sediments
- Genomics application in environmental risk assessments of genetically modified organisms and other biotech products
- Development and standardization of test methods using environmental genomics techniques
- Gene expression technologies applications to wildlife toxicology
- Development and validation of a lobster toxicogenomic array – correlation of gene expression profiles with traditional toxicological end-points for contaminant exposure
- Aquatic toxicogenomic tools for risk assessments and environmental effects of chemicals and complex mixtures
- Development and application of novel genomicsbased micro-array techniques for the detection of environmental microorganisms in wastewater
- Breeding behaviour and population history of the red-listed Yellow-breasted Chat in British Columbia: a pilot study
- Establishing molecular assessment techniques for emerging infectious diseases in native amphibians; laboratory and sampling technique comparisons
- Comparative genetic diversity of captive and wild of Loggerhead Shrikes
- Conservation genetics of Leach's Storm-petrels
- Conservation genetics of Northern Gannets
- Conservation genetics of Haida Gwaii Thrushes
- Hybridization between eastern wolves (Canis lycaon) and other canids: An example of contemporary evolution in human-modified landscapes
- Genetic characterization of strains of Pasteurella multocida isolated from large-scale avian cholera outbreaks across Canada
- Ontario Canada goose population harvest discrimination
- Characterization and sequencing of avian influenza viruses from birds in eastern Newfoundland
- Inter-island movements of introduced black-tailed deer in Haida Gwaii

Fisheries and Oceans Canada

Genome-based monitoring to help in the management of two important fisheries:

- Using genetics to improve conservation of beluga whales (Delphinapterus leucas) in the western Canadian Arctic
- Genomics of migratory fitness in wild salmon

Increased understanding of population genetic and structure of important economic fisheries:

- Conservation genomics of Atlantic salmon in Newfoundland and Labrador: assessment of genetic differences between wild and aquaculture strains and analyses of genetic structuring for the identification of important within-species biodiversity
- Discriminating capelin populations in the northwest Atlantic
- Redfish (Sebastes sp.) species identification and stock structure based on genetic analysis of archived otoliths
- Dolly Varden char population structure and genetic diversity in the western Arctic
- Investments in the Aquatic Biotechnology Service Lab at the Bedford Institute of Oceanography

Increase understanding of the behavioural, physiological and immunological responses to the environment:

- Microbial characterization of produced water and its influence on the microbial community in the marine environment around the Hibernia production platform
- Application of genetic markers to resolve species identification and population structure of aquatic invasive species

Management of aquatic animal diseases, important for both the wild fisheries and the aquaculture industry:

- Immune function of salmon and disease resistance against infectious salmon anemia virus (ISAV) – phase 2
- The effects of wild and captive rearing environments, and associated parasite and pathogen regimes, on the diversity and nature of genetic variation in Atlantic salmon
- Host parasite interactions: a functional genomics approach to characterising salmonid responses to the salmon louse

Appendix A Supplemental Performance Details

Annex 2 - Highly Qualified Personnel (HQP) by Department

National Research Council Canada

171 research and technical personnel were active under the initiative:

- 35 research officers
- 62 technical officers
- 48 research associates
- 6 visiting scientists
- 20 students

Agriculture and Agri-Food Canada

135 research and technical personnel were active under the initiative:

- 75 scientific and technical staff
 (16 adjunct professors in 7 universities)
- 27 PDF
- 4 visiting scientists
- 29 university students (graduates)

Health Canada

55 research and technical personnel were active under the initiative:

- 16 Principal Investigators
- 14 indeterminate positions
- 10 technical positions
- 5 PDF
- 10 university students
 (1 PhD, 2 MSc and 7 undergraduates)

Public Health Agency of Canada

42 research and technical personnel were active under the initiative:

- 17 Principal Investigators
- 8 technical positions
- 8 PDF
- 9 university students

Natural Resources Canada

89 research and technical personnel were active under the initiative:

- 12 research scientists
- 31 biologists/technicians
- 21 PDF
- 3 visiting scientists
- 22 university students (12 MSc and PhD, 10 undergraduates)

Environment Canada

33 research and technical personnel were active under the initiative:

- 16 research scientists
- 2 research professionals
- 2 research technicians
- 1 chemist
- 2 PDF
- 10 students (2 PhD, 2 MSc, 6 undergraduates)

Fisheries and Oceans Canada

49 research and technical personnel were active under the initiative:

- 23 research scientists
- 20 technical staff
- 6 students

Appendix A Supplemental Performance Details

Annex 3 – Planned Results versus Achieved Results (2008-09)

Planned Result 1

Develop commercially relevant advances in areas of genomics R&D related to human health (e.g. genetic testing, diagnostics, microbial genomic applications, treating and preventing human diseases such as cancer and cardiovascular disease, and pathogen detection)

Achieved Result 1

Integrated devices that provide rapid, point of care diagnosis of pathogens based on their genomic signature are a goal of the NRC Biochips project. Central to the success of these devices are on-chip assays that can achieve detection with the sensitivity and specificity necessary to inform sound clinical decisions. In 2008-2009, the Biochips team developed conditions for simultaneous polymerase chain reaction (PCR) amplification and hybridization of target molecules on the chips, allowing detection of less than 5 molecules of pathogen DNA sequence with a specificity distinguishing a single nucleotide mismatch. This advance brings the detection sensitivity of the assay within the useful clinical range of less than 10 molecules of pathogen per assay, and represents a breakthrough in actualizing on-chip real-time PCR, hybridization and detection of biological samples.

Building a sustainable pipeline of protein-based tumour-targeting agents that will act as prospective therapeutics is the goal of the NRC Cancer project. In July 2008, Alethia Biotherapeutics, a Canadian biotechnology company engaged in the discovery and development of therapeutics in areas of unmet medical needs, signed an option to license anti-Clusterin monoclonal antibodies developed by the project team. In 2008-2009, in vivo animal studies showed that three of the anti-Clusterin antibodies caused a significant reduction in metastatic nodule production. In addition, an isolated clusterin-binding peptide has been shown effective as an optical imaging agent for tumour cells in animal models and a provisional patent has been filed.

Planned Result 2

Realize crop value improvements in cereals, soybean and canola through improvements in areas related to adaptation to biotic and abiotic stresses (e.g. resistance to disease, tolerance to drought and cold), as well as seed development and metabolism (e.g. related to oil content for biofuels and nutraceutical applications)

Achieved Result 2

As part of a team of 23 researchers from 6 countries AAFC scientists contributed to constructing a physical map of wheat chromosome 3B which is the first step toward sequencing the first chromosome of wheat. Each wheat chromosome is about the size of the entire rice genome so sequencing of wheat is a massive project. The expertise in genetic mapping of AAFC was used to assist colleagues at INRA (France) with ordering more than 1,400 genetic markers on chromosome 3B, which was critical for future sequencing of the chromosome. The work was reported in the prestigious journal *Science*.

A serious fungal pathogen of cereal crops such as wheat, barley, and corn, *Fusarium graminearum* produces a number of toxins that accumulate in infected grain. Researchers were able to identify hundreds of Fusarium proteins that were present when the fungus was induced to synthesize these mycotoxins. Using proteomics, seventy-two proteins were identified as being associated with toxin production and they provide leads in the search for mechanisms of plant diseases as well as provide novel targets for new antifungal agents.

Sclerotinia sclerotiorum is a plant pathogen that infects important agricultural crops including canola, soybean and sunflower. It secretes a battery of enzymes that break down plant tissues including polygalacturonases (PG). Most plants have a limited set of polygalacturonase inhibitor proteins (PGIP) that may inactivate the PG secreted by pathogens. Scientists at AAFC characterized a diverse set of 16 PGIP canola genes. Several genes responded to infection by S. sclerotiorum or were responsive to other stresses. The large number of PGIP genes and the different manners in which they are regulated likely ensures that canola can respond to attack

from a broad spectrum of pathogens and pests. These are currently being examined for their ability to provide resistance to diseases caused by fungal pathogens.

Baculoviruses are insect specific and have proved to be effective insect control agents that are safe to non-target organisms and humans. Baculoviruses have been identified for many insects of economic importance and represent a significant resource for the future development of organic insecticides. The baculovirus *Autographa californica nucleopolyhedrovirus* has the broadest host range of any known baculovirus. Scientists have investigated genes that are present in all baculovirus species completely sequenced to date, as they may have a critical role in virus replication. Indeed, deletion of some of these genes has prevented virus replication. Such increased understanding will lead to improved use of these natural agents as insect control agents.

The NRC Biorenewable Oil for Food and Fuel team is characterizing 29 genes that may play an important role in canola crop improvement. Elite candidate genes will be incorporated into pre-commercialization programs. Five prototypes were tested in the field in collaboration with AAFC. Compared to the controls, two prototypes confirmed improved oil content and one prototype confirmed early flowering and increased seed size. Formal international collaborations were established with scientists from Germany, the Netherlands, China and India.

Planned Result 3

Implement the sustainable management of aquatic resources through the use of genomics tools to: manage fishery openings; generate increased understanding of population genetics and structure; further understanding of behavioural, physiological and immunological responses to the environment; and through the management of aquatic animal diseases

Achieved Result 3

Following a competition to select the projects that respond most to the department's priorities and strategic outcomes, twelve projects were initiated in fiscal year 2008-09 as described below.

1 – Through the GRDI, DFO has initiated activities that seek to use genome based monitoring to help in the management of two important fisheries.

Genome based monitoring of beluga whales (Delphinapterus leucas) in and connected to proposed marine protected areas within the Beaufort Sea

The beluga whales of the Beaufort Sea constitute an important subsistence fishery for the local Inuit populations, with an average Canadian annual landed catch of 111 per year (1990-1999). This study was undertaken in order to determine the population structure of these Beluga such that the sustainability of the population can be maximized through a harvesting plan based on sound scientific data, ensuring that this important fishery is open and productive into the future. A better understanding of beluga whale population structure will be important to ensure that a proposed new marine protected area contributes to their conservation.

Genomics of migratory fitness in wild Salmon

Salmon fisheries management practices are undergoing radical change in British Columbia due in part to declines in abundance of many stocks and in part to the increasing difficulty in predicting escapement in a rapidly changing environmental backdrop. Genomic technologies are being used to determine the migratory fitness of Fraser River salmon. This work will help fisheries managers to determine which populations are strong enough to harvest as the salmon return to their natal breeding streams and which groups will not return to spawn successfully due to diminished fitness.

2 – DFO has initiated several projects to generate increased understanding of population genetics and structure of important economic fisheries. These include:

Genetic identification of Atlantic salmon from Newfoundland and Labrador in relation to nearby aquaculture and escapes into the wild

On a worldwide basis, an estimated 2 million farmed Atlantic salmon escape annually. Most of this escapement occurs in areas where wild populations are greatly outnumbered by the farmed salmon in cages and hatcheries. Given the environmental severity in some farming regions, such as Newfoundland, some level of escapement may be inevitable. In light of the fact that artificial selection of aquaculture stock modifies gene expression profiles, gene flow from farmed escapes may affect the genetic integrity of nearby wild populations. This work will help to determine if the introgression of genes from aquaculture stock into wild populations is accruing and begin to monitor potential impacts.

Discriminating capelin populations in the northwest Atlantic

The genetic stock structure of capelin has never been clarified despite its ecological role as a primary forage species and their economic role in commercial fisheries. In recent years, capelin has returned to spawn on Labrador beaches. It is unknown whether this reappearance is a re-colonization from the south or an expansion by Arctic capelin populations – both scenarios having implications related to climate change. Recent findings have detected genetic barriers between the Southeast Shoal, Scotian Shelf and Newfoundland beaches. Given the role of capelin as a key forage species, this work seeks to genetically differentiate between different breeding populations of capelin to advise decision makers regarding ecosystem management initiatives.

Redfish species (*Sebastes* sp.) identification and stock structure based on genetic analysis of archived otoliths

Redfish are slow growing and long-lived species for which recruitment success is extremely variable and occurs at intervals of 5 to 12 years. In the northwest Atlantic, there has been almost no important recruitment in the last 20 years and most stocks are depleted or collapsed. Determining the genetic characteristics of these species over decades is important particularly in periods during which major changes in population size and recruitment patterns have occurred. This work is critical to our understanding of the ecology of these species and for providing the best possible advice for the management and conservation of these resources under a precautionary approach.

Genetic variability in wild populations of chars in the Arctic

Dolly Varden is a species of chars found in western North America with at least two sub-species and perhaps two more distinct subspecies present throughout their range. In the north-western Canadian Arctic, the northern group is found only in rivers of the north-western Northwest Territories and Yukon Territory, with coastal populations known from five rivers, and two additional inland populations known. This study seeks to enhance understanding of the taxonomic complexity, genetic diversity and coastal mixing among populations to facilitate and inform for the purposes of conservation, assessment and management actions.

Alongside the projects undertaken, DFO has made investments into its Aquatic Biotechnology Service Lab at the Bedford Institute of Oceanography

Prior to the establishment of the Aquatic Biotechnology Lab (ABL), biotechnology in the Maritimes region was available only through individual researchers' programs, limiting its availability to many researchers. The ABL was established at the Bedford Institute of Oceanography as a core facility, allowing DFO researchers to access biotechnology tools to address their research questions without establishing their own biotechnology labs. This capacity is available to researchers that require the adoption of genomic technologies into their studies but do not have the capacity on hand and supports a number of projects in this phase.

3 – Several new projects serve to increase our understanding of the behavioural, physiological and immunological responses to the environment. These projects include:

Microbial characterization of produced water and its influence on the microbial community in the marine environment around the Hibernia production platform

The long-term impacts from petroleum operations on our continental shelf and in the Arctic must be determined in order to apply and enforce responsible environmental management of our natural resources. The advent of molecular techniques and their application in microbial ecology enables the characterization of entire microbial communities and the monitoring of changes in the community structure resulting from stress or recovery from insult. Since microorganisms play essential roles in global processes ranging from the recycling of matter in our air, water and soil, to causing or preventing disease in plants, animals, and humans, the ability to reliably monitor these key players is critical. This project will apply and adapt molecular techniques to characterize and profile changes in the indigenous microbial community structure and function, and determine if the release of produced water is impacting the natural ecosystem around offshore oil and gas production platforms. Produced water will also be characterized to identify whether there are any unique microorganisms that could be used as tracers to study the microbiological impact on the surrounding ecosystem in the marine environment following release of produced water.

Application of genetic markers to resolve species identification and population structure of aquatic invasive species

Globally, invasive species are one of the greatest threats to biodiversity and ecosystem health. Managing and mitigating the impacts of invasive species depends on having the ability to identify these species, including larval or juvenile forms, and understanding their patterns of dispersal. For invasive species this dispersal may be natural or human-mediated and can occur over long distances depending on the introduction site and larval duration. Recently, in the marine environment, tunicates have received much attention due to their negative impacts on shellfish aquaculture. Developing molecular markers will provide the tools necessary to resolve these issues. When combined with human-mediated transport data, the population genetic data should allow for more focused policy and management options.

4 – The management of aquatic animal diseases is important for both the wild fisheries as well as the aquaculture industry. Research under the GRDI at DFO continues to focus on issues such as:

Immune function of salmon and disease resistance against infectious salmon anemia virus

Infectious salmon anemia virus (ISAV) is considered a major pathogen of Atlantic salmon, and despite efforts to contain and control its spread, ISAV continues to cause significant losses to the aquaculture industry of Atlantic Canada. An increasing number of genetically distinct ISAV isolates continue to be identified. The viral mechanisms leading either to fish death or survival and resistance are not well understood at the immune or molecular levels. In order to gain further understanding of these mechanisms, this study will examine the immune response and global gene expression patterns in fish following exposure to isolates of ISAV.

The effects of wild and captive rearing environments, and associated parasite and pathogen regimes, on the diversity and nature of genetic variation in Atlantic salmon

Endangered Inner Bay of Fundy salmon are presently being maintained under captive and semi-wild conditions to prevent their imminent loss. However, captive rearing can result in the loss of genetic variation and fitness. Research indicates that existing recovery programs are minimizing the loss of neutral genetic variation. They have not yet assessed their ability to maintain potentially adaptive variation. By assessing levels of variation over time (in the parents and

offspring), rates of loss of the major histocompatibility complex class II gene variation can be estimated, and contrasted with existing data from neutral genetic markers for these same fish. By comparing rates of loss of genetic variation, and MHC II allele types, the effects of captive breeding on the loss of non-neutral genetic variation can be determined.

Host parasite interactions: a functional genomics approach to characterising salmonid responses to the salmon louse

The salmon louse (*Lepeophtheirus salmonis*) is a common and economically important parasite of farmed and wild salmon. As such, it is critically important to both the salmon farming industry as well as the wild salmon fisheries, that these interactions be characterized in order to mitigate potential damage to either population. Preliminary data obtained from pooled Atlantic, chum and pink salmon samples demonstrated differences in gene expression profiles following exposure to *L. salmonis*. This information can be used to develop sound management plans to optimize control strategies for sea lice in order to minimize the risk of transfer between aquaculture and wild populations of salmonids.

Planned Result 4

Position the Canadian regulatory system for health to enable innovation while minimizing the risks to Canadians through a focused genomics R&D program aimed at strengthening research in priority areas such as genetic information, biotechnology products, human genomics and microbial genomics, related to human, animal and environmental health. Improve knowledge and understanding of human infectious and chronic diseases for public health-related applications including the development of improved or new diagnostic tools.

Achieved Result 4

Work is undertaken to generate, synthesize, and translate new knowledge in pathogen and human genomics to: strengthen infectious disease surveillance, prevention and control through applications such as diagnostics, molecular risk assessment, vaccines, intervention strategies, mitigation of antimicrobial resistance; and, develop applications to diagnose and prevent diseases and promote health through predictive genetic screening and/or modulation of gene-environment interactions.

In 2008-09 genomics research within PHAC continued to focus on the development and application of "omics" tools to reduce exposure to food borne pathogens. For example, a generalized approach for genetic fingerprinting of bacterial pathogens using comparative genomics has been developed. The approach is being used to develop a series of assays that are adaptable to different existing and emerging platforms, providing a range of solutions that can be tailored to available resources of laboratories. A computer program to analyze genome sequence data and facilitate the design of assays was developed and a series of assays for Campylobacter jejuni, Verotoxigenic Escherichia coli (VTEC), Listeria monocytogenes and Helicobacter pylori are currently in various stages of development. The method is currently being field-tested by collaborators at PulseNet Canada and the Centre for Disease Control. Additional work on emerging platforms has also been undertaken and a series of protoype assays have been designed and fabricated, and protocols were developed and validated.

Shiga toxin-producing Escherichia coli (STEC) can cause massive outbreaks and the potentially fatal hemolytic uremic syndrome. Although O157:H7 is the most common STEC serotype, more than 200 virulent non-O157 isolates have emerged globally that are associated with human disease. While some non-O157 STEC strains may also be fatal, others are associated with only mild diarrhea or with no human disease at all. The lack of full genome sequence data for non-O157 STEC has hampered scientific discovery into the genetic basis for these virulence differences. Research at PHAC seeks to identify the critical STEC genetic elements and virulence factors associated with severe and epidemic disease. This will enable the development of a molecular risk assessment strategy using specific nucleic acidbased diagnostic tests to rapidly identify and respond to emerging non-O157 STEC that pose a serious public health risk to humans.

Health Portfolio projects continued to build on existing research focusing on environmental toxicogenomics. Toxicogenomics is the application of genetic methods to the study of toxicology. New array technologies were applied to identify DNA binding sites of thyroid receptors, and have led to the development of a high throughput assay for screening chemicals that may disrupt binding to result in disease. This work has shed light on the mechanisms leading to neurodevelopmental effects of hypothyroidism, and provided targets for analysis in humans. Global transcriptional profiling was used to compare the efficacy of a cell culture model to

reflect the in vivo response, providing validation of the in vitro tool. Results from 2008-09 have provided insights specific to gene expression changes driven by exposure to toxic substances. Several types of toxins and environmental contaminants were examined using microarray technology in a "genome-wide" test for induced gene expression, microRNA and DNA methylation changes, allowing the development of models of their modes of action and potential health effects. For example, two papers developed models for new biomarkers and models for mechanisms of action leading to cardio-pulmonary disease in smokers. Further toxicogenomic and proteomic work in particle exposure experiments revealed that inhaled carbon black and diesel exhaust particles do not result in the induction of the acute phase response pathway in mouse liver and revealed the critical importance of understanding the effects of restraint stress in characterizing the pulmonary response using nose-only inhalation exposures.

In 2008-09 research focussed on the development of new diagnostic technologies applicable to both large scale surveillance screening and clinical monitoring. For example, the development of a high throughput, rapid, inexpensive real-time PCR based chip array for HIV drug resistance testing (applicable to both large scale surveillance screening and clinical monitoring) has been initiated. The 52 primer and probe sets required to detect the designated HIV drug resistance mutation have now been designed. All control plasmids containing the relevant HIV drug resistance mutations have been designed and synthesized. Current work involves the optimization and validation of the primers/probes against control reagents. Next steps include the validation of reactions under nanolitre conditions.

Other scientists studied the main divergent responses (clinical phenotypes) to antiviral treatment of Hepatitis C Virus infection: "Responders" and "Non-responders", as a significant proportion of infected patients fail to respond to the best antiviral therapy currently available. Numerous studies have demonstrated that therapeutic outcomes are influenced by patient genetics. Scientists are applying state-of-the-art technologies, namely high density DNA microarrays, DNA sequencing, and bioinformatics were applied to identify candidate host genetic polymorphisms (biomarkers) associated with treatment response.

The majority of cystic fibrosis patients are colonized with *Pseudomonas aeruginosa*; however their respiratory infections are poly-microbial in nature. The role of host oropharyngeal flora bacteria has been investigated and clinical studies have recently revealed that *Strepto-coccus milleri* levels are contributing to acute respiratory exacerbations in some cystic fibrosis patients. Currently there are no reliable diagnostic assays or tools to assess the level of pathogenic *S. milleri* isolates in chronic lung infections. Scientists at PHAC continue to assess bacterial genomes of each *S. milleri* species to facilitate the development of targets for diagnostic and therapeutic assays for cystic fibrosis.

Researchers at PHAC propose to identify genetic polymorphisms associated with severe influenza using a genome-wide association strategy in 2000 adults (1000 cases and 1000 controls) with laboratory confirmed influenza. An extensive recruitment network that includes approximately 20 hospitals in Ontario and the Provincial Laboratory for Public Health in Calgary, Alberta has been formed and sample collection is underway. Recruitment efforts are also underway in other provinces as well as in the European Union.

Researchers at PHAC investigated newly discovered regulatory molecules produced following viral and prion infection, that contribute to the regulation of innate immune responses. These molecules are potential prime targets for therapeutic interventions in immune related diseases or infections in which excessive or chronic inflammation is damaging. In addition they may 'fine-tune' responses induced by vaccination.

Scientists at PHAC explored high mutation rates in RNA viruses, including Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus that result in the generation of variant genomes, called *viral quasispecies*. Characterization of these viral quasispecies genome populations from infected individuals, such as diversity, recombination and evolution, is important for understanding these viruses and for developing control strategies, diagnostics, vaccines, and antiviral therapies.

Viruses have an absolute reliance on host cells for their replication cycle and therefore must physically and functionally interact with their host proteome. These protein-protein interactions not only create cellular environments conducive to virus replication, but also affect normal cellular functions the consequences of which often result in life threatening pathologies. A team of PHAC scientists is attempting to identify human proteins that virus proteins interact with in order to provide insight into the mechanisms of virus replication and pathogenesis and to uncover novel host therapeutic targets.

Health Canada used genomics research to analyze the ability of radiofrequency fields emitted by cellular phones to modulate transcriptional responses in a series of human-derived cell lines. This information has helped to strengthen HC's knowledge base on possible non-thermal effects of wireless communication signals and strengthens the scientific knowledge base upon which existing HC human exposure limits to such electromagnetic energy are based.

Nutrigenomics research at HC generated samples that will form the basis of an analysis of the genetic response of the cells lining the lower gastrointestinal tract in response to dietary fibre and resistant carbohydrates. We predicted that both dietary fibre and resistant carbohydrates would vield similar results since both materials are fermented by the lower bowel bacterial populations and produce very similar end products, which are utilized by the colon cells. Initial results showed a profound difference in cellular response to dietary fibre and resistant carbohydrates. This information is helping to shape a new definition for dietary fibre by providing information on the health benefits that can be expected from fermentation events alone. This helps Health Canada regulate these products and provides Canadians with information on healthful food choices.

Planned Result 5

Increase knowledge for forest generation and protection methods, and for addressing environmental impact considerations, through a focused genomics R&D effort on species and traits that are of economic importance to Canada.

Achieved Result 5

Increased knowledge of genomics-based pest control and diagnostics

NRCan's genomics program provides basic knowledge of forest pests and their pathogens, including pathogen modes of action, host defence mechanisms, and host-pathogen interactions. In 2008-2009 the foundation was laid for the examination of pathogen groups of three economically important invasive coleopteran species: emerald ash borer (EAB), mountain pine beetle (MPB), and brown spruce longhorn beetle (BSLB). Assays based on PCR were optimized for the detection of viral pathogens and new microsporidian species were found in EAB and MPB. A new project to understand the chemical communication of the EAB was initiated by the development of cDNA libraries. Research on balsam fir

sawfly viruses led to the identification of 18 proteins, three of which were novel. Early evidence has shown that the co-evolution of insects and their viruses saw a co-dependency of the interacting proteins to initiate and establish infection in the host. These are the first steps in identifying candidates for release to control established pest populations.

New knowledge generated under the GRDI included the identification of proteins related to plant defence in Douglas fir, pathogenicity-related genes in laminated root rot fungus, and the molecular characterization of key signalling processes of poplar-rust interactions. Proteomics research generated unique resources (peptide libraries) for genome annotation. The use of peptide libraries of a leaf rust that attacks conifers and aspen is explored as a reliable model to study treedisease interactions. In collaboration with the USDA Forest Service and BC Ministry of Forest and Range, several white pine candidate genes were investigated for single nucleotide polymorphisms (SNPs) and SNP genetic association with resistance phenotypes in multiple white pine families with quantitative resistance phenotypes. The comparison of proteome profiles from white pine blister rust resistant and susceptible seedlings revealed seven proteins of interest in the resistant seedlings.

Research on genomics-based pest control products for species that are of economic importance involves searching for active ingredients, target sites, and new or improved strains for the development of environmentally benign pest control methods. The creation of cDNA libraries allowed scientists at NRCan to work towards the development of molecular markers for the identification and monitoring of two economically important defoliating species (hemlock looper and white-marked tussock moth). Proteomics research at NRCan advanced our understanding of the role of certain proteins, such as P74. It was found that P74 plays a role in viral infectivity of lepidopteran pests. This is an important step towards the optimization of species specific biological control products.

Identification of genes controlling desirable attributes in economically important tree species

Canada's forests will increasingly experience changes in local temperatures and precipitation, affecting the growth rate and distribution of trees as a result of climate change. The genomics program at NRCan-CFS directs research towards the development of methods, tools and databases for the discovery of genes in forest trees

coding for attributes favouring fibre quality and forest sustainability: growth; wood quality characteristics; resistance to biotic and abiotic factors; and adaptation to environmental change. 2008-2009 saw the identification of specific regions of the spruce genome coding for features such as resistance to insect and diseases and adaptation to climate change. This will allow the development of selection tools, such as molecular markers, for tree breeders. CFS researchers performed and continue to perform experiments on select candidate genes to identify and validate these potential molecular markers.

NRCan scientists investigated a selection of candidate genes that are involved in growth and adaptation in spruce. Linkage mapping positioned 1800 SNPs from gene coding sequences onto spruce genomics maps. Mapping bud phenology and growth traits continues to integrate data across environments and season to define robust quantitative trait loci (QTL). In addition, expression profiling studies identified 214 high priority genes for wood formation in white spruce from a list of a few thousand candidate genes. Identification of single nucleotide polymorphisms (SNPs) for these high priority genes for the development of a genotyping array is underway.

Planned Result 6

Develop genome-science applications to support regulatory and enforcement activities in key areas such as environmental risk assessment and management; enforcement and compliance; pollution detection, monitoring and prevention; conservation biology and wildlife genetics; technology forecasting and assessment; and the responsible and sustainable development and use of bio-based products and industrial processes.

Achieved Result 6

In 2008/2009 EC made significant advances in the application of the genomic tools and data that have been generated over the life span of the GRDI. Using GRDI funding, EC has developed and/or applied genomics tools to:

 Investigate molecular-level effects of environmental contaminants (priority substances and emerging contaminants) on wild species to improve environmental risk assessment/ monitoring;

- Conduct molecular characterization of communities of microbes in contaminated soil so as to enhance bioremediation and validate a new national guidance document under the Canadian Environmental Protection Act;
- Detect pathogenic micro-organisms in wastewater so as to assess the effectiveness of sewage treatment;
- 4) Investigate the toxic effects of environmental contaminants on aquatic microbial communities;
- Provide scientific data in which conservation and wildlife management decisions (i.e. for bird species Yellow-breasted chats, Ontario's goose populations, Loggerhead Shrikes etc.) have been based (both at the federal and provincial level);
- 6) detect the presence of genetically modified organisms and bacterial genes in aquatic ecosystems; and
- 7) Determine the ecological effects of biotechnology products at the genomic level.

In 2008-09 investments continued in environmental genomics foresight, knowledge development, instrumentation, infrastructure, and outreach (e.g. periodic comparative analysis of international environmental genomics activities via bilateral exchanges with US EPA). Environment Canada is also working closely with the Organization for Economic Co-operation and Development (OECD) and the International Programme on Chemical Safety (IPCS) of the World Health Organization (WHO) in developing strategies and work plans on several fronts to lead and co-ordinate international efforts to attempt to see how toxicogenomic methods and approaches might be applied within in a regulatory context. Strengthening of partnerships and joint projects between federal departments continues (i.e. Environment Canada and Fisheries and Oceans Canada).

The methods developed for detecting biotechnology products formed the basis of a new provincial monitoring program (Quebec environment and sustainability); microarray technology was used to analyze microbial community compositions; toxicogenomic methods were applied to aquatic systems (marine and freshwater) using relevant Canadian indicator species (fish, daphnids, amphibians). These results are used by Environment Canada's regulatory and enforcement branches to evaluate environmental microbial contamination, and by the City of Hamilton for the management of recreational waters.

Appendix A Supplemental Performance Details

Annex 4 – R&D Outputs by Department

National Research Council Canada

- 43 publications in refereed journals
- 37 publications in refereed conference proceedings
- 54 invited presentations
- 24 technical reports
- 9 other publications
- 14 participation in national conference / workshops
- 36 participations in international conferences / workshops
- 2 genomics-related database
- 9 patent applications
- · 2 patents issued
- 6 material transfer agreements
- 47 formal collaborative agreements

Agriculture and Agri-Food Canada

- 54 publications in refereed journals
- 55 invited presentations (of which 32 international)
- 72 posters
- 5 book chapters
- 82 papers reviewed by scientists for national and international journals
- 22 peer review panels with GRDI scientist membership
- 13 scientists holding editorial posts for national and international journals

Health Canada

- 10 publications in refereed journals
- 75 presentations, of which 18 were invited
- 1 book chapter
- 2 books edited
- 3 technical reports
- 1 patent application filed
- 2 material transfer agreements

Public Health Agency of Canada

- 5 publications in refereed journals
- 6 invited presentations
- 8 international conference/workshop presentations
- 12 posters presented at national and international conferences and workshops

- 6 formal collaborative agreements initiated and negotiated
- 1 genomics-related database developed and launched
- 1 bioinformatics program rolled out
- 1 "Emerging Pathogens Response Policy" developed and refined
- 1 new bacterial genome annotation pipeline inaugurated
- 1 new annotation standard operating procedure developed
- 1 material transfer agreement negotiated
- 30 whole genome sequence bacterial databases created
- Several new and exhaustive comparative pathogenomics toolsets (bioinformatics) inaugurated

Natural Resources Canada

- 24 publications in referred journals
- 8 publications in conference proceedings
- 21 invited presentations
- 4 book chapters
- 59 national conference presentations and posters
- 23 international conference presentations and posters
- Numerous GenBank deposits (spruce budworm, baculoviruses)

Environment Canada

- 19 publications in refereed journals
- 3 publications in refereed conference proceedings
- 5 invited presentations
- · 2 technical reports
- 8 other publications
- Participants in 2 National Networks
- Participants in 2 International Committees

Fisheries and Oceans Canada

- 6 publications in refereed journals
- 1 technical report
- 10 invited presentations

Appendix A Supplemental Performance Details

Annex 5 – Outreach by Department

National Research Council Canada

- 8 media interviews
- 1 press release
- 1 external website
- 6 citizen engagements activities (participation in science fairs, student mentorships, Sanofi-Aventis Biotech Challenge)
- 13 community presentations and tours (student laboratory tours, Ministerial tour, university/educational presentations, Canadian-Wide Science Fair: Hands-On Science Day)
- 1 brochure created to promote the initiative
- 1 NRC Outstanding Achievement Award

Agriculture and Agri-Food Canada

- 3 media interviews
- 11 reports to industry or organizations
- Demonstrations to the general public through open houses
- Presentations in public schools
- Participations in science fairs

Health Canada and Public Health Agency of Canada

- Increased the internal and external awareness and understanding of genomics research results and applications
- Detailed research results and achievements at intergovernmental conferences

Natural Resources Canada

- 7 media interviews
- 3 web pages
- 1 factsheet
- 5 exceptional achievement awards

Environment Canada

- community presentations and tours conducted at GRDI participating institutes across Canada
- official designation by the DG for Environmental Science and Technology of a Centre of Expertise for Aquatic Genomics
- Environment Canada Genomics Science Policy Workshop

Fisheries and Oceans Canada

- 10 press releases
- 2 community presentations

Appendix B Genomics R&D Initiative: RMAF Overview

Overview

In fulfillment of the requirements and guidelines of the Treasury Board Secretariat, a Results-based Management and Accountability Framework (RMAF) has been developed for the interdepartmental GRDI. The RMAF formalizes the commitment of the six departments involved in the Initiative regarding common measurement and accountability requirements.

A logic model has been developed (**Figure 1**) that reflects the overall objectives of the Initiative, recognizing that there are significant differences in particular needs and priorities of each department. The key objective of the GRDI is to sustain intramural genomics research in support of departmental mandates and key federal public policy objectives in areas of national interest (human health, agriculture and food safety, environment and natural resources management), to strengthen innovation, promote global competitiveness, and ensure sustainability for the benefit of all Canadians. Key results are related to four important program areas:

Management – while good management is an important aspect of any government programming, it is particularly important to recognize for this initiative because of the number of players: there are six departments and agencies involved and it is important that the practices in place support effective departmental and interdepartmental coordination. It is also critical that departmental and initiative priorities be well defined so that the projects are selected to ensure that government-wide priorities for genomics research information are addressed and to ensure that genomics research adequately supports policy, regulatory, and other types of decisions.

Capacity Building – capacity building was the focus of the earlier phases of this initiative and it is critical that this continue. The hiring of highly qualified personnel (HQP), training of existing personnel, and provision of effective and efficient tools to enable research are essential components to successfully undertake research projects as well as be credible participants in genomics research and applications.

Research and Development – Research and development is the central component of this initiative. All activities surrounding the actual conduct of R&D, the transfer and adoption of the technologies developed, and the dissemination of the research results and scientific knowledge, are critical to ensuring progress towards all outcomes and ensuing impacts.

Outreach (communications) – While the previous three components are important to ensuring that the right research is done at the right time and that the research results are disseminated to the scientific community, it is also important for genomics to be well understood and accepted by Canadians. Direct and indirect public communications are therefore an important aspect of this initiative.

Performance Measurement Plan

Table 5 outlines the performance indicators, sources and responsibility for the outcomes outlined in the logic model presented in **Figure 1**. Information outlined in this table will be collected and reported annually.

Table 6 outlines the performance indicators, sources and responsibility for the outcomes outlined in the logic model which should be examined at the time of a future impact evaluation. While information in this table may be collected annually, it will be analyzed and reported upon at the time of the impact evaluation.

Individual departments may also report on their individual progress in their Departmental Performance Report and use the information to adapt their programming and priorities.

Tables 5 and **6** therefore outline specific data that needs to be collected by all departments, where appropriate. While some of the data will only be collected and analyzed at the time of the impact evaluation, the tables outline the following ongoing departmental requirements:

Interdepartmental information: Departments must maintain a record of all minutes of meetings, decision records, planning documents, etc. of an interdepartmental nature that has affected the way in which the initiative has been implemented in their own departments.

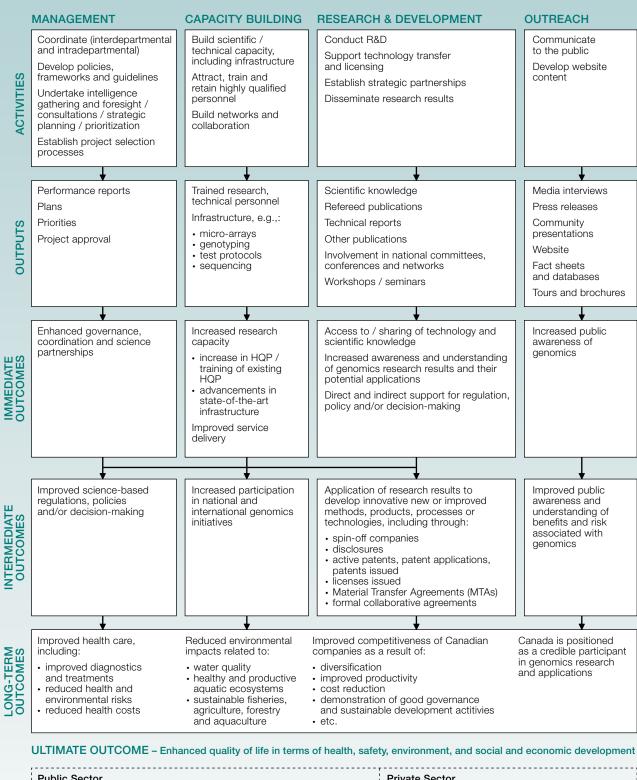
Departmental information: Departments also need to maintain a record of internal information that has affected the way in which the initiative has been implemented in their department. This includes program-level funding information (A-base and B-base funding), human resource information (hiring, training), non-project specific participation in national and international committees, conferences and networks, and website statistics.

Project-specific information: This includes the following information on projects:

- project applications (proposals, peer review assessments, etc.);
- projects approved (title, scope, funding level, description, objectives, lead scientist, team members);
- interdepartmental projects (title, scope, funding level, number of departments, description, objectives, lead scientist, team members);
- partners, collaborators on projects (names, type, financial contribution, in-kind contribution, role);
- regulators, policy makers, others accessing research results (names, titles, contact information);
- use of project funds (budgets including overhead charges or corporate taxes);
- infrastructure projects (types, funding level, % of total);

- # of papers in refereed journals (names of journals);
- # of papers in refereed conference proceedings;
- # of invited presentations;
- # of technical reports;
- # of book chapters;
- # of other publications;
- # and type of participation in national and international committees, conferences and networks related to projects;
- # and type of genomics related databases, libraries, etc. resulting from projects;
- application of research results and technology transferred;
- new products, tools, processes developed;
- spin-off companies (#, types, names, contact information);
- # of disclosures;
- # of active patents, patent applications, patents issued;
- # of licenses issued:
- # of material transfer agreements (MTAs);
- # of formal collaborative agreements; and
- # of standard operating protocols.

Figure 1 - Logic Model for the Interdepartmental Genomics R&D Initiative



Public Sector Private Sector Government scientists and Universities (Canadian and international): Industry (Canadian REACH Not-for-profit organizations decision / policy makers: · scientists ` · other faculty and international): Canadian general public federal municipal scientists Other research organizations · provincial · international · decisionmakers (Canadian and international)

Table 5: Annual Performance Measurement Strategy

AREA ONGOING INDICATORS SOURCES RESPONSIBILITY **IMMEDIATE OUTCOMES** Project information # of interdepartmental research initiatives (table Enhanced governance, Departments coordination and science summarizing initiative, scope, funding level, # of partnerships departments involved, description) # of partnerships / collaborations on projects Project information Departments by type, e.g.: • OGDs · universities · international organizations · private sector • Genome Canada • etc. Internal funds leveraged: A-base and B-base funding Departmental records Departments Other funding and in-kind contributions by type Project information Departments (complementary to previous information on collaborations), e.g.: • OGDs • universities · international organizations · private sector • Genome Canada • etc. Increased research capacity: # and type of new research personnel: Departmental records Departments • Increase in HQP / • permanent and temporary (PDFs, students) training of existing HQP · scientific and technical support \$ and % of allocation to training and related Departmental records Departments **HQP** activity # of existing staff trained (genomics related) Departmental records Departments # of existing departmental staff working on Departmental records Departments GRDI funded projects (increasing expertise by doing research) · advancements in state-of-Type of infrastructure: Project reports Departments the-art infrastructure • acquired adapted upgraded maintained \$ and % of allocation to infrastructure Departmental records Departments Access to and sharing of • # of papers in refereed journals Departments Project reports technology and scientific (hard copy / electronic) knowledge · information about journals available on request # of papers in refereed conference proceedings Departments Project reports # of invited presentations Project reports Departments # of technical reports Project reports Departments # of book chapters Project reports Departments # of other publications Project reports Departments # and type of participation in national and inter-Project reports Departments national committees, conferences and networks Departmental records # and type of genomics related databases, Project reports Departments libraries, etc. Public awareness of genomics Web presence / # website hits / Analysis of website Departments other website statistics statistics

AREA ONGOING INDICATORS SOURCES RESPONSIBILITY

INTERMEDIATE OUTCOMES	3		
Increased participation in national and international genomics initiatives	Extent to which scientists in departments participate in other projects • national vs international • role on projects • leveraging • # of partners • OGDs vs universities vs private sector vs Genome Canada vs others • etc.	Project information	Departments
	Other types of participation in national and international genomics initiatives • number of initiatives • types of initiatives • role of departments / scientists	Departmental records	Departments
Application of research results to develop innovative new or	Description of application of research results (internal and external) and technology transferred	Departmental records	Departments
improved methods, products, processes or technologies,	# and types of spin-off companies	Project reports	Departments
including through:	# of disclosures	Project reports	Departments
 spin-off companies disclosures active patents, patent applications, patents issues licenses issued material transfer agreements (MTAs) formal collaborative agreements 	# of active patents, patent applications, patents issued	Project reports	Departments
	# of licenses issued	Project reports	Departments
	# of MTAs	Project reports	Departments
	# of formal collaborative agreements / # of standard operating protocols	Project reports	Departments

Table 6: Impact Evaluation Performance Measurement Strategy Requirements

AREA ONGOING INDICATORS SOURCES RESPONSIBILITY

AREA	ONGOING INDICATORS	SOURCES	RESPONSIBILITY
IMMEDIATE OUTCOMES			
Enhanced governance, coordination and science partnerships	Evidence of coordinated planning (interdepartmental and intra-departmental), priority setting and management approaches (e.g., GRDI ADM Coordinating Committee, GRDI Working Group, linkages to the Canadian Regulatory System for Biotechnology)	Minutes of meetings, decision records, planning documents, etc.	Departments GRDI ADM Coordinating Committee GRDI Working Group
	# of interdepartmental research initiatives (initiative, scope, funding, # of departments involved, description)	Project information	Evaluators based on departmental information
	# of partnerships / collaborations on projects by type, e.g.: OGDs universities international organizations private sector Genome Canada	Project information	Evaluators based on departmental information
	Internal funds leveraged: A-base and B-base funding	Departmental records	Evaluators based on departmental information
	Utilization of funds for intended purposes	Project information	Evaluators based on departmental information
	Other funding and in-kind contributions by type (complementary to previous information on collaborations), e.g.,: OGDs universities international organizations private sector Genome Canada	Project information	Evaluators based on departmental information
Increased awareness and understanding of genomics research results and their potential applications	Extent to which projects have addressed key genomics information needs within the departments	Comparison of project objectives to departmental priorities; interviews with departmental managers	Evaluators based on departmental information
	Extent to which regulators, policy makers, decision-makers are aware of projects, their results and their potential applications • within departments • in other departments • in other levels of government • in other organizations	Interviews with regulators, policy makers, other managers and others	Evaluators based on departmental information
Direct and indirect support for regulation, policy and / or decision-making	Extent to which scientific evidence related to genomics is available and used in the development of regulations and policies as well as in other types of decisions • within departments • in other departments • in other levels of government	Interviews with regulators, policy makers and other managers, review of decision records, discussion documents, White Papers	Evaluators based on departmental information
Public awareness of genomics	Level of public awareness of genomics	Survey of general public	Evaluators
	Web presence / # website hits / other website statistics	Analysis of website statistics	Evaluators based on departmental information

AREA ONGOING INDICATORS SOURCES RESPONSIBILITY

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INTERMEDIATE OUTCOMES	;		
Improved science-based regulations, policies and / or decision-making	Evidence of contribution of scientific evidence to regulatory, enforcement, environmental assessment, public health and policy discussions and decisions • within departments • in other departments • in other levels of government	Interviews with regulators, policy makers and other managers, review of discussion documents, White Papers	Evaluators based on departmental information
Increased participation in national and international genomics initiatives	Extent to which scientists in departments participate in other projects • national vs international • role on projects • leveraging • # of partners • OGDs vs universities vs private sector vs GC vs others.	Project information, interviews with scientists and partners	Evaluators based on departmental information
	Other types of participation in national and international genomics initiatives number and types of initiatives role of departments / scientists	Departmental records, interviews with dept reps / reps of other initiatives	Evaluators based on departmental information
Application of research results to develop innovative new or improved methods, products, processes and technologies through: • spin-off companies • disclosures	Description of application of research results (internal and external) and / or technology transferred	Departmental records	Evaluators based on departmental information
	# and type of products, tools and processes developed due to application of research results; description of use	Departmental records, interviews with recipient organizations	Evaluators based on departmental information
 active patents, patent applications, licenses issued Material Transfer Agreements formal collaborative agreements 	# and types of citations	Citation analysis	Evaluators based on departmental information
Public understanding of	Change in the level of public understanding	Survey of general public	Evaluators
genomics as an important contributor to their quality of life	Change in media reporting	Content analysis of newspapers, other publications	Evaluators

AREA **ONGOING INDICATORS** SOURCES RESPONSIBILITY

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LONG-TERM OUTCOMES			
Improved health care, including: • improved diagnostics and	Extent to which research results are used for diagnostics, treatments, prevention, etc.	Case studies, interviews	Evaluators based on departmental information
treatments reduced health and environmental risks reduced health costs	Specific health care impacts (refer to Departmental RMAFs for specific indicators)	Case studies, analysis of secondary data on health care	Evaluators
Reduced environmental impacts related to: • water quality	Extent to which research results are used to refine environmental regulations and improve pollution detection, monitoring, and enforcement activities	Case studies, interviews	Evaluators based on departmental information
healthy and productive aquatic ecosystems sustainable fisheries, agriculture, forestry and aquaculture	Specific environmental impacts (refer to Departmental RMAFs for specific indicators)	Case studies, analysis of secondary data on environment	Evaluators
Improved competitiveness of Canadian companies as a result of: • diversification • improved productivity • cost reduction	Extent to which research results are used by Canadian companies	Case studies, interviews	Evaluators based on departmental information
	Performance of companies using research results vs others in that sector (refer to Departmental RMAFs for specific indicators)	Case studies, analysis of secondary data	Evaluators
demonstration of good governance and sustainable development	Improved performance of specific sectors affected by research results	Case studies, analysis of secondary data	Evaluators
Canada is positioned as a credible participant in genomics research and applications	Level of participation in international initiatives	Departmental records, interviews with departmental reps and reps of other initiatives	Evaluators based on departmental information
	Opinions of experts regarding participation of Canada	Literature review, interviews with experts	Evaluators based on departmental information
	Level of public and private investment in genomics R&D	Case studies, analysis of secondary data	Evaluators
ULTIMATE OUTCOME			
Enhanced quality of life in terms of health, safety, environment, and social and economic development	Miscellaneous quality of life indicators (e.g., improved health services / treatments, employment opportunities, lifestyle improvement, environmental benefits, etc.)	Case studies, secondary data, special studies, etc.	Evaluators