


Genomics R&D Initiative

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GENOMICS R&D INITIATIVE

ANNUAL PERFORMANCE REPORT

2011-2012

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.

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EXECUTIVE SUMMARY

The Genomics R&D Initiative (GRDI) is a federal program that coordinates science departments and agencies in the field of genomics research to contribute solutions to issues that are important to Canadians. Focusing specifically on issues that involve living organisms, the Initiative contributes solutions to protect and improve human health, develop new interventions related to prevention, control or treatments for chronic and infectious diseases, protect the environment, and manage agricultural and natural resources in a sustainable way. It supports evidence-based decision making, policy development, formulation of standards and regulations, and the development of S&T innovation for Canada, in line with the specific role of federal government research.

The GRDI has been funded for three-year cycles: Phase I (1999-2002), Phase II (2002-2005), Phase III (2005-2008), and Phase IV (2008-2011). Since the initiative was first funded in 1999, it has delivered insights into pests and diseases for Canada's important wheat and canola crops; contributed to water, forestry and fisheries management; identified cancer genetic signatures that allow better targeted treatments; and developed new methods to assess viruses such as influenza for the targeted release of vaccines.

Phase V (2011-2014) continues to support mandated research in participating departments. It also supports two highly coordinated interdepartmental projects along shared priorities and common goals:
1) Strengthening Food and Water Safety in Canada through an Integrated Federal Genomics Initiative; and
2) Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species.

This Annual Performance Report for 2011-2012 follows the Performance Measurement Framework that was developed for the GRDI in 2011. It presents the GRDI program profile and planned results, its links to departmental objectives and program activity architecture, its governance, coordination and accountability structures. It then reports on performance for 2011-2012 in terms of governance, research and development, and maintenance of capacity. Annexes present summary statistics as well as a summary narrative account of R&D achievements for 2011-2012.

ACRONYMS

AAFC	Agriculture and Agri-Food Canada
ABL	Aquatic Biotechnology Laboratory
ADM	Assistant Deputy Minister
ADM CC	ADM Coordinating Committee
AIV	Avian influenza virus
cDNA	Complementary DNA
CEPA	Canadian Environmental Protection Act
CFIA	Canadian Food Inspection Agency
CFS	Canadian Forest Service
CFU	Colony forming units
CIHR	Canadian Institutes of Health Research
CORE	North American Collaborative Oat Research Enterprise
COSEWIC	Committee on the Status of Endangered Wildlife in Canada
CRTI	Chemical, Biological, Radiological-Nuclear, and Explosives Research and Technology Initiative
DFO	Fisheries and Oceans Canada
DNA	Deoxyribonucleic acid
EC	Environment Canada
eQTL	Expression quantitative trait loci
FTEs	Full time equivalents
FWS	Food and water safety
GHI	Genomics and Health Initiative
GRDI	Genomics Research and Development Initiative
HC	Health Canada
HIV	Human immunodeficiency virus
IHNV	Infectious hematopoietic necrosis virus
ISAV	Infectious salmon anemia virus
MHC	Major histocompatibility complex
mRNA	Messenger RNA
NGO	Non-governmental organization
NRC	National Research Council Canada
NRCan	Natural Resources Canada
OGD	Other government departments
OTU	Operational taxonomic units
PCR	Polymerase chain reaction
PHAC	Public Health Agency of Canada
PMF	Performance Measurement Strategy Framework
PWEF	Photonic wire evanescent field
QIS	Quarantine and invasive species
qPCR	Quantitative PCR
QTL	Quantitative trait locus
R&D	Research and Development
RAD	Restriction site Associated DNA
RNA	Ribonucleic acid
RT-PCR	Reverse transcription polymerase chain reaction
S&T	Science and Technology
SMV	Soybean mosaic virus
SNP	Single nucleotide polymorphism
SSC	Shared Services Canada
SSR	Single sequence repeats
STAGE	Strategic Technology Applications of Genomics in the Environment
STEC	Shiga-toxin producing
TB	Tuberculosis
TOR	Target of rapamycin
US EPA	United States Environmental Protection Agency
USA	United States of America
WG	Interdepartmental Working Group

GENOMICS R&D INITIATIVE – PROGRAM PROFILE

The GRDI was established in 1999 to establish and maintain core genomics R&D capacity in federal departments and agencies and provides $19.9M/year, based on a three-year cycle, to: Agriculture and Agri-food Canada (AAFC); Environment Canada (EC); Fisheries and Oceans Canada (DFO); Health Canada (HC); Public Health Agency of Canada (PHAC); National Research Council Canada (NRC); and Natural Resources Canada (NRCan).

Projects funded under the GRDI are focused on departmental mandates and government priorities, and are strategically aligned with the objectives of the departments. They seek to uphold regulatory, public policy, and operational mandates in important areas such as health, food safety, sound management of natural resources, a sustainable and competitive agriculture sector, and environmental protection, with strong collaborations with university and private sectors.

New to this phase of the GRDI (2011-2014), is the mobilization of resources for concerted research on issues that are beyond the mandates of single departments. It supports highly coordinated interdepartmental projects along shared priorities and common goals. Two projects were identified for priority action: 1) Strengthening Food and Water Safety in Canada through an Integrated Federal Genomics Initiative; and 2) Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species. All GRDI participating departments, as well as the Canadian Food Inspection Agency, have the opportunity to participate in these shared priority projects.

Resources

Table 1: Funding Allocations ($000)

DEPARTMENT/AGENCY	PHASE I 1999-2002	PHASE II 2002-2005	PHASE III 2005-2008	PHASE IV 2008-2011	PHASE V 2011 - 2014
Agriculture and Agri-Food Canada	17,000	18,000	18,000	18,000	15,300
Environment Canada	3,000	3,000	3,000	3,000	2,295
Fisheries and Oceans Canada	2,500	2,700	2,700	2,700	2,295
Health Canada / Public Health Agency of Canada	10,000	12,000	12,000	12,000	10,200
National Research Council Canada	17,000	18,000	18,000	18,000	15,300
Natural Resources Canada	5,000	6,000	6,000	6,000	5,100
Shared Priorities					8,955
Medical Research Council[1]	500	-	-	-	-
Total	**55,000**	**59,700**	**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.

All departments have levered the GRDI with allocations from their Abase resources and from successful collaborations. Table 2 provides an overview of resources invested in 2011-2012 in support of GRDI projects, and shows that non-GRDI funds represented more than twice the GRDI investments. Additional in kind investments estimated to close to $2 million included the sharing of technology platforms, materials, and expertise with a variety of collaborators in research areas that cut across traditional departmental sectors.

Table 2: Overall Investment in support of GRDI projects in 2011-2012 ($000)

DEPARTMENT/AGENCY	GRDI	NON-GRDI	TOTAL
National Research Council Canada	5,966	6,241	12,207
Agriculture and Agri-Food Canada	5,700	1,373	7,073
Health Canada	1,900	1,805	3,705
Public Health Agency Canada	1,900	3,914	5,814
Natural Resources Canada	1,900	2,815	4,715
Environmental Canada	950	1,360	2,310
Fisheries and Oceans Canada	855	1,493	2,348
SHARED PRIORITY PROJECT	**GRDI**	**NON-GRDI**	**TOTAL**
Quarantine and Invasive Species	399	626	1,025
Food and Water Safety	330	39	369
Total	**19,900**	**19,666**	**39,566**

Planned Results

As part of NRC's 2011-2012 Report on Plans and Priorities supplementary tables for the GRDI, the participating departments established a collective set of planned results:

- Commercially-relevant advances in genomics R&D related to human health;
- Concerted interdepartmental research along shared priorities and common goals on issues that are beyond the mandates of single departments, and where the CFIA has the opportunity to participate;
- Using genomics to improve the value of cereal, canola and legume crops;
- Genomics knowledge and advice for the management of fisheries and oceans;
- Genomic knowledge for the Canadian health regulatory system;
- Genomic knowledge for forest generation and protection;
- Genomics knowledge to strengthen Public Health programs and activities related to infectious and chronic disease; and
- Enhance Environment Canada's applications of genomics-based tools and technologies for responsible decision-making.

To deliver on these planned results, departments and agencies have developed the following research program plans and activities:

Agriculture and Agri-Food Canada

Project supported by the GRDI at AAFC will continue to align with the Canadian Crop Genomics Initiative, with some expansion into additional key crop kinds and related activities. Investments will continue to be made in three main areas 1) biodiversity, gene mining and functional analysis for the identification and extraction of genes for desirable traits; 2) delivery of genomics discoveries through bioinformatics and physical tools in order to improve access to both biological materials and data sets, and to assist and accelerate the adoption and commercialization of new technologies; and 3) enhanced efficiency of plant breeding. The program will continue to focus on addressing biotic and abiotic stress through functional genomics of disease and insect resistance and tolerance to stress such as cold, enhanced

quality attributes in cereals (wheat, oat and triticale), oilseeds (*Brassica* and *Arabidopsis*) and legumes (soybeans, pulses), as well as platform technologies.

Fisheries and Oceans Canada

Genomics-enabled research within DFO will continue to be aligned within the following themes: 1) *Genetic Profiling of Aquatic Resources*: DFO has responsibility for providing scientific advice and research for over 650 fish, invertebrate, and mammal species. There is enormous potential for the development of genomic tools relevant to those species under management, and particularly those that are of management concern; 2) *Research and Development of Genomic Approaches for Aquatic Animal Health Diagnostic Tools to Protect Aquatic Ecosystems*: Aquatic animal health research under this theme includes the genomics research concerning the health of aquatic animals that fall under DFO legislative authority. Further research incorporating genomics approaches to aquatic animal health will better position Canada to respond and manage aquatic animal resources, particularly under changing environmental conditions; and 3) *Aquatic Ecosystem Health*: Genomics approaches offer opportunities for increasing our understanding of the aquatic ecosystem, and are anticipated to be an important tool for applying an ecosystem approach to managing aquatic resources and healthy and productive aquatic ecosystems.

Environment Canada

The *Strategic Technology Applications of Genomics in the Environment* (STAGE) program aims at enhancing EC's applications of genomics-based tools and technologies to support the department's policy, regulatory decision making, and enforcement mandates. Environment Canada will continue to show leadership in environmental genomics and foster collaboration in other departments and external institutions. Genomics research supports the current Strategic Outcomes of the department's Program Activity Architecture, *Canada's Natural Environment is Conserved and Restored for Present and Future Generations* and *Threats to Canadians and their Environment from Pollution are Minimized,* thereby meeting departmental priorities. This will assist the delivery of EC's obligations as a signatory of, and regulator for, major environmental legislation and agreements such as the *Fisheries Act,* the *Toxic Substance Management Policy*, the *Chemical Management Plan*, and the *Canadian Environmental Protection Act*.

Research priorities for 2012-2014 were approved for STAGE by the department in March 2012, as follows: *Strengthen predictive models* (*e.g.,* tools to address the transport, fate, effects and risks of existing and emerging chemical, biological, and physical influences on organisms, biodiversity, ecosystem function, and water availability); *Understand and monitor ecosystems* (tools to understand and monitor aquatic and land-based ecosystems); *Understand cumulative risks/impacts* (*e.g.,* tools to understand and predict cumulative impacts on, and risks to, ecosystem health from multiple stressors interacting over time); and *Manage environmental risks* (*e.g.,* tools to manage environmental risks of chemical, biological, physical, and genetic pollutants).

Health Canada

Genomics research will continue to focus on four priority areas of investment for strengthening the department's regulatory role: 1) *Regulatory knowledge on therapeutics and biologics*: Studies will be conducted for the identification of biomarkers associated with the safety evaluation of health products; 2) *Regulatory knowledge on food safety and nutrition*: Genomics research will be undertaken to detect food-borne contaminants, to characterize the health effects of food contaminants, nutrients, novel foods/food ingredients, and pre- and pro-biotics for enhanced regulatory decisions, and to develop biomarkers to monitor cellular and physiological responses in the context of nutrition and disease susceptibility of defined populations; 3) *Regulatory knowledge to protect human health from potential adverse effects of environmental contaminants, consumer products, and pesticides*: Research will focus on effectively and efficiently assessing the hazards of environmental contaminants, occupational health hazards, pesticides, and consumer products; and 4) *Research on socio-ethical impacts of genomics technologies and products*: Bioethics and benefit-sharing best practices will be developed for genetic research, with studies pertaining to ethical, legal, and social issues of genomics to address the use of DNA samples for research purposes.

National Research Council Canada

The NRC Genomics and Health Initiative (GHI) is focused on genomics and health-related technologies – key enabling technologies that support NRC and federal priorities in health, energy and environment. NRC-GHI provides a mechanism to bring to bear multi-disciplinary competencies and converging technologies in NRC research institutes, while ensuring that research projects are linked to market needs and opportunities for Canadian companies. The GHI has four primary goals: 1) To translate scientific and technical knowledge within genomics and health-related research into social and economic well-being for Canada; 2) To create and use new genomics and health-related technologies to contribute to the global competitiveness of Canadian industry in key industrial sectors (e.g. biopharmaceuticals and agriculture); 3) To support and participate in regional, national and international genomics and health-related innovation networks through cooperation and integration across NRC institutes and with external partners from industry, academia, government departments and other research organizations; and 4) To foster excellence in horizontal research program management and accountability.

Natural Resources Canada

Genomics research addresses the challenges faced by Canada's forest sector by using that knowledge for commercial innovation. Canada's capacity and expertise in forest genomics will address the needs of the forest sector by: 1) identifying genes of commercially important traits such as wood quality, growth and resistance, giving tree breeders the ability to select superior trees in seedlings as young as a year; 2) the production of innovative molecular technologies that will allow the identification or diagnosis of potentially invasive pests; 3) furthering our understanding of the interactions between hosts and pests or hosts and beneficial microorganisms for the development of environmentally-friendly forest management approaches, including biological control methods; and 4) investigating bioenergy solutions via improved feedstock and/or novel enzymatic processes and associated value-added bioproducts.

Public Health Agency of Canada

For Phase V, PHAC has selected research projects that target high priority issues in the areas of infectious and chronic diseases. Projects related to infectious diseases address priority issues such as increasing our knowledge related to the emergence of drug-resistant bacterial pathogens, and related to emerging and re-emerging pathogens such as Ebola virus and *Mycobacterium tuberculosis*. PHAC also directs GRDI support to the priority area of food safety, enabling the public health networks that monitor and respond to food-borne pathogens to deploy innovative tools for rapid and accurate characterization of pathogens leading to improved responses to food-borne pathogens. In addition, PHAC researchers are creating automated bioinformatic processes for genomic sequence analysis. The tools produced will provide PHAC researchers, public health partners and federal researchers in other government departments with methods needed to accommodate burgeoning genomic data that can now be generated more rapidly than it can be analysed. The effect of nutritional status on the development and outcome of chronic diseases is being investigated by other GRDI supported projects at PHAC. In particular, researchers are investing the effect of vitamin D status on the development of type-2 diabetes and the role that variation in folate metabolism plays in risk of chronic disease. The GRDI projects at PHAC apply genomics approaches to generate leading edge knowledge to inform public health decisions and to develop innovative tools in response to the public health needs of the federal government and of our provincial partners.

Shared Priorities

The project *Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species* (the Quarantine and Invasive Species project) aims at developing diagnostic tools based on DNA barcoding for the early detection, surveillance and management of hundreds of species, focusing on those that are or quarantine concern. It is coordinated by AAFC and involves CFIA, DFO, EC, NRCan, and NRC. The project *Strengthening Food and Water Safety in Canada through an Integrated Federal Genomics*

Initiative (the Food and Water Safety project) aims at developing increased speed and reduced cost of genomics-based methods for pathogen isolation, detection and characterization; and developing a federally integrated database to manage, store and provide access to genomic data and related information from food and water-borne pathogens, focusing on *Escherichia coli* and *Salmonella* Enteritidis. It is coordinated by HC and involves AAFC, CFIA, EC, NRC, and PHAC.

Alignment with Government Priorities

The GRDI seeks to support increasingly complex federal evidence-based regulatory and policy decisions required by the respective mandates of participating departments and agencies, as well as the development of new policies and standards, within the realm of the specific role of federal research as presented in the federal science policy framework (S&T Strategy, 2007), and focusing activities in areas where government is best able to deliver results. It also seeks to support the ability to anticipate and respond to the needs of Canadians in relation to areas of government responsibility for public health, the economy and the environment. For example, research funded by the GRDI has: 1) allowed genomics datasets to be developed and used for the most intensive real-time management of mixed-stock fisheries in the world, thus greatly increasing the effectiveness of conserving threatened Pacific salmon while harvesting more abundant stocks sustainably; 2) led to the development of methods to detect microbial contamination of water to aid municipal and provincial governments in the management of water resources; and 3) produced a Salmonella identification method that reduces costs by 70% and identification time from 4 days to 7 hours. Provincial and municipal governments are also users of GRDI knowledge for the management of public resources.

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

All research and innovation activities at AAFC (including those of the GRDI) directly support the achievement of prioritized research outcomes. Funding from the GRDI has enabled AAFC to develop and strengthen the Canadian Crop Genomics Initiative through investments in plant genomics and the formation of multi-disciplinary teams across Canada. Under the agriculture portfolio, CFIA will contribute to shared projects to support its regulatory mandate, and will benefit from interdepartmental integration of common functions.

National coordination for genomics research at DFO is provided by the National Aquatic Biotechnology and Genomics R&D Program. This Program supports genomics research directly related to Economically Prosperous Maritime Sectors and Fisheries, one of the three pillars of the department's Program Activity Architecture.

The GRDI has contributed to the foundation of EC's Strategic Outcomes *Canada's Natural Environment is Conserved and Restored for Present and Future Generations* and *Threats to Canadians and their Environment from Pollution are Minimized*, as defined in EC's Program Activity Architecture. Environment Canada carries out its genomics research through the Strategic Technology Applications of Genomics in the Environment (STAGE) program.

The GRDI at HC contributes to the generation of knowledge that is required for the effective regulation of health and food related technologies. The Departmental Science Plan describes the contribution of genomics research towards improving policy development and regulations, informing and engaging the public on emerging technologies and supporting HC's efforts in harmonizing policies nationally and internationally. The GRDI addresses a number of strategic objectives under the Program Activity of Emergent Health Issues.

The Genomics and Health Initiative (GHI) is the largest horizontal R&D initiative of NRC and supports one of NRC's two Strategic Outcomes: *Advancements in*

innovative technologies and increased innovation capacity in targeted Canadian industries and national priority areas. This is accomplished by contributing to program activities under Health and Life Science Technologies that support Canadian R&D priorities in health (chronic diseases and agri-food), energy (biofuels), and the environment (environmental technologies and bioproducts).

At the Canadian Forest Service (CFS) of NRCan, the GRDI has developed the foundation for contributing to the Strategic Outcome *Economic Competitiveness* and to the Program Activity *Economic Opportunities for Natural Resources*. It contributes to the CFS Intended Outcome: *Advancing Forest Product Innovation*. Resulting from this foundation are important amounts of data, infrastructure, and collaborations that are delivering practical applications.

Within PHAC, projects funded by the GRDI support the over-arching strategic outcomes of promoting health, reducing health inequalities, as well as preventing and mitigating injuries and disease. Researchers create innovative tools that apply genomic and bioinformatic technologies for more effective public health interventions targeting infectious and chronic diseases. In addition, the GRDI generates leading edge scientific knowledge to support public health decision making and program development. By driving collaboration and knowledge exchange among public health professionals working in federal, provincial, territorial, municipal and non-government organisations, the GRDI facilitates the integration of reliable and current information into public health decision making and interventions at all levels across Canada. The development and application of leading-edge public health science and of tools to provide specialized laboratory testing and reference services that will contribute to better public health and improved responses to emerging health risks fall directly within the Program Activity of *Science and Technology for Public Health*.

The federal science policy framework is currently provided by *Mobilizing Science and Technology (S&T) to Canada's Advantage* (hereafter referred to as the S&T Strategy), a strategy released by the Federal government in May 2007 that is committed to position Canada for global knowledge leadership. The GRDI contributes to the three S&T advantages for Canada outlined in the S&T Strategy (knowledge, people, entrepreneurial) with its focus on knowledge generation for evidence-based decision making, the recruitment and training of highly skilled personnel, and major collaborative relationships with academia and the private sector to deliver concrete results. It is also congruent with the vision presented in the S&T Strategy of what research should be pursued inside federal laboratories. It generates knowledge that helps support governmental mandates, formulates standards and regulations, facilitates evidence-based decision making and policy development, and develops novel applications related to key federal public-policy objectives in all life science sectors. Transformational research aims to support the competitive needs and economic viability of Canadian enterprises, including small and medium-size enterprises. The GRDI supports federal regulators in their evaluation of genomics data, as well as outreach activities to facilitate access to clear and accurate information on genomics R&D.

Governance, Coordination and Accountability

Departments are vertically accountable in terms of authority to deliver on their mandate and to spend resources. Accountability is thus often viewed as a challenge to the management of shared programs that have a collective sense of purpose. Indeed, programs involving more than one department to jointly pursue common objectives present unique complexities for setting priorities and sharing resources.

To ensure sound management of the GRDI, the interdepartmental governance framework established under the leadership of NRC for previous phases of the GRDI will continue to oversee the collective coordination of the GRDI. The governance structure for GRDI includes three main elements: an ADM Coordinating Committee, an Interdepartmental GRDI Working Group and a Coordination Function, with support from Ad Hoc Advisory Committees when particular needs for expert advice arise.

ADM Coordinating Committee (ADM CC)

An interdepartmental ADM CC, chaired by the lead agency (NRC) with membership at the ADM-level from each of the organizations receiving funding, the CFIA, and guest representatives from Industry Canada and Genome Canada. It is responsible for the overall strategic direction for the GRDI and approval of investment priorities. It ensures that effective priority setting mechanisms are established for the GRDI, and that government objectives and priorities are addressed. The Committee also ensures that common management principles are implemented and collaborations between organizations are pursued wherever relevant and possible. It typically meets three times a year at the call of the Chair, more often when warranted by specific needs for decision-making.

Interdepartmental Working Group (WG)

An interdepartmental GRDI WG supports the work of the ADM CC. It is chaired by the lead agency (NRC) with membership at the Director level from all participating departments/agencies, the CFIA, and Industry Canada. The mandate of the WG is to provide recommendations and strategic advice to the ADM CC regarding strategic priority setting and overall management of the GRDI. The WG is responsible for providing direction to GRDI program activities related to operational delivery, implementation planning and investment priority setting. The WG also supports evaluation and reporting requirements related to the GRDI. It meets about every two months, more often when warranted by specific needs for recommendations and advice, as well as to develop the GRDI Annual Performance Report.

GRDI Coordination Function

The Coordination Function for the GRDI is housed at NRC, the GRDI lead agency. It provides GRDI-wide program coordination, communication, networking and outreach support. This includes support to the ADM CC and the GRDI WG, transparent and effective communication to departments of the planning cycle, process requirements, financial administration and other project management requirements, and support for interdepartmental shared project planning and implementation. This function is also responsible for conducting studies and analyses to serve as input to determination of GRDI-wide research priorities, and providing management and administration support, as well as support for performance management, reporting, evaluation, and communications. It will be funded through the shared priorities portion of the GRDI.

Advisory Function

An advisory function is required, especially when it comes to engaging stakeholders and potential end users to address needs in the planning stages, and to seek strategic advice on priorities. The GRDI uses several means of seeking expert input: planning workshops; one to one meetings with stakeholders and end-users; or by convening ad hoc committees when particular needs arise (for example, to advise on common functions for the GRDI).

Performance Measurement Strategy Framework

Consistent with the concept of modern comptrollership that focuses on results-based control systems, a horizontal Performance Measurement Strategy Framework was developed for the GRDI in 2011 to formalize the commitment of the eight departments and agencies involved in the GRDI regarding the common measurement and accountability requirements associated with this Initiative. An overview of the Performance Measurement Strategy Framework is provided in Appendix B, as well as the logic model that reflects the overall objectives for the GRDI, leading to the uptake and application of the knowledge and tools it generates for policy and regulatory decisions, for addressing key public policy priorities, as well as for supporting private sector innovation.

PERFORMANCE

Governance

Fiscal year 2011-2012 was the first year of Phase V programs. Funding was released with considerable delay, which caused difficulties for the recruitment of highly qualified personnel and the establishment of new projects. Departments and agencies were also faced with uncertainties with strategic and operational reviews, as well as institutional reorganizations. Still, cash management decisions within departments and agencies, and in some cases, continuation of Phase IV projects for one year, allowed research to proceed.

GRDI Interdepartmental Coordination

The document entitled *Genomics R&D Initiative (GRDI) Governance Framework Phase V* was developed to provide a management framework for the GRDI, and approved by the ADM CC on 23 November 2011. It presents GRDI principles; decision-making criteria; governance, coordination and accountability; supporting structures including terms of reference; process and decision flow chart for interdepartmental shared priority projects; mitigation of risks; as well as an overview of commitments related to the GRDI for 2011-2014.

The document entitled *Genomics R&D Initiative (GRDI) Phase V- Mandated Research Best Practices* details the governance structures developed by departments to manage and deliver research funded through the GRDI, as well as project selection and approval processes. It also presents a variety of templates, drawn from existing processes, which are meant to provide examples of best practices, and was approved by the ADM CC on 20 February 2012.

The document entitled *Companion Document to the Performance Measurement Strategy for the Genomics R&D Initiative (GRDI) - Information to be collected by departments for Annual Performance Reports* provides guidelines on data collection details to address performance indicators and to improve performance tracking and reporting for the initiative. It presents a common understanding of annual performance report requirements to facilitate a coherent approach for departments, and was approved by the GRDI WG on 30 March 2012.

Four meetings of the ADM Coordinating Committee and 14 meetings of the GRDI WG were held to allow for timely collaborative decisions.

Planning meetings and interdepartmental workshops were also organized for the development of shared priority projects. These meetings involved research directors and senior research staff to identify specific objectives and key research participants to lead the development comprehensive project proposals, including work and expenditure plans. Templates, directives, logistic and financial support were provided for project development and peer review processes, and funding agreements were put in place according to formal Project Charters approved by the ADM CC.

Under guidance from the ADM CC, the GRDI WG commissioned an online survey within GRDI departments to highlight existing strengths, as well as gaps, needs, and potential collaborative models in relation to bioinformatics and research computing. The survey was completed in December 2011 and key areas that could be strengthened were identified around: infrastructure, sustainability, data integration, reference data, interoperable software, standardized approaches, and the need for more flexible government IT policies.

This was followed by the organization of an interdepartmental bioinformatics workshop, held in Ottawa on 28 March 2012 to discuss future operating models in light of the creation of Shared Services Canada (SSC). Genomics projects are heavily dependent on bioinformatics. For example, both shared priority projects require early collaboration between their bioinformatics sub-project and other sub-projects to create a cyber-infrastructure platform to manage, store, and analyze data, with a short development timeframe. The creation of SSC thus raised concerns about the ability of the GRDI project teams to deliver on their commitments. It also presents a unique

opportunity to strengthen the established scientific computing capacity within government, with a research computing strategy and solution designed in collaboration between SSC and departmental research computing staff. The meeting was well attended with 65 participants including several senior officials from Shared Services Canada. At the workshop, SSC committed to work with the science community as collaborators and partners rather than as service providers and the basis of a working relationship was created. A report was produced, sent to all participants, and presented to the GRDI ADM CC.

Mandated Research

Departments renewed their strategic directions and held competitions for the allocation of funds to new projects, according to practices developed to define priorities, support departmental coordination, and select projects to specifically address the identified priorities where federal scientists had distinct expertise, using balanced portfolio approaches. Departments and agencies frame their GRDI program within the scope of existing program areas aligned with their respective Strategic Outcomes, Activities, and Sub-Activities defined in their Program Activity Architecture.

While detailed governance approaches vary by department, all research projects were approved internally based on formal approval processes.

Shared Priorities

For Phase V of the GRDI, the ADM CC envisioned targeting a portion of the funds to one or two projects that would address shared priorities. The distribution of funding would reflect existing strengths and activities, and would support specific departmental contributions to the selected projects, based on a collaborative approach. A truly interdepartmental approach was used for the development of these shared priority projects. The GRDI Working Group worked to develop project options, and ten thematic areas based on potential synergies between departments were developed and consolidated at a one-day scientific workshop.

These themes were analyzed using agreed upon decision-making criteria, resulting in the selection by the ADM CC of two themes to be pursued: 1) Improved ability to detect, diagnose and monitor microbial organisms to ensure a sustainable supply of safe and healthy food and water for human consumption; and 2) Improved ability to detect, identify and understand Canadian biological diversity to prepare Canadian natural and managed resources and markets for global change.

Based on this guidance, the GRDI research community self-assembled to develop thorough project proposals. These were then presented to the GRDI WG and to the ADM CC as part of a pre-approval step towards their finalization. Revised proposals were then sent out for external scientific peer review to validate the scientific approaches and for quality control and enhancement purposes. Input from the peer review was integrated into the proposals and these were developed into formal project charters, approved by the ADM CC.

Project charters define research objectives, milestones and deliverables, establish responsibilities and performance expectations, set milestones, establish resource and communication networks, and form the basis to demonstrate progress and results.

The charter for the project Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species (the Quarantine and Invasive Species project) was approved by the ADM CC on 10 January 2012. The charter for the project Strengthening food and water safety in Canada through an integrated federal genomics initiative (the Food and Water Safety project) was approved by the ADM CC on 15 March 2012.

Research and Development

Research and development is the central component of this initiative to respond to priorities, support governmental mandates, inform policy and regulatory decisions, and foster innovation. All activities surrounding the actual conduct of R&D, the transfer of technologies and results to stakeholders for uptake and application, and the communication of these results are critical to ensuing impacts and are thus included in the performance measurement framework.

Direct scientific outputs for 2011-2012 and quantitative indicators for performance evaluation are enumerated in Annex 2 by department/agency, for: collaborations, scientific contributions, communications, knowledge and technology transfer, as well as research tools and processes. Highlights of the results achieved in 2011-2012 against planned results are provided in Annex 3, and Annex 4 presents a list of research tools and processes developed under the GRDI.

Maintenance of Capacity

Highly Qualified Personnel

In 2011-2012, the GRDI supported the work of 258 scientific and technical staff, 62 post-doctoral fellows, 110 students (PhD, MSc, BSc, and Co-op) and 4 administrative officers, for a total of 634 active research and technical personnel. Annex 2 provides additional detail presented by department.

Facilities

Departments continued to invest in core infrastructure facilities and funding was allocated towards the purchase, maintenance and upgrading of laboratory equipment. For example:

At AAFC, service contracts were issued for the maintenance of mass spectrometry and transmission electron microscopy equipment. An Illumina next generation sequencer was purchased.

At DFO, genetic analyzers (2 – ABI 3130xl) are maintained and repaired as needed by manufacturer's technical staff; one of the instruments was repaired in 2011-2012 due to software communication failure. Acquisition of infrastructure consisted in: a Bioruptor; a BioAnalyzer; a larval incubator; a Liquid handling robot (epMotion 5070); a Tissue Lyser; and semi-conductor chips for Ion torrent.

At HC, GRDI funding supported the maintenance of bioanalytical capacity in the Bureau of Food Surveillance and Science Integration. Non-capital items, including computer hardware and software and application licenses, were purchased to update and expand capacity for genomics data analyses.

Similarly, non-capital computer hardware and application licenses were purchased to support proteomics infrastructure. The Environmental Health Research Group maintains a state-of-the science DNA microarray facility including: Agilent DNA microarray scanner and associated labware and software; Agilent Bionalyzer; Nanodrop spectophotometer; two CFX real-time PCR machines; GeneSpring Gx microarray analysis software; Ingenuity Pathway Analysis; NextBio; and a core informatics including two high end workstations (T7500) and three Dell R-900 servers. Two MacBook pro computer systems were purchased to enable NGS sequence data analysis and use of open-source unix-based software. A ViiA 7 real-time high throughput PCR system was purchased to provide additional capacity in readiness for large numbers of samples generated by Food Directorate GRDI projects. A yellow-green laser was added to the existing flow cytometer. This will provide increased sensitivity for the instrument thus allowing the detection of mesenchymal stem cell biomarkers that are expressed at very low levels on the cell surface. The addition of this new laser also allows the instrument to conform with newly purchased cell isolation equipment that is necessary for the validation of mesenchymal stem cell biomarkers.

At NRC, the GHI continued to invest in core infrastructure facilities: DNA microarray and proteomics. These facilities support NRC-GHI projects by undertaking research and client-oriented "service" activities utilizing state-of-the-art technologies. Annual operational and equipment funding was provided for each facility with approximate expenditures of $43k for

each. The majority of funding was used to cover salaries of personnel. No major capital acquisitions were made; total minor capital expenditures were $13.5k and funding was used for computer-related equipment.

At NRCan, laboratory equipment was purchased including a PCR set-up hood, a centrifuge, a heating/chilling dry bath, an electrophoresis unit real time PCR machines, and a bioinformatics platform was established.

PHAC uses a combined approach of long-read Roche GS pyrosequencing complemented with data from lower cost, higher coverage Illumina GAIIx sequencing system when sequencing bacterial genomes. A system update in 2011 to PHAC pyrosequencing capacity now allows for sequence reads up to 1000 bases. Characterisation and comparison of bacterial genomes is facilitated by bioinformatic tools that create graphic outputs such as heat-maps and blast-atlases. PHAC analyses pathogen genomic diversity with a variety of data visualisation tools developed or refined in-house. In addition, PHAC continues to maintain and improve the high performance computing environment required for genomic computational biology. The Laboratory for Foodborne Zoonoses (Lethbridge) acquired a Graphics Processing Unit-based personal super computer to enable the assembly and analysis of genomic sequence data. The computing infrastructure is professionally managed with full networking services including user access control, fully encrypted network traffic, intrusion detection and prevention systems, firewall, and network monitoring systems.

For the Qarantine and Invasive Species project, an antivibration table and an Applied Biosystems Step-one plus thermo-cycler for end-point and real-time PCR were purchased. The QIS funding catalyzed a much larger, coordinated bioinformatics infrastructure investment. Funding was invested to purchase 13 new servers to form a new compute cluster attached to a large modular storage device (108TB) to meet GRDI and other project bioinformatics needs. A new Biodiversity Bioinformatics Training and Design Studio was built with capacity for 15-18 bioinformaticians.

APPENDIX A

Annex 1 – GRDI Projects and Funding Allocations from GRDI funds

GRDI FUNDS ($)	PROJECT TITLE
QUARANTINE AND INVASIVE SPECIES	
398,791	Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species
FOOD AND WATER SAFETY	
327,064	Strengthening food and water safety in Canada through an integrated federal genomics initiative
AGRICULTURE AND AGRI-FOOD CANADA	
Addressing biotic stress to develop germplasm and varieties with resistance to economically important diseases and insect pests	
86,800	Proteomic approaches for identifying pathogen and host factors eliciting disease or resistance in the wheat-leaf rust interaction
76,000	Genomics of priming-induced resistance in wheat
130,880	Exploring wheat leaf rust fungus molecular resources to combat cereal rust diseases
239,860	Defining molecular virulence in fusarium and unique resistance mechanisms in wheat and maize towards reducing fusarium mycotoxins in Canadian cereals
74,400	Characterization of new virulent races of *Puccinia striiformis* that threaten the Canadian wheat industry
34,520	Characterization of the *Puccinia triticina* population in Canada
80,000	Bamboozling the flea beetle: functional genomics of trichome development
67,680	Harnessing information on disease resistance in the Genome Canada project 'Creating Pulse'
47,200	Food, feed, and fermentation: identifying toxin targets through yeast genomics
246,400	Identifying novel sources of resistance to Brassica crop diseases
25,000	Strategies to control broad host range fungal pathogen *Sclerotinia sclerotiorum* II: functional analysis of candidate plant defence genes and fungal pathogenicity factors
72,640	Toward control and beneficial uses of Soybean mosaic virus (SMV): genomics and genetics of soybean-SMV interactions
173,600	Soybean root rot caused by *Phytophthora sojae* : genetics of host resistance and pathogen virulence
200,000	The Bertha Armyworm (*Mamestra configurata*) midgut: a target for development of novel control strategies and improved biological control agents
49,260	Detection and quantification of seed-associated pathogens and commensal microorganisms in Canadian crop plants and novel bioinformatic approaches for exploiting metagenomic data
125,600	Molecular understanding of plant virus infection processes and design of novel strategies for plant virus disease control
Addressing abiotic stress to uncover novel and complementary avenues to increase cold and heat tolerance as well as frost resistance of crops	
89,360	"Symbionomics" for sustainable crop production: fixated on nitrogen fixation
240,000	Programming gene expression networks for enhancement of sustainable crop production
164,640	Unravelling low temperature adaptation through comparative genomics strategies in the Brassicaceae
135,320	DNA-marker technologies to maximize contributions of forage legumes to sustainable agriculture

Addressing quality attributes in cereals (wheat, oat, triticale), oilseeds (Brassica, Arabidopsis) and Legumes (soybeans, pulses) to decipher the genes that control seed development, carbon partitioning, protein quality, starch quality, and the accumulation of anti-nutritional compounds	
39,200	Functional genomics of soybean seed proteins: reducing allergens, identification of beneficial proteins
32,800	Genomic investigation of cadmium accumulation in soybean seeds
67,200	Genetic and epigenetic mechanisms controlling the expression of seed maturation genes in soybean and Arabidopsis
79,960	Managing crop reproduction
64,000	Wheat retroelements and insertion site based polymorphisms
99,224	Transcript profiling of S-methyl-cysteine biosynthesis in developing seeds of common bean (*Phaseolus vulgaris*)
39,800	Transcriptome and proteome analyses of triticale reproductive tissues
Platform technologies to enable present or future research and development in plant agriculture	
253,066	Platform for producing industrial proteins and improved feed
69,120	Validation and application of candidate genes and marker-trait associations in oat
63,200	Next-generation genomics for oat improvement
215,000	Associative expression and systems analysis of complex traits in oilseed rape / canola
160,000	DNA recombination biology and applications for developing next generation crops
ENVIRONMENT CANADA	
15,942	Characterization and sequencing of avian influenza viruses from birds in Newfoundland: focus on the 2011 H1 outbreak in common Murres
42,921	Use of shotgun proteomics to assess fish health at the Thunder Bay Area of Concern
24,526	Molecular ecology and evolution of *Pasturella multocida* strains isolated from large-scale avian cholera outbreaks across Canada
49,053	Avian Toxicogenomics – new tools for hazard assessment programs
85,842	Using gene expression analysis and the amphibian toxicity test system to evaluate genotoxicity of environmental contaminants in aquatic wildlife
67,447	Effects of contaminants on aquatic microbial diversity as indicated by expression profiling and proteomic analysis
30,658	Development of genomic tools to evaluate impacts of emerging contaminants on the gene expression of aquatic organisms
24,526	Towards metagenomic characterization of microbial water quality in Canadian aquatic ecosystems
73,375	Development and validation of a crustacean microarray and correlation of gene expression profiles with traditional toxicological end-points for contaminant exposure
122,632	Continuation on the development of denaturing gradient gel electrophoresis and clonal restriction fragment length polymorphisms for the characterization of microbial consortia and communities
60,089	Identification of pathogenic larval parasites in fish and amphibians through DNA barcoding
40,468	Application of DNA genotyping to assessment of priority wildlife populations
93,404	Application of aquatic toxicogenomic tools for risk assessment of aquatic contaminant impacts on early life stage of fish and amphibians
23,300	Quantifying the consumption of Fraser River sockeye salmon by Rhinoceros Auklets using genetic markers and fatty acid profiles
26,673	An assessment of the feasibility of using functional markers to distinguish between sub-arctic and temperate-breeding Canada Geese
18,395	Genetic of Lyngbya wollei and toxin production
88,295	Aquatic toxicogenomics of emerging substances
5,949	Genetic characterization of the western chorus frog (*Pseudacris triseriata*)
20,000	Development of report “Environmental Genomics at Environment Canada”

FISHERIES AND OCEANS CANADA	
60,000	Stock delineation of redfish (*Sebastes mentella*) based on genetic analyses of archived otoliths
139,000	Rapid SNP discovery and genetic mapping using next-generation RAD sequencing: fostering the tools and expertise for genomic based management in model and non-model marine organisms
134,000	Development of molecular genetic markers for investigations into climate induced selection and usage in genetic mixed stock analysis of Atlantic salmon in the Northwest Atlantic
26,000	A genomic and telemetric approach to measure Atlantic cod population structure, and its application to Marine Protected Area effectiveness
154,000	Genomic characterization of physiologically compromised wild salmon
83,000	Identification and characterization of infectious hematopoietic necrosis virus (IHNV) carrier state in sockeye salmon using genomic tools
145,000	Arctic fish genomics as 'sentinels' of ecosystem integrity and change
50,000	Low pathogenic infectious salmon anemia virus (ISAV) variant in vivo: a comparative genomic study

HEALTH CANADA	
200,000	Genomic characterization of clinically important foodborne isolates of *Campylobacter* and *Listeria* impacting public health
234,000	Immunotoxicogenomics and food allergy: developing a genomics assay to assess chemical food contaminants that modulate pathways leading to food allergy
226,000	Genomic characterization of tissues from P53+/- transgenic mice exposed to genotoxic and non-genotoxic carcinogens for developing short term cancer bioassays
326,000	Genomic analysis of mesenchymal stem cells to develop high throughput diagnostics for measuring the medicinal ingredient and tumourigenic contaminants in stem cell based health products
453,000	Integrating genomics endpoints into regulatory toxicology
264,000	Toxicogenomics for mixture toxicology: genomics-guided proteomic approach to identifying biomarkers of exposure and effect for carcinogenic complex mixtures in the environment

NATIONAL RESEARCH COUNCIL CANADA	
2,424,016	Next generation canola: meeting environmental challenges
168,048	Photonic wire sensors and instrumentation for bacterial identification and food pathogen detection
2,597,680	Developing protein-based therapeutics targeting key mechanisms underlying tumour invasion and treatment resistance
50,000	Proteomics platform support
50,000	Microarray platform support
192,320	Coordination Office

NATURAL RESOURCES CANADA	
270,000	Applied genomics for tree breeding and forest health
210,000	Spruce budworm eco-genomics: from population dynamics to population suppression
236,500	Genomics-enhanced next generation forest disease diagnostic and monitoring
30,000	Development of a method to detect mRNA by reverse transcription loop mediated isothermal amplification as an indicator of viability of pinewood nematode in wood products
184,000	Genomics of tree-microbe interactions
210,000	H*Ap*lnomics: host, *Agrilus planipennis* integrative genomics
54,500	Bioinformatics platform

	PUBLIC HEALTH AGENCY OF CANADA
86,000	The modifying effect of genetic polymorphisms involved in folate and B12 metabolism on the relationship between folate/B12 intake and vitamin status
100,000	Prospect for proteomic biomarkers of inflammation to predict early risk of type II diabetes and to monitor response to nutritional intervention by vitamin D
99,672	New technology for HIV drug resistance testing – a model for integrating next generation sequencing and data analysis
88,750	Identification of targets to monitor the dissemination of carbapenem-resistance genes in enterobacteriaceae
150,000	The association of vitamin D insufficiency and related genetic variants with tuberculosis infection and disease in a Canadian cohort
200,000	Uncovering the signatures of *Mycobacterium tuberculosis* specific immune responses to distinguish active versus latent tuberculosis infection
74,287	Genomic and proteomic profiling in *in vitro* and *in vivo* models of Filovirus infection
120,000	Molecular characterization of *Salmonella* Enteritidis for surveillance and control of foodborne illness
88,000	Improving the accuracy of automated prokaryotic genome annotation
250,000	A rapid geno-serotyping tool for the classification of *Salmonella* serovars
300,000	High-throughput genomics and proteomics for public health molecular epidemiology: next generation laboratory workflow for the investigation and response to food and waterborne bacterial outbreaks and endemic disease
220,000	Application of comparative genomics to the identification of shiga-toxin producing *Escherichia coli* subgroups and pan-genomic markers frequently associated with human disease

APPENDIX A

Annex 2 – Quantitative Indicators for Performance Measurement

Research and Technical Personnel

Research and technical personnel by department/agency expressed in terms of number of persons engaged in projects funded by the GRDI. It includes everyone who worked on the project, including but not exclusive of personnel financed through GRDI funds.

								NUMBER OF PERSONS
Research and Technical Personnel	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	**Total**
Research scientists	59	11	20	17	40	14	32	**193**
Research professionals	0	8	12	19	14	15	13	**81**
Research technicians	79	12	17	11	64	17	7	**207**
Post-doctoral fellows	19	0	6	3	22	13	2	**63**
Graduate students	30	1	18	5	8	5	2	**69**
Undergraduate students	16	0	7	5	0	10	5	**43**
Administrative officers	0	0	1	0	4	0	0	**5**
Total	**203**	**32**	**81**	**60**	**162**	**74**	**61**	**661**
Total FTEs	**76.8**	**24**	**56**	**46.6**	**84.3**	**38.6**	**21**	**347.3**

Collaborations

Collaborations by department/agency, expressed in terms of number of research collaborators. Research collaborators are considered to be collaborators from an organization that is different from that of the project's lead scientist, and who are directly involved in the delivery of the project. The GRDI involves many research collaborative relationships among government-based science organizations, universities, industry, and other research institutes, both nationally and internationally.

	NUMBER OF COLLABORATORS							
Organization type	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	**Total**
Universities (Canadian)	23	6	30	8	5	7	12	**91**
Universities (international)	22	0	0	3	4	6	0	**35**
Other international research organizations	22	6	2	3	6	4	2	**45**
Other Canadian research institutions	3	1	0	0	2	2	3	**11**
Private sector	5	3	2	3	12	0	2	**27**
Other government departments (OGDs)	8	3	9	4	5	1	13	**43**
Other public sector organizations such as provinces and municipalities and NGOs	0	5	5	0	0	2	20	**32**
Participation in national or international genomics-related committees	3	0	0	1	1	0	0	**5**
National or international genomics research peer review committees served on	13	0	0	0	0	0	0	**13**
Total	**99**	**24**	**48**	**22**	**35**	**22**	**52**	**302**

Scientific Contributions by Department

Scientific contributions include scientific information and publications produced in 2011-2012, accepted, in press, or published, including online. They include contributions from any of the project team member as long as they are related to the GRDI project. They also include contributions deriving from a previous phase of the project, if produced in the fiscal year being reported on. They do not include submitted papers or publications in draft form. They do not include contributions that were reported in previous years.

NUMBER OF R&D OUTPUTS								
	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	Total
Publications in refereed journals	61	8	45	6	33	28	9	**190**
Publications in refereed conference proceedings	4	0	1	3	17	2	2	**29**
Technical reports	7	9	2	0	2	0	2	**22**
Books (edited, written)	1	0	1	0	2	0	0	**4**
Other publications (ex. book chapters, monographs, abstracts, notes, etc. industry magazines)	26	1	5	0	1	15	1	**49**
Poster presentations at conferences	29	5	15	15	-*	23	8	**95**
Invited presentations	16	10	19	8	34	21	5	**113**
National conference presentations	16	1	11	0	-*	14	2	**44**
International conference presentations	17	8	16	9	-*	8	6	**64**
Active participations in national conferences (organizer, chair, panel discussion etc.)	11	0	2	0	2	4	1	**20**
Active participations in international conferences (organizer, chair, panel etc.)	2	0	6	1	0	1	2	**12**
Editorial posts for national and international journals (excludes peer reviewers)	11	0	3	0	-*	6	2	**22**
Deposits in genomics related databases or libraries	11	7	6	0	0	16	17	**57**
New genomics related databases or libraries	0	0	0	0	0	1	1	**2**
Awards, prizes	1	0	14	1	1	1	0	**18**
Total	**213**	**49**	**146**	**43**	**92**	**140**	**58**	**741**

* Information not collected

Communications Products

NUMBER OF COMMUNICATIONS PRODUCTS								
	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	Total
Media interviews	-*	0	0	0	0	4	0	**4**
Press releases and announcements	1	0	0	0	3	1	0	**5**
Newspaper and magazine articles	2	0	0	0	1	3	0	**6**
Community presentations	0	6	0	3	0	1	0	**10**
Brochures, fact sheets, web pages	1	1	1	0	2	1	2	**8**
Total	**4**	**7**	**1**	**3**	**6**	**10**	**2**	**33**

* Information not collected

Knowledge/Technology Transfer

	NUMBER OF KNOWLEDGE/TECHNOLOGY TRANSFERS							
	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	**Total**
Outreach activities	1	5	6	0	0	0	9	**21**
Material transfer agreements	2	0	0	0	3	1	0	**6**
Transfer of standard operating procedures	0	1	0	0	-*	0	3	**4**
Disclosures	0	0	0	0	2	0	0	**2**
Active patents, patent applications, patents issued	1	0	0	1	11	0	0	**13**
Licenses issued	0	0	0	0	1	0	0	**1**
New formal collaborative agreements / standard operating protocols	11	0	0	0	4	1	0	**16**
Knowledge transfer workshops with stakeholders/end-users	6	1	0	0	-*	0	1	**8**
Requests for research results, papers, collaborations	-*	7	0	0	-*	10	2	**19**
Total	**21**	**14**	**6**	**1**	**21**	**12**	**15**	**90**

* Information not collected

Research Tools and Processes

Research tools and processes include those produced in 2011-2012, deriving from previous phases of the GRDI if produced in 2011-2012, as well as produced in previous years if they have been improved since last reported on.

	NUMBER OF RESEARCH TOOLS AND PROCESSES							
	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	**Total**
Research tools	19	3	10	4	4	9	4	**50**
Research processes	15	1	2	0	4	4	2	**28**
Total	**34**	**4**	**12**	**1**	**8**	**13**	**6**	**78**

APPENDIX A

Annex 3 - Highlights of Achieved Results

Commercially relevant advances in areas of genomics R&D related to human health

Developing protein-based therapeutics targeting key mechanisms underlying tumour invasion and treatment resistance

Research at NRC has focused on the discovery and development of protein-based therapeutic candidates targeting key mechanisms underlying tumor metastasis and therapeutic resistance, pushing NRC's technology platforms to remain at the leading edge of their fields. Protein-based therapeutic candidates were prioritized by assessing their correlation with the aggressive mesenchymal phenotype of tumor cells, and by testing their ability to reverse this phenotype, thereby resensitizing tumor cells to chemotherapeutics. Network biology was applied to select new tumor targets, and protein engineering approaches were used to optimize priority protein-based therapeutic candidates and transfer them to industry.

A discovery by researchers with NRC is playing a key part in what may prove to be a new and more effective way to treat one of the most serious types of cancer. A new drug candidate being developed by Helix BioPharma is based on a lung cancer antibody discovered at NRC. It has been performing as hoped in both laboratory and animal testing, and has recently been approved for Phase I Clinical trials – to ensure it is safe for humans – in patients with advanced lung cancer.

Antibodies discovered as part of NRC cancer research have been licensed by the Montreal-based company Alethia Biotherapeutics. The company is conducting pre-clinical trials with these antibodies as potential new treatments for a number of cancers. A US patent was issued in November 2011, entitled "Methods and compositions for modulating tumor cell activity", whose inventors are NRC personnel.

In 2010, NRC had provided crucial experimental validation for an innovative technological platform from an emerging Canadian company. This led the company to secure the multi-million financing required to move ahead, and sign a collaborative deal with a large pharmaceutical partner for the development of novel antibody therapeutic candidates. This enabled the company to engage in a far larger collaboration with NRC to further advance a number of their technologies and products.

Using the Multiple Survival Screening algorithm developed at the NRC, a robust set of predictive markers were identified that can accurately identify breast cancer patients who will not respond to treatment with paclitaxel. These novel markers constitute a powerful tool to help physicians to select alternate chemotherapeutic agents, thereby optimizing treatment early. Negotiations are ongoing with two Canadian companies to commercialize this technology.

Using genomics to improve the value of cereal, canola and legume crops

Next generation canola: meeting environmental challenges

Scientists at NRC focused on understanding and improving the growth performance of Canada's major oilseed crop, canola (*Brassica napus*), when water and nutrients are limiting. Major canola-growing regions in Canada suffer from chronic soil moisture deficiencies that prevent the crop from approaching optimal yields, and high costs of fertilizers to growers have created a market demand for increased nutrient use efficiency. Drought stress protocols have been developed to compare the drought tolerance of three Brassica species (*B. napus*, *B. juncea* and *B. tournefortii*). The expression of the Brassica transcripts was analyzed and many drought response genes were identified. Once validated, these will greatly enrich Brassica genomic resource for next generation canola breeding. Signaling of a specific gene, TOR (target of rapamycin), is an important component of nutrition and energy sensing in plants. Molecular and functional understanding of this signaling may lead to development of new molecular tools and strategies relevant to improving water utilization and crop performance. Transgenic *B. napus* and Arabidopsis lines were produced with TOR expression constructs and these lines are currently tested in greenhouse conditions. In low potential field environment these lines showed

more “nitrogen” and seed protein compared to wild type suggesting some functions in nitrogen assimilation under partly simulated challenging conditions. Scientists at NRC focused on selected genes that could have an important biological role in nitrogen use efficiency in *B. napus*. These genes were cloned and vectors were used to transform *B. napus*. The plants are currently being harvested and analyzed for single copy insertion and the effects of transgenes on nitrogen use.

The team has nearly completed the public data acquisition and analysis task for the construction of a genome-scale network of gene-gene-trait map (CanolaNet). It has also acquired 40 *Arabidopsis thaliana* gene expression datasets under various abiotic stress conditions from public databases; using a recently developed software, the team identified *A. thaliana* abiotic stress responsive genes and genetic pathways, and has incorporated the results into the newly developed Arabidopsis Stress Knowledge Base.

Canadian scientists have helped sequence part of the genome of canola. Results from this international collaboration were published in the August 2011 edition of the peer-reviewed science journal, *Nature Genetics*. Determining the DNA sequence of crops allows researchers to understand the mechanisms of the plant, and to map traits of interest. This information can then be used by breeders to develop crops for Canadian farmers that are more disease resistant, drought tolerant, location-suitable and with increased yields. Scientists from NRC and AAFC contributed to an international consortium that has sequenced the genome of *Brassica rapa* (*B. rapa*), and have developed a 60k Infinium array that will be available for the global research community in June 2012.

Successful research collaboration continues with Valent Biosciences to identify an important novel plant growth regulator. The team has screened in excess of 240 compounds using an NRC assay and has identified a number of interesting target compounds related to accelerated rates of growth and possibly improved seed oil levels.

Agrisoma Biosciences, in collaboration with NRC and other partners, has flight-tested jet fuel derived from the new oilseed crop *B. carinata*. Agrisoma is employing gene technology discovered as part of the NRC canola research for their second generation industrial oilseed crops.

Crop adaptation to biotic stress

At AAFC, three projects focused on the fungus *Fusarium graminearum*, an organism that infects wheat plants and constitutes one of the major problems in wheat crops grown in temperate climates worldwide. A fourth project was the first to use yeast genome heterozygous deletion arrays to screen against Fusarium mycotoxin. The characterization of candidate plant genes for Fusarium resistance or susceptibility is well underway, and significant progress has been made towards characterizing the genes involved in mycotoxin biosynthesis, regulation and pathogenicity. Understanding the molecular mechanisms exploited by the pathogen to overcome the plant’s defenses can be used to develop novel strategies for resistance. An alternative way to enhance host resistance to a pathogen is to induce the plant defense mechanisms by treatment with a disarmed strain of *F. graminearum*, a process called ‘priming’. A better understanding of the mechanisms of priming in wheat will allow the design of novel sustainable crop management protocols. Another genetic approach in the fight against Fusarium being explored is modification of the circadian clock. A transcription factor conferring resistance to infection by *F. graminearum* as well as potentially improving yield through modifications of leaf cell architecture was successfully transferred from Arabidopsis to wheat. It was determined that the Arabidopsis transcription factor is involved in the regulation of the circadian clock in Arabidopsis. Because over 50% of all plant genes are regulated by the circadian clock, its modification through overexpression of the transcription factor has the potential to modulate the expression of key genes involved in plant related processes including disease resistance.

GRDI investments supported four projects at AAFC to address genetic mechanisms of cereal rust diseases caused by *Puccinia* spp. Proof-of-concept for a transient assay that can be used for functional analysis of suspected rust fungus pathogenicity genes (in an indirect way since direct genetic manipulation of these fungi is not yet possible) has been completed. It was shown that the targeting of such essential fungal virulence factors using an *in planta* gene silencing approach can suppress disease development in wheat of leaf, stripe and stem rust fungi; this could include novel invasive and potentially catastrophic isolates, such as those from the Ug99 stem rust lineage.

The GRDI is supporting research at AAFC on three key soybean diseases prevalent in Canada. Root rot is caused by a fungal pathogen, *Phytophthora sojae*. Average annual yield losses in North America rest around 1M tonnes, representing a value of approximately $300M. Research has resulted in the identification of *P. sojae* virulence factors Avr5 and Avr1d that control race-cultivar specific compatibility through their interaction with soybean resistance genes. As the complexity and number of the different races of *P. sojae* continue to increase in areas of soybean production, defining *P. sojae* virulence determinants is essential for effective pathogen diagnosis and disease management. Work also continued on *Sclerotinia sclerotiorum,* the causal agent of stem rot, as well as on the Soybean Mosaic Virus, a viral pathogen for which genetic resistance is conferred by a single dominant gene, a very fragile form of resistance. Genomic studies revealed that durable resistance to this virus may be achieved through gene pyramiding.

Diseases caused by fungi and fungal-like pathogens cause substantial yield losses in crucifer crops such as canola, mustard and vegetable Brassicas (e.g broccoli, cauliflower and cabbage). *Albugo candida, Leptosphaeria maculans* and *Plasmodiophora brassicae* are causal agents of the most destructive diseases in Brassica species, referred to respectively as white rust, blackleg and clubroot. Outcomes from this research include the first draft genome reported for *A.candida*, significant progress cloning of the *L. maculans* avirulence gene AvrLepR1, and advances in the first genome sequencing of *P. brassicae*. Improved understanding of the genetics of obligate plant pathogens increases the potential for scientists to improve resistance to the diseases caused by these organisms.

Lentil production in Canada is hampered by the fungal pathogen anthracnose (*Colletotrichum truncatum*) and control of this pathogen is particularly important as it does not occur in importing countries. A lentil line with resistance to the two anthracnose races found in western Canada was generated for the first time. Subsequently, one recessive and three dominant anthracnose resistance genes were characterized. Ascochyta blight is a damaging disease of both lentil and chickpea and is caused by *Ascochyta lentis* and *Ascochyta rabiei*, respectively. The objective was to map loci conferring resistance to these diseases using molecular markers based on single sequence repeats (SSR) and single nucleotide polymorphism (SNP). The first SSR linkage map in lentil was developed, and a quantitative trait locus (QTL) for ascochyta blight resistance was identified including flanking markers useful for marker-assisted selection in breeding programs. In chickpea, the first integrated SSR linkage map with location of eight QTLs conferring ascochyta resistance was developed including markers needed for pyramiding of resistance genes in new cultivars. Several lentil and chickpea mapping populations are being developed for more precise mapping of disease resistance loci using new SNP technologies currently under development at NRC in Saskatoon.

Two projects focused on resistance to insect pests. In the area of plant defense to insects, significant progress was made towards determining novel genetic trichome lines in an Arabidopsis enhancer population developed earlier through GRDI funds. Trichomes are plant hairs that protect some plant species from insect feeding. Once their function is determined, newly identified genes have the potential to be useful in protecting canola from flea beetle and diamond back moth feeding, and could potentially also have application around the world in other crops damaged by insect species that are easily disrupted from completing specific feeding or egg laying behavior patterns. Research was also supported on control strategies for Bertha Armyworm (*Mamestra configurata*). This project considerably enhanced understanding of the interaction of host gut cells and pathogens at the molecular level, including the infection process for baculovirus strains under consideration for development as biopesicides, and increased genomic and proteomic resources for the pest.

Crop adaptation to abiotic stress

A comparative genomics approach was used to examine freezing tolerance in the Brassicaceae. Progress was made in: identifying diverse germplasm to map QTL underlying low temperature tolerance; establishing transcriptome datasets in a range of stress tolerant Brassicaceae species; identifying novel Brassicaceae genes and metabolites imparting freezing and cold stress tolerance; determining eQTL underlying enhanced freezing tolerance in an Arabidopsis mutant; and beginning to elucidate the role of polyamine and gamma-amino butyric acid metabolism in the low temperature response.

Significant insight was gained into the role of the plant genome in promoting symbiotic, nitrogen fixing associations with beneficial soil microorganisms. Improved understanding of processes that regulate nitrogen fixation has the potential to support the development of a biofertilizer strategy which will contribute to agricultural sustainability by reducing the need for industrial fertilizers to prevent nutritional stress in plants.

Scientists at AAFC showed that transposable elements are activated in wheat when plants are under stress and can cause genome changes responsible for quick adaptation, a phenomenon that may become increasingly important given climate change. Active transposable elements are an excellent source of highly polymorphic markers and are responsible for the creation of genetic variability, the basis for plant breeding.

Research into the molecular basis of both abiotic and stress tolerance in forage crops such as alfalfa and red clover has produced knowledge that can be used to enhance cold and salinity tolerance, and Phytophthora resistance in these species. The research has shown, for example that breeding for freezing tolerance can be effective based on cold-induced molecular changes in the parents. Forage production is an important tool in sustainable agriculture systems

Quality attributes in cereals (wheat, oats, triticale), oilseeds (Brassica, Arabidopsis) and legumes (soybeans, pulses) including seed development and metabolism

Advances were made towards the production of fertility management systems in members of the Triticeae and more specifically for the development of triticale as a bio-industrial platform. The Affymetrix GeneChip® Wheat Genome Array was used to gather high throughput data on the genes expressed in triticale reproductive tissues. A database of tissue-specific and tissue-enriched genes was assembled. The microarray analyses were supplemented by more than 2.5 million high quality whole transcriptome shotgun sequences; this knowledge arguably represents the most comprehensive transcriptome profiling resource worldwide within the Triticeae. In addition, the conditions for extracting the total triticale stigma proteins were tested and optimized, and a reference two-dimensional polyacrylamide gel electrophoresis map of the triticale stigma proteome was generated and is being analysed. Studies are also underway to investigate genetic mechanisms behind pollen heat tolerance using Arabidopsis.

A high density microarray platform was developed to study gene expression in common bean. The microarray was used to profile gene expression in developing seed between two genotypes of common bean which differ in composition of seed storage proteins and concentration of essential sulphur amino acids. A global activation of sulphur metabolic genes was identified. The results provide candidate genes for alternative strategies to improve concentration of essential sulphur amino acids and protein quality in common bean.

A study of the genetic and epigenetic mechanisms controlling the expression of seed maturation genes in soybean and Arabidopsis revealed the involvement of microRNA in controlling seed genes and that a polycomb protein is key in repressing seed genes, suggesting functional diversification of polycomb proteins in plants.

Soybeans grown in certain Canadian environments accumulate cadmium in their seeds to a level above international standards, constituting both a health risk to humans and a barrier to export markets. Low accumulating germplasm exists but converting all Canadian lines to low cadmium accumulation could be a lengthy process, especially since the measurement of cadmium concentration is expensive. This project investigated the genetics of low cadmium accumulation with the long term objectives of identifying the genes responsible, understanding the biological mechanism(s) and identifying molecular markers linked to those genes that could facilitate breeding of low cadmium accumulating varieties. Two

candidate genes are under investigation, in an effort to identify the exact gene and biological mechanism responsible and also to develop extremely efficient markers. DNA sequencing of the candidate genes from multiple high and low cadmium lines is testing the correlation between the alleles at these two loci and the low cadmium accumulating phenotype.

Crop platform technologies

Developing low cost systems for producing clean commercial proteins in plants has many advantages over traditional systems such as microbial fermentation or cell culture and will stimulate a broad spectrum of novel industrial applications. Proof-of-concept of seed protein depletion (Empty Seed) for developing a seed protein production platform was established. Universal technologies to selectively repress the expression of seed storage protein genes and to target heterologous proteins to seed protein storage vacuoles were developed, as were plant lines expressing human growth hormone and human serum albumin.

An international project on associative expression and systems analysis of complex traits in oilseed rape/canola (the ASSYST consortium) involving collaboration with NRC and with groups in Germany, and the United Kingdom led to establishment of a large, genetically and geographically diverse collection of germplasm and SNP array resources that are being applied in multiple projects to examine genotypic and phenotypic diversity, and traits such as nutritional and antinutritional seed compounds. Considerable added value was realized within the consortium particularly in terms of the combination of highly complementary expertise on breeding, genome sequencing, gene expression, metabolomics, quantitative genetics and bioinformatics.

An unprecedented amount of new genomic sequence information has been developed for oats. Detailed knowledge of oat genomic DNA and allelic variability in 25 key oat varieties was gained, robust marker-trait associations for use in oat variety improvement were validated, expertise and training in high throughput sequence analysis were developed, and a new bacterial artificial chromosome library in oat was established. The results from this project were also used as a foundation for building a large North American Collaborative Oat Research Enterprise (CORE) involving AAFC, the United States Department of Agriculture, growers, private industry and universities, worth $1.65M over three years.

The epiphytic microbiota associated with crop seeds can exert dramatic effects on crop yields, either through antagonistic effects on pathogens or by potentiating disease. Metagenomic approaches have the potential to identify new pathogens and to provide critical data on the connection of microbial communities to health and disease. Scientists at AAFC have developed molecular tools that enable the metagenomic analysis of microbial communities by traditional and next-generation sequencing technologies, the quantification of specific microorganisms of interest by quantitative PCR, and the simultaneous detection of many microorganisms in a single sample by bead-based multiplexing techniques. Through the use of specific algorithms and software, biologically valid Operational Taxonomic Units (OTU) can be computationally assembled directly from DNA sequencing data, and completely unknown novel organisms can be worked with, thereby deriving specific, sequence-based markers. By assembling OTU de novo it is possible to detect the signature of an unknown organism in the context of a disease and have the assembled sequence available for development of diagnostics specific to that organism all without the need for a related organism to be present in a reference database. In addition, by evaluating the abundances of OTU from a community, it is possible to track changes in a microbiome in a computationally similar way to how microarrays have enabled the study of gene expression at a whole genome level. This work will result in a generalized platform for tracking plant diseases through the seed microbiota and may lead to the identification of novel biocontrol agents and the development of molecular assays for a wide range of organisms inhabiting Canadian seeds.

DNA recombination and repair are fundamental biological processes responsible for maintaining the fidelity of genomes as well as evolution of organisms through controlling mutation rates and genetic exchange in vegetative cells and during meiosis. These processes directly influence the efficiency of plant breeding since they affect recombination frequency and the integration of DNA cassettes into the genomes of vegetative cells. Novel discoveries were made including proof-of-concept for increasing and decreasing recombination frequency through engineering altered biochemical activity of key enzymes in the recombination pathway and through

chemical treatment of plant tissues. Several members of protein complexes that facilitate sensing and repair of DNA damage were identified.

Genomics knowledge and advice for the management of fisheries and oceans

For Phase V of the GRDI, DFO initiated eight new genomics research projects to: increase understanding of the impacts of fisheries and/or potential for climate based selection on the population genetics and structure of Redfish, Atlantic cod, Atlantic salmon and Arctic fish; develop new genetic markers using next generation sequencing for the genomics-based management of aquatic resources; evaluate the immune response of salmon to HPRO non-pathogenic infectious salmon anemia virus (ISAV) and subsequent exposures to pathogenic strains; and characterize the genomics of infectious hematopoietic necrosis virus (IHNV) carrier state in Sockeye salmon and physiologically compromised Pacific salmon. Seven of the eight projects met the majority of their research milestones and are on-track to achieve their intended results; the objectives of one project were modified in response to unanticipated sampling problems.

For Phase IV of the GRDI, examples of the emerging results and outcomes of DFO's genomics research projects including the following studies:

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

Redfish is an important commercial species, with landings worth over $27 Million making it the fourth most valuable Canadian groundfish fishery in 2010. Research results contributed significant information to the "Assessment of redfish stocks (*Sebastes fasciatus* and *S. mentella*) in Units 1 and 2 in 2009" (DFO Can. Sci. Advis. Sec. Sci. Advis. Rep. 2010/037), (i) confirming the redfish stock structure described with contemporary samples, (ii) demonstrating that stock structure is stable through time, and (iii) confirming the recruitment failure of historic strong year-classes in Units 1 and 2. Results informed the Committee on the Status of Endangered Wildlife in Canada's (COSEWIC) evaluation of redfish population using designatable units, and facilitated the establishment of the first industry-led monitoring program for the identification of redfish species in the commercial fishery. Genomics knowledge generated by this study may also influence further changes to the management of redfish fisheries.

Genetic variability in wild populations of chars in the Arctic

Dolly Varden fisheries form a significant portion of DFO's responsibilities for fishery co-management, conservation, and habitat management activities. Research results contributed to the Integrated Fisheries Management Plan (2009-2014) developed by DFO and its co-management partners and to a Stock Advisory Report for Big Fish Dolly Varden (2012). Advice to fisheries co-management partners (Inuvialuit and Gwich'in) has provided key information for sustainable fishing management policies regarding the source stock and mixed-stock Dolly Varden fisheries, with results integrated into harvest level decisions for the 2012 subsistence harvest. Genetic assignment of catch composition to stock-of-origin has altered fishery management practices with respect to individual populations of Dolly Varden, with findings considered in decision-making to re-open fisheries that have been closed for >10 years. Co-management partners have supported genetics analysis and coastal fishery monitoring programs for an additional two years to examine temporal stability of these fisheries.

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

Preliminary project results indicate that non-neutral MHC variation may be lost at a greater rate in completely captive groups of Atlantic Salmon relative to counterparts maintained for part of their life cycle in wild-native-river habitat. Results were provided to DFO's Population Ecology Division and Live Gene Bank managers and are contributing to modifications of management strategies for endangered inner Bay of Fundy Atlantic Salmon, including: a) increasing the duration of wild-exposure of early juvenile salmon; b) adjusting several specific operations so that the number of adults exposed to natural selection as juveniles that are available at spawning time is increased, and c) changing spawner selection criteria to increase the weight given to wild exposure of broodstock relative to Mean Kinship values.

Immune function of salmon and disease resistance against infectious salmon anemia virus (ISAV) - Phase 2

While avirulent ISAV, known as HPR0, can be detected by molecular methods such as PCR, it is unclear how fish infected with the avirulent strain should be managed. Researchers determined that fish that were exposed to and survived an infection by HPR0 are much more resistant to future infections by high virulence strains, indicating a form or acquired immunity. Gene expression patterns in the head kidney are dependent on the viral load in that organ, but the viral load in the head kidneys of "resistant" fish rises much more slowly than in naïve fish; this suggests that the salmon immune system blocks viral entry into the head kidneys of immune fish, at least in the early stages of the infection. Research results were discussed with Canadian Food Inspection Agency National Aquatic Animal Health Program officers to inform a disease response plan.

Genomics of migratory fitness in wild salmon

Research determined that return migrating salmon were conditionally compromised before entering the Fraser River to spawn, and that a single genomic signature was predictive of premature mortality in the river. Genomic research identified a novel salmon parvovirus emanating from freshwater and carried by multiple life-history stages of sockeye salmon, with highest loads in the early marine environment. A novel high-throughput genomics approach lea to the discovery of sequences of variant of orthomyxovirus with high homology to ISAV present in BC salmon. Retrospective analysis of previous microarray studies revealed a genomic response associated with salmon positive for the British Columbia ISAV variant. The project notably contributed knowledge to technical reports commissioned by the Cohen Inquiry on the role of diseases and parasites (Kent report) and salmon farms (Dill and Noakes reports), and to the "Synthesis of evidence from a workshop on the decline of Fraser River sockeye salmon" (Peterman) from a DFO/Pacific Salmon Commission workshop.

Aquatic Biotechnology Lab – Bedford Institute of Oceanography

The maintenance of the existing capacity in the Aquatic Biotechnology Lab (ABL) allowed several projects to be successfully undertaken by the ABL in GRDI Phase IV. These projects were funded by both GRDI and other funding sources. Forensic genetics analysis results were provided to Conservation and Protection Fisheries Officers for two cases (one in Maritimes Region and one in Newfoundland and Labrador Region). One case involving the seizure of Atlantic salmon from a fish vessel boat resulted in a guilty plea from the suspects, a $6000 fine and the avoidance of a full trial prosecution; DNA evidence significantly influenced the suspects' plea.

Genomic knowledge for the Canadian health regulatory system

Genomic assessment of chemical food contaminants leading to food allergy

A cell culture assay was successfully developed to measure the effects of chemical contaminants on immune pathways related to food allergy. The assay was used to test two different carbon-based nanomaterials that may contaminate foods. The results indicate that one of the nanomaterials alters immune cell responses. Using high-throughput plate-based PCR arrays, immune cells treated with nanomaterials are now being subjected to genomic analyses to link changes in immune function with changes in gene expression. Immune cells have also been prepared for proteomic analyses using mass spectrometry techniques to determine changes in expressed protein levels and levels of proteins that have been post-translationally altered; methods for protein extraction, purification and analyses are currently in progress. This research will contribute to the search for the underlying causes behind the increasing incidence of allergic disease and allow government regulators to identify chemicals that may contribute to this problem.

Development of short term cancer bioassays using transgenic mice exposed to carcinogens

Supplies relating to miRNA PCR arrays and PCR arrays have been obtained and preliminary experiments are underway with test rodent samples to establish Standard Operating Protocols. The isolation of miRNA is underway from control samples and from kidney samples from mice treated with the carcinogenic mycotoxin ochratoxin, known to have acute toxicity to mammalian kidneys. Analysis data from control and ochratoxin treated mice from microarray experiments, and gene specific RT-PCR arrays has been summarized and presented at meetings and conferences. Purchase and setup of a new gel imaging system has been completed.

Genomic approach for risk-benefit analyses of stem cell based health products

Stem cells present tremendous potential to treat diseases for which there are currently no cures. Stem cells from adults are a particularly promising source as they provide a means to avoid the social and ethical issues involved with the use of embryo derived cells. However, potential risks associated with the use of adult stem cells in a health care environment must be evaluated and HC is responsible to ensure that stem cell-based health products are both safe and effective. This newly developed infrastructure has increased Health Canada's capacity for knowledge generation and will be an important driver for projects both within and outside the scope of GRDI. In 2011-2012, HC has established international and national collaborations; upgraded equipment; and provided training and education to staff. In collaboration with researchers in Spain and University of Western Ontario, quantitative proteomic methods were optimized for stem cell analysis, epigenetic changes that occur in mesenchymal stem cells as they transform into tumourigenic entities were documented, and the tumour forming capacity of 13 different mesenchymal stem cell cultures was established. The tools developed from this research are currently being utilized to study human adult stem cells with the goal of identifying biomarkers for measuring their ability to treat diabetes as well as their potential to form cancerous tumours.

Integrating genomics endpoints into regulatory toxicology

Cell- and animal-based tests using global transcriptional profiling of RNA are being developed to derive toxicogenomic signatures that predict specific modes of action of environmental contaminants and disease onset. The research utilizes chemicals that exert well-known health effects and molecular changes to establish predictive expression signatures anchored against the phenotypic changes (e.g., genetic damage, cancer, hormone alterations). The research is primarily designed to develop new toxicology methods that can be used by government regulators to test individual chemicals on a case-by-case basis, develop modes of action and adverse outcome pathways, and facilitate chemical categorization to reduce health impacts of environmental pollutants. Scientists at HC demonstrated the feasibility of using a cell culture assay to screen for the potential of chemicals to cause DNA damage and mutation, and to identify the primary mechanisms involved. This work is part of an international consortium that includes government, academic and industrial partners to develop new/improved regulatory toxicology methods that will advance toxicological risk assessment through collaborative harmonized efforts. Pilot experiments have demonstrated that archival tissues available from two-year cancer bioassays may be useful for the study of gene expression. Once protocols are optimized, these tissues may be used to explore whether genomics endpoints can be used in shorter-term (e.g., one or two month) experiments to predict cancer at the 2-year time point. The development of predictive signatures for various toxicities will be explored in the upcoming fiscal years. Six chemicals selected from the panel of chemicals tested in the US EPA's ToxCast cell-based testing program have been screened in rats. Liver samples from these tests have been to determine at the genomic level if the predicted molecular pathway perturbations are observed. This work will provide validating support to the ToxCast approach and identify potential inconsistencies.

Proteomic approach to identify biomarkers of exposure and effect of complex mixtures in the environment

Scientists at HC use *in vivo* animal exposures and 'omics' tools to characterize and compare changes in gene expression elicited by coal tar extract (a carcinogenic complex mixture abundantly present in the environment), select chemical fractions of coal tar extract and individual polycyclic aromatic hydrocarbons contained in the coal tar, to identify biomarkers of exposure and adverse effects. In 2011-2012, HC acquired crude coal tar from the Electrical Power Research Institute (USA) and from CanmetENERGY (NRCan), prepared purified coal tar extract and analyzed its chemical composition, and completed a dose-range finding study to determine the actual experimental doses of coal tar. Collection of biological samples and gene expression profiling of various tissues from mice exposed to individual polycyclic aromatic hydrocarbons were completed. Preliminary results indicate that the various chemicals contained in the mixture act via different mechanisms of action impacting multiple biological pathways, which will complicate the quantitative risk assessments of such complex mixtures.

Genomics knowledge to strengthen Public Health programs and activities related to infectious and chronic disease

Photonic wire sensors and instrumentation for food pathogen identification

Scientists from NRC work to produce a highly multiplexed instrument that reads a single photonic wire evanescent field (PWEF) microarray chip with more than one hundred sensors. The overall goal is develop a compact, storable chip that will shorten and simplify the protocol for pathogen detection identification, and also explore the use of the sensors in complex samples so that the sample purification and concentration process can be streamlined. A new silicon biochip has been developed that can reveal hidden disease causing microorganisms by testing for the presence up to 128 independent molecular markers that act as a fingerprint for the presence and type of microorganism. Software has been developed and tested to collect and analyze the sensor outputs from 128 different sensors on a 128 microarray sensor chip. The reader instrument and software were able to extract signals from 128 sensors simultaneously and in real time, and display (on screen) any desired subset of sensor response curves. The biochip and reader system are self-contained and computer automated, and can be deployed in permanent or field lab settings. This is driven by a marketplace pull for highly multiplexed instruments for drug screening and proteomics.

The NRC team collaborates with the CFIA and the National Microbiology Laboratory of PHAC to make PWEF sensor array chips for detecting and serotyping bacteria strains. Serotyping tests have been repeated several times using 16 sensor array chips functionalized with antibodies for different *E. coli* serotypes and showed a clearly specific capture response. Capture and identification were confirmed when only the *O157* sensors responded positively to secondary antibody amplification with *O157* antibodies in free solution. Specificity to *O157* was much better than a factor of ten (response of *O157* sensors relative to sensors targeting other serotypes) in both the initial capture step and the subsequent antibody amplification steps. Similar results were obtained using samples containing *O55 E. coli* bacteria. Work has begun on dilution studies to determine the sensitivity of the bacteria assays. The experiments described above used sample containing 10^8 (10 million) colony forming units (CFU) per ml; a rather high bacteria concentration used to facilitate preliminary assay development. In more recent measurements the team has been able to demonstrate a measurable capture response to samples containing as low as 10^4 CFU/ml (10 thousand).

The team also works with the CFIA to integrate the use of PWEF sensors with magnetic bead technology for pathogen separation from food samples, as well as the use of secondary antibody amplification methods to guarantee strain specificity in complex samples. Initial experiments demonstrated that the sensor gives a clear response when exposed to beads extracted from samples containing *E. coli.* Most importantly, the sensor registers no response to identical beads that have not been exposed to *E. coli*. This experiment is therefore the first clear demonstration that the PWEF sensor chips can be combined with paramagnetic bead based extraction of microorganisms from samples. As these are the first set of experiments, much work remains to demonstrate reproducibility, specificity to bacteria serotype, and detection limits.

Food-borne pathogens

Genomic characterization of foodborne isolates of Campylobacter *and* Listeria

Full genome sequence data obtained from strains of *Listeria* and *Campylobacter* are used to identify signature sequences associated with epidemiological (geographic, temporal, environmental or animal origin) and biological properties (ability to infect, ability to survive) of isolates. Diagnostics developed based on this information will be critical for tracking sources of harmful bacteria as they enter the Canadian food supply, as well as for early identification of strains with greater potential for severe human health impacts. Objectives were modified in light of the late transfer of funds, which were received in January 2012. Funds were allocated to the procurement of laboratory consumables, to sequencing service contracts from the BC Genome Centre and to short term technical contracts to isolate nucleic acids from target *Listeria* and *Campylobacter* isolates for sequencing. Two post-doctoral fellows were hired through the visiting fellowship program to carry out the bulk of the analyses required. Funds were obtained from the CRTI Technology Acquisition grant to purchase a Next-Generation sequencer (Illumina MiSeq), which will enhance the capacity to deliver on milestones for years 2 and 3. Publically available data were used to develop a framework for bioinformatic analyses of

whole genome data for assessing microbial typing methodology for *Campylobacter jejuni* and *C. coli*.

Development of rapid methods for molecular typing of Salmonella

Two complementary projects focus on the development of rapid methods to increase the efficiency of typing and characterization of *Salmonella* and thereby reduce the impact of outbreaks and burden of disease. The sequence data obtained from 42 *Salmonella* isolates was used to expand a *Salmonella* Geno-Serotyping Array. This updated and improved array layout is undergoing validation by the Animal Health and Veterinary Laboratories Agency in the UK, and the Austrian Institute of Technology in Austria alongside PHAC's Laboratory for Foodborne Zoonoses in Guelph. Approximately 1000 *Salmonella* isolates will be tested in the validation study to assess repeatability, sensitivity, specificity and evaluate the utility of the array as a rapid alternative to the current gold standard of serotyping. In an alternative approach, comparative genomic fingerprinting and single nucleotide polymorphism assays are being evaluated for their capacity to provide rapid, reliable and high resolution molecular subtyping of *S.* Enteritidis.

Genomic tools and methods to more accurately identify disease-associated E. coli *strains*

A Canada-wide beef recall in 2011 presented an opportunity to initiate sequencing and research directives using a "real-time" event. Notably, traditional subtyping methods indicated an underlying high degree of genetic complexity and variability from clinical and food isolates sampled during the event. With project partners including the CFIA, a sequencing panel of about 100 *E. coli* O157:H7 isolates was selected from various sources with specific focus on the recent beef recall event, and including past Canada-wide outbreaks. Historic isolates with similarity to the beef recall were chosen to provide evolutionary context and insight into genome evolution. To date, six *E. coli* O157:H7 isolates from the beef recall have been sequenced and genome assembly and sequence analysis is underway. Sample preparation is in progress for sequencing the remaining isolates. Other studies are investigating the environmental dynamics of *E. coli* strains in order to better understand the potential reservoirs of Shiga-toxin producing (STEC) *E. coli* commonly associated with human disease. More than 300 STEC strains are in the process of being sequenced. Based on preliminary analyses of these 300 STEC sequences, a second set of about 200 strains will be selected in the coming year to target host-biased clusters of strains for further genomic sequencing. Researchers at PHAC are also developing bioinformatic tools to automate the annotation of genomes and enhance the ability to determine the relatedness of different bacterial isolates.

Other Infectious Pathogens

Tuberculosis (TB) research

Relationships between the GRDI funded TB research group and other local health clinics have been built. Services to capture and follow TB and suspected TB infections in Manitobans and new immigrants have been established. A bio-repository for sample collection, handling, and storage has been set up, and 150 skin test positive samples have been examined with the current state of the art assay (the Quantiferon® TB Gold In Tube Test) to determine its utility for diagnosing TB. Results from skin test negative control samples have also been collected. Pilot studies on blood cells have indicated differences in the function of immune cells between active and latent TB infection and uninfected controls. These studies are currently being expanded to all samples. In a related project that will examine the association between vitamin D status and tuberculosis infection and disease, study samples were collected, and samples were genotyped for host genetic factors involved in vitamin D biological pathways.

Investigation of antibiotic resistance in E. coli *and* Klebsiella *bacteria*

The rapid emergence of carbapenem-resistant bacterial infections in Canada and throughout the world poses serious health concerns. To investigate the emergence and molecular epidemiology of antibiotic resistance in *E. coli* and *Klebsiella* bacteria, 50 plasmids harbouring carbapenemase genes were isolated and typed. Thirty plasmids are currently being sequenced. Six carbapenemase-producing clinical isolates of interest were selected and submitted for full genome sequence analysis.

Analysis of cellular genomic and proteomic profiles following infection by the Ebola virus

The analyses of changes in cells infected by Ebola virus has identified some general features that all viruses use to grow and reproduce and promises to shed light on some of the processes that are unique

to the Ebola virus. An *in vitro* system for the evaluation of genomic and proteomic profiles in Ebola virus infected cells has been defined. This system models targets for infection in a host animal and permits the analysis of the host cell proteome to identify infection-associated changes in protein expression. By better understanding the processes by which viruses replicate and cause disease it will be possible to design strategies for intervention in infection to improve the outcome in infected individuals and reduce the risk that highly pathogenic viruses pose to humans.

Chronic Diseases

Investigation of the effects of vitamin D on insulin resistance

To investigate the effect of vitamin D on the development of insulin resistance, PHAC researchers are building a cohort of study subjects that are pre-diabetic and also deficient in serum vitamin D. Studies in years 2 and 3 of the project will determine the expression of biomarkers associated with type 2 diabetes, and identify genomic signatures that can predict the response to vitamin D supplementation.

Genomic knowledge for forest generation and protection

Identification of genes controlling desirable attributes in economically important tree species

The genomics program at the Canadian Forest Service of NRCan 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. Association studies performed in 2011-2012 showed that 100-200 single nucleotide polymorphisms (SNPs) were significantly associated with single traits relating to early, late or total wood in spruce. Analyses showed that 20-25% of the phenotypic variation could be explained by using 40-60 SNPs. In collaboration with scientists of the Genome Canada SmarTForests project, NRCan scientists initiated work to examine the genes involved in the transcriptional regulatory pathway of wood formation. Building on the Genome Canada Arborea project, 500 progeny were genotyped and a genetic map of each parent was assembled. Genes involved in bud development and butset are also being investigated to further our understanding of genes that govern naturally occurring phenotypic variation and adaptive traits in white spruce.

Increased knowledge of genomics-based pest control and diagnostics

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. Spruce budworm is considered by many to be one of the greatest threats to our forests due to the periodic nature of its outbreaks, which can cause devastating damage and severe economic losses. Modeling their dispersal and the development of novel control options could offer forest managers new tools in the management of this pest. To that effect, moths were collected across their range in Canada and their DNA was extracted. DNA samples are being sequenced for the construction of restriction-site associated DNA libraries that will allow the rapid identification of thousands of SNPs. Transcriptomics analysis of eggs, 1st instar, and 2nd instar larvae, were initiated to elucidate the genes involved in diapause. A similar approach is being used with transcripts from pheromone glands and antennae of spruce and jack pine budworm to identify species specific genes. Investigation of 14 genes associated with antifreeze proteins also continues, and scientists are studying a gene that may enhance baculovirus amplification in budworm for the development of biological controls.

Canada's ash resources are threatened by the emerald ash borer. Three different approaches for potential control are underway at NRCan. One approach relates to the identification of genes essential in emerald ash borer development that could be used for control purposes, focusing on genes relating to moulting and hormone receptors that are essential for their survival and growth. A second approach studies the genetics of the olfactory system for development of optimal chemical lures. The final approach examines naturally occurring fungi that may be lethal to insects: to date, 102 fungal strains have been obtained and are being examined.

NRCan-CFS scientists are studying tree pathogen interactions: genes in fungi that may cause disease (pathogenicity genes) and genes in trees that may offer resistance. Research has focused on identifying and confirming these roles in specific genes. The identification of these types of genes could lead to the development of molecular markers that could be integrated into marker-assisted breeding programs.

For genomic data to be translated into DNA-based diagnostic tools, the genomic sequences of target pathogens need to be obtained. The genomes of seven fungal pathogens have been sequenced and in-depth comparative bioinformatics analyses in two species have been performed. To reconstruct the epidemiology of invasive pathogens and to understand and predict migration pathways of invasive pathogens, knowledge of population genetic patterns is important. Pathogens can evolve rapidly and develop novel adaptation that could affect their ability to infect and spread. These adaptations will leave a signature in the genomes of pathogens, and routes and patterns of migration can be inferred by these signatures. Population re-sequencing of the genomes of three targeted invasive pathogens was initiated in 2011-2012 with the acquisition of samples from a wide variety of geographic and host sources and SNP genotyping is ongoing. A list of criteria was established in consultation with plant protection agencies to initiate the establishment of a list of the Top 50 most unwanted pathogens.

Pine wood nematode is native to North America but its introduction overseas has caused devastation in pine forests. Internationally traded wood products may be subject to trade disruptions should dead nematodes be found in the wood. Accurate detection that differentiates between live and dead pine wood nematode is essential. Scientists designed and tested pine wood nematode specific primers and optimized an assay to test the stability of the target mRNA.

Investigation of bioenergy solutions via improved feedstock and/or novel enzymatic processes and associated value-added bioproducts

Key genes are being investigated in an effort to improve biofuel production efficiency, as well as to increase the quantity and quality of biomass. Using activation-tagged poplar, traits were screened which may impact bioenergy production and key traits such as biomass production, tree architecture and phenology. Wood chemistry analyses have identified poplar clones with increased capability for cellulosic ethanol production, whereas ten genes relating to cell wall formation are being investigated in an effort to facilitate biomass conversion.

Enhanced Environment Canada's applications of genomics-based tools and technologies for responsible decision-making

In 2011-2012, Environment Canada developed genomics tools and approaches for assessing the environmental risk of potentially toxic substances, identifying parasites, and tracking microbial sources. These tools will help inform environmental management decisions as well as enforcement and compliance decisions. Tools and approaches were also developed to learn more about individual species (e.g., population structure and mating behaviour), which helps support the development of wildlife conservation and management plans for species of concern. Highlights from EC's STAGE projects are described below.

Development of denaturing gradient gel electrophoresis and clonal restriction fragment length polymorphisms for the characterization of microbial consortia and communities

Screening assessment techniques are needed for microbial consortia substances on the current Domestic Substances List, as well as future newly notified consortia substances. Improvements were made by EC researchers to genomics tools to detect and identify microorganisms in a consortium containing more than one microorganism, which will allow scientists to properly screen microbial consortia for pathogens under the CEPA New Substance Notification Regulations for Living Organisms. Methods to assess microbial consortia will be reviewed by risk assessors in EC and HC, which may lead to regulations to protect the environment from pathogens.

Towards metagenomic characterization of microbial water quality in Canadian aquatic ecosystems

This EC research seeks to accelerate EC's understanding of the importance of natural microbial diversity in aquatic ecosystems serving as source water for drinking, recreation, food production, and wildlife needs. Current use of *E. coli* testing provides only a narrow window for assessing implications of changes in microbial water quality for human or animal health. In 2011-2012, progress was made in microbial

source tracking for identifying human sewage and seagull fecal contamination in Great Lakes near shore areas. Microbial source tracking results are providing valuable guidance for remediation of fecal pollution sources impacting beaches in Great Lakes Areas of Concern.

Application of DNA genotyping to assessment of priority wildlife populations

Preliminary EC research has shown that coastal river otters, among other top predators, are being exposed to high levels of industrial pollutants in the marine environment. The ecological impacts of these pollutants are not yet known, but there is concern that if coastal predator populations decline the whole ecosystem could be compromised. Research in 2011-2012 applied a multidisciplinary approach combining genetic, toxicological and hormone analyses, using the river otter as a valuable top predator sentinel species to better understand the impacts and potential implications of persistent contaminants in Victoria Harbour. This is permitting risk assessors and responsible managers to make determinations of the ongoing and future risk of residual sediment and soil contamination in the harbour, as a basis for determining the need for remedial action. Potential remedial liabilities have been estimated to be as high as $ 800 million.

Aquatic toxicogenomics of emerging substances

Assessment techniques are needed to more accurately and efficiently understand the ecosystem impacts of emerging substances associated with anthropogenic development, including municipal wastewaters, oil sands development, and the increased use of nanoparticles in applications of daily living. In 2011-2012, genome-wide effects in male fish were explored in association with municipal effluent exposure, deciphering the mechanisms by which physiological processes (such as decreased sperm functions) are affected. The toxic properties of treated and untreated municipal wastewaters to rainbow trout cells were examined for 12 cities applying different wastewater treatment processes. This EC study identified factors affecting toxicity, and highlighted treatment processes with the least toxic effects. In addition, a suite of gene targets in rainbow trout cells were developed to serve as toxicogenomic fingerprints of oil sands processing water contamination and, separately, of adverse response to silver nanoparticles.

Assessment of the feasibility of using functional markers to distinguish between sub-arctic and temperate-breeding Canada geese

Southern breeding Canada geese cause numerous conflicts and are present in growing numbers. Genomics techniques were under development by EC researchers in 2011-2012 to distinguish between different stocks of Canada geese and inform hunting regulations. If Canada geese from different populations can be reliably distinguished, harvest regulations can be refined to increase harvest (at specific locations and times) of temperate-breeding geese responsible for crop depredation and risk to air traffic, without the risk of over harvesting protected geese from northern-breeding populations.

Development and validation of a crustacean microarray and correlation of gene expression profiles with traditional toxicological end-points for contaminant exposure

More efficient and accurate methods are needed for evaluating the safety of chemical samples being considered for discharge at sea according to the CEPA 1999 Disposal at Sea Regulations. Research is ongoing at EC to characterize lobster gene expression profiles resulting from exposure to various chemicals. Information generated from this project will be integrated in the department's monitoring plans and may contribute to fisheries management activities, under the Disposal at Sea program.

Effects of contaminants on aquatic microbial diversity as indicated by expression profiling and proteomic analysis

Better understanding of the sublethal toxicity of priority substances and new existing substances in microbial communities is needed to manage overall ecosystem health. Microbial biodiversity and microbial function/activity were assessed by EC researchers in response to applied environmental stressors (such as pharmaceuticals). This provides an effective approach for detecting changes to microbial communities as a result of stressors, which, in the longer term can protect healthy ecosystem processes like nutrient cycling.

Identification of pathogenic larval parasites in fish and amphibians through DNA barcoding

In freshwater fish, many larval trematodes cause pathology and mortality or reduce product quality. The

taxonomy and life cycling of these larval parasites are poorly understood because they are morphologically indistinct, unlike their adult stages that are found in birds and mammals. Research at EC in 2011-2012 continued to link larval parasites to their adult forms, advancing a standardized genetic database on common species of parasites to include geographical representation across Canada, and elucidating important patterns in host and site specificity.

Diagnostic barcodes were developed for nearly 300 species of parasitic flatworms pathogenic in fish, amphibians, birds, and mammals, including humans. This knowledge will vastly improve diagnostic abilities and will be used to inform ecosystem health management processes in the longer term.

Establishing molecular assessment techniques for emerging infectious diseases in native amphibians: establishing PCR techniques for disease incidence and distribution assessments

Diseases of amphibians are globally recognized as being of conservation concern as they cause amphibian population declines and even species extinctions. Genomics-based techniques were used by EC researchers to assess the distribution, prevalence, strain-based virulence and transmission dynamics of two significant diseases in Canadian amphibian species. Results revealed that these diseases are widely distributed in Canada and have the ability to cause mortality in several amphibian species, providing information for ecosystem managers.

Using gene expression analyses and the amphibian toxicity test system to evaluate genotoxicity of environmental contaminants in aquatic wildlife

Better techniques are required to assess the impacts of contaminants on amphibian species. Research is ongoing at EC to study genes associated with development, growth and metamorphosis of amphibians. By measuring the levels of expression of these genes in amphibians exposed to environmental contaminants, and relating these changes in gene expression to physiological, individual and population level effects, the genotoxicity of these environmental contaminants to common model amphibian species is examined. This research will provide important information for risk assessors.

Characterization and sequencing of avian influenza viruses from birds in Newfoundland

Understanding the dynamics of avian influenza virus (AIV) in seabirds has important human health and ecosystem management ramifications. Significant progress was made in 2011-2012 by EC researchers to trace the origin and strains of the AIV in seabird colonies off the coast of Newfoundland, capturing for the first time a comprehensive set of low-pathogenicity viruses from an active outbreak in wild birds for further study and to inform future management efforts. This research on AIV in Newfoundland birds is demonstrating the importance of eastern Canada, and specifically Newfoundland, as a potential entry point of Eurasian strains of AIV into North America. Regulators across government, both in the public health, environmental and agriculture (poultry) are recognizing the potential importance of this trans-Atlantic route.

Use of shotgun proteomics to assess fish health at the Thunder Bay Area of Concern

Monitoring techniques are required to assess fish health in remediated Areas of Concern. Research in 2011-2012 assessed White Sucker in the Thunder Bay Area of Concern for health, demonstrating where white sucker health had benefited from the remediation at one site, whereas white sucker from another site were still being impacted by ongoing contaminant discharges. The study provided breakthrough methods for use in the monitoring of fish health at “Areas in Recovery” in the Great Lakes and elsewhere and will help government regulators set priorities and implement coordinated management approaches. As well, this EC research provides information on a novel genomics technique that is anticipated to be widely adopted for a wide range of applications.

Avian toxicogenomics – new tools for hazard assessment programs

Accurate and efficient methods are required to determine and predict the effects of industrial chemicals that are of high priority for environmental and human health risk assessments by Environment Canada and Health Canada. In 2011-2012, genomics tools were used to determine and predict the effects of industrial chemicals and their byproducts on

embryo birds, linking effects to contaminant levels actually detected in particular areas of the Great Lakes, and providing risk assessors with information needed to address toxicological data gaps for chemicals of concern.

Molecular ecology and evolution of Pasturella multocida *strains isolated from large-scale avian cholera outbreaks across Canada*

Avian cholera is emerging in new environments in the Canadian Arctic and east coast, causing massive outbreaks of mortality in wild migratory birds. Research at EC in 2011-2012 used genomics tools to track the source and movement of bacterial strains of cholera in migratory birds, identifying carrier strains in certain populations. Understanding the dynamics of outbreaks will be useful to ecosystem managers of Canada's northern environment, and will contribute to improved food security for Inuit First Nations communities.

Genetic characterization of the cyanobacteria Lyngbya *wollei and toxin production*

The benthic cyanobacterium Lyngbya wollei forms mats of filaments at the bottom of rivers, whose proliferation causes degradation of aesthetics and quality of drinking water (volatile organic compounds, toxins). Research at EC demonstrated that populations of invasive benthic cyanobacteria inhabiting a wide range of environmental conditions are part of the same genetic clade. Further development of the method for quantification of toxins in this species is underway to inform management and monitoring programs.

Genetic characterization of the Western Chorus Frog

The Western Chorus Frog has recently been listed as "Vulnerable" by the Province of Ontario, and federally, as "threatened under COSEWIC". In 2011-2012, genomics tools were used to begin demarcating populations of the Western Chorus Frog. This EC research will provide information to species management planning on distribution abilities of this species in the face of increasing habitat fragmentation.

Concerted interdepartmental research along shared priorities and common goals on issues that are beyond the mandates of single departments

The first year was mostly devoted to planning and initiating the projects through workshops and meetings, organizing external peer reviews, hiring qualified personnel, and finalizing formal project charters. The distribution of funds to interdepartmental projects reflects existing strengths and activities, and supports specific departmental contributions to the projects.

Strengthening Food and Water Safety in Canada through an Integrated Federal Genomics Initiative (Food and Water Safety)

Participating Departments/Agencies: AAFC, CFIA, EC, HC, PHAC and NRC
Scientific Coordination: HC
Project Management: HC

The Food and Water Safety project was initiated in late March 2012 with the procurement of all necessary laboratory consumables needed to isolate, detect and prepare templates and strains for use in fiscal year 2012-2013. Regular conference calls between the theme leaders, project manager and scientific coordinator were held to ensure open communication between all sections of the project and to confirm that objectives were being achieved in a timely manner as described in the Project Charter.

Isolation-Detection Theme

Building on work funded under a previous project at HC, a small footprint and computer-controlled prototype PCR platform has been assembled and tested for the heating of a first version of PCR adapted chip for nucleic acid amplification of desired targets. An advanced temperature control algorithm has been adapted to achieve a high temperature accuracy as well as faster temperature cycling when compared to traditional thermal-based amplification. Cycling between the three required temperature zones (95°C, 48°C, and 72°C) can be achieved in less than 30s with an overshoot of less than 0.3°C. The time required to reach the target temperature inside the microfluidic devices was found to be approximately three times faster using the developed platform compared to the conventional bench top PCR station. Several preliminary on-chip PCR amplification tests have been performed using the developed platform and

polymer-based microfluidic devices. Work is underway (at HC and NRC Boucherville) to identify appropriate blocking agents to prevent nonspecific absorption.

Information Generation Theme

All the funds intended for staffing were re-directed towards the procurement of laboratory consumables due to the late approval of the Project Charter.

Bioinformatics Theme

Anticipatory staffing has been initiated and workshops were organized for planning and collaboration building purposes. A two-week "hands on" focused workshop on microbial informatics was organized and held twice to PHAC and GRDI scientists. Consumables have been purchased for pathogen handling as well as a graphics processing unit to accelerate data processing, and a new version of a specialized software for shotgun proteomic analysis.

Protection of Canadian biodiversity and trade from the impacts of global change through improved ability to monitor invasive alien and quarantine species (Quarantine and Invasive Species)

Participating Departments/Agencies: AAFC, CFIA, EC, DFO, NRC, NRCan
Scientific Coordination: AAFC
Project Management: CFIA

The Quarantine and Invasive Species project was initiated in early January 2012, following approval of the formal Project Charter by the GRDI ADM CC. It has already reached considerable visibility through several national and international invited presentations.

Optimization and standardization of nucleic acid extractions

Several primers and pre-treatments prior to DNA extractions were tested on mollusc and finfish tissue preserved in ethanol to optimize PCR reactions. This is mostly used as positive control. Model organisms to be used for the optimization of DNA extraction from field samples were selected. Different types of soil were selected and prepared for soil inoculation with fungi, to optimize methodologies before using field soil and water samples. Probes specific to fungi and *Phytophthora* were designed. Culture material of *Phytophthora* and *Verticillium* were grown to test DNA extraction methods. Experimental designs for sample purification and pre-concentration were prepared using inertial size separation, DNA extraction with lyses chip and purification and pre-concentration of DNA. For the sample purification, several typical soil samples were characterized and particle size was analyzed by optical microscopy.

Barcoding of aquatic invasive species of highest risk to Canadian native fauna and trade

The team obtained an updated list of "banned" species and identified candidate species to work on to ensure complementarity with work undertaken by other research teams. It has compiled a first list of "closely related" species to the ones listed, as these species will have to be discriminated from the banned species. Work has focused on collecting specimens of introduced species and making contacts with collaborators to obtain specimens from their regions and countries of origin.

Barcoding of quarantine and invasive species in terrestrial ecosystems

Staffing has been initiated, priority lists of target organisms have been developed to guide the acquisition of specimens from field work, and to focus the mining of material from collections.

Direct detection of quarantine and invasive species

Forest insect trapping supplies were purchased and traps have been set in British Columbia to collect large numbers of individuals to develop initial protocols and determine detection limits for 454 sequencing. Infested logs were also harvested and moved to rearing chambers to collect emerging insects. Agricultural insect traps have been set up in the Ontario region in preparation for collection later in the year. Dormant wood samples of healthy and infected grapevine and tree-fruit have also been collected and double stranded RNA extracted to provide control samples.

Bioinformatics

The $169K for 2011-2012 provided the catalyst for a much larger, coordinated bioinformatics infrastructure investment. In total, $350K from 17 research projects spanning 2 centres and including recipients of the traditional targeted GRDI funding was invested to purchase 13 new servers to form a new compute cluster attached to a large modular storage device (108TB) to meet GRDI and other projects bioinformatics needs. The team was also able to leverage close to $60K in additional investment including renovations to provide a Biodiversity Bioinformatics Training and Design Studio to permit 15-18 bioinformatics professionals, students and researchers to work together in a uniquely collaborative environment. On March 27th 2012, two Bioinformatics workshops were hosted at AAFC in order to coincide with the GRDI-SSC Bioinformatics workshop. The first related to the classification of bioinformaticians, and was organized to address difficulties experienced at AAFC related to the CS positions requested for GRDI. It also addressed federal coordination and standardization of bioinformatics roles, responsibilities and work descriptions. The second workshop related to bioinformatics training, which was identified as a cross-cutting concern between the two GRDI shared priorities projects. Participating federal bioinformaticians discussed existing bioinformatics training curriculum, short-term and long-term training requirements, and methods for addressing these training requirements. A draft report for both workshops has been prepared and the final copy will be shared with the GRDI Working Group. This concerted effort in bioinformatics is a perfect example of how federal scientists can leverage equipment, funds, efforts and knowledge.

APPENDIX A

Annex 4 – Research Tools and Processes Produced by the GRDI

Research tools:

- Novel antibody specific to rust fungus haustorial infection structures that allows high-level purification (AAFC);
- Gene sequences for wheat leaf rust fungus released into public domain (AAFC);
- A functional molecular marker linked to superior freezing tolerance in alfalfa (AAFC);
- Populations of red clover with improved freezing tolerance (AAFC);
- A novel suite of tools for characterizing microbial communities (AAFC);
- Plant lines expressing human growth hormone and human serum albumin (AAFC);
- Polyclonal antibody against alpha subunit of asparaginase ASPGB1 from soybean and common bean (AAFC);
- High-density CustomArray 96K microarray for common bean (AAFC);
- Expanded suite of molecular markers to survey leaf rust isolates (AAFC);
- Cumulative phenotype data from a specific *B. napus* population for subsequent genome-wide association studies (AAFC);
- A foundational platform to enable the engineering of abiotic stress tolerance in canola to support breeding (AAFC);
- Transcriptome profiling of triticale reproductive tissues for the development of novel crop fertility management systems (AAFC);
- A reference two-dimensional polyacrylamide gel electrophoresis map of the triticale stigma proteome (AAFC);
- A novel constitutive promoter for expression in all plant tissues (AAFC);
- A suite of plant vectors for transient expression in leaves to enable a high-throughput assay (AAFC);
- Protein complexes that facilitate sensing and repair of DNA damage, providing candidate proteins to engineer DNA recombination potential (AAFC);

- A novel vector for assessing soybean and legume gene functions and producing proteins of interest in legumes (AAFC);
- Candidate defense related genes introduced into soybean for functional analysis (AAFC);
- Novel germplasm for use in research and breeding programs nationally and internationally (AAFC);
- Molecular markers (microsatellite loci, mitochondrial DNA and nuclear markers) for Dolly Varden and other char species (DFO);
- Database of genes up- and down-regulated in head kidney following infection with infectious salmon anemia in Atlantic salmon, publicly available for consultation (DFO);
- Fluidigm BioMark nanofluidics platform to conduct simultaneous high throughput quantitative PCR biomarker screening of salmon transcriptome and pathogens (DFO);
- New avian influenza isolates (cDNA) for researchers (EC);
- Functional marker methods to distinguish between stocks of migratory birds for EC Canadian Wildlife Services and other regulators (EC);
- PCR assays for identification of fecal pollution from human sewage and seagull fecal droppings for municipalities near Great Lakes Areas of Concern (EC);
- Metagenomic and transcriptomic analysis tools to assess river microbial communities (EC);
- Aligent 44 K chicken microarray used for screening for potential toxic effects of priority environmental contaminants (dioxin compounds) in birds, of use to risk assessors (EC);
- qPCR array for toxic fingerprinting of oilsands processed water in rainbow trout to discriminate between oil sands effects and natural background effects, of use to regulators (EC);
- qPCR array to screen for the effects of municipal effluents on rainbow trout and *Lymnea stagnalis* snails, of use to regulators (EC);
- Diagnostic sequences of partial cytochrome *c* oxidase I, developed for 80 species of wildlife parasites, of use to monitoring programs (EC);
- Diagnostic markers, biomarkers for fish health effects, antibodies for cancer regulator p35 in rainbow trout, for risk assessment of exposure of wild fish populations to environmental stressors (EC);
- Denaturant gradient gel electrophoresis and clonal restriction fragment polymorphism to detect microbial species within a mixed microbial community, for risk assessment of new substances (microbial consortia) for environmental and human health (EC);
- Biomarkers of fungal toxicity and carcinogenicity (HC);
- Biomarkers of food allergenicity (HC);
- Mesenchymal stem cells using novel protein markers (HC);
- Cell culture screening tool for in vitro prediction of genotoxic modes of action (HC);
- Loop prediction tool for advancing computational design of protein-based therapeutics (NRC);
- Multiplexed sensor chip and reader instrument capable of functioning as a serotyping assay for *E. coli* (NRC);
- A 60k Infinium array for the *Brassica* global research community (NRC and AAFC);
- Multiple Survival Screening (MSS) algorithm that uses a robust set of predictive markers to accurately identify breast cancer patients who will not respond to treatment with the cancer treatment drug paclitaxel (NRC);
- TaqMan probe for the detection of fungus in poplar leaf and canker samples (NRCan);
- Database containing wood properties of 1800 white spruce from two breeding groups, created through a partial diallel mating design (NRCan);
- Genetic map for white spruce parents via the genotyping of 500 progeny (NRCan);
- Poplar activation tagged collection for assessment of bioenergy traits (NRCan);
- Transcription profiles of various spruce budworm life stages (egg, 1st, 2nd instar) for the identification of genes involved with the induction of diapause (NRCan);

- Spruce budworm bacterial artificial chromosome library and fosmid library; cDNA library of adult spruce budworm heads (NRCan);
- Transcriptome profiles of western white pine, between genotypes resistant and susceptible to rust (NRCan);
- Transformed *Brassica napus* for characterization of resistance genes in pine (NRCan);
- Emerald ash borer genomic fosmid library (NRCan);
- Pan-genomic analysis software PanSeq (PHAC);
- Genomic analysis software BASys, GView, ACT2 (PHAC);
- Salmonella geno-serotyping assay (PHAC);
- Automated genome annotation software (PHAC).

Research processes:

- An assay system to link candidate proteins to fluorescent proteins(AAFC);
- A bioassay for the isolation of avirulence proteins and corresponding genes (AAFC);
- Universal technology to selectively repress the expression of seed storage protein genes (AAFC);
- Universal technology to target heterologous proteins to seed protein storage vacuoles (AAFC);
- Parameters for elevating recombination frequency of vegetative cells through chemical treatment of plant tissues (AAFC);
- Proof-of-concept for increasing and decreasing recombination frequency in meiotic and vegetative cells of plants (AAFC);
- Proof-of-concept for increasing accumulation of PCR products (AAFC);
- Proof-of-concept for increasing effectiveness of gene targeting substrates (AAFC);
- Proof-of-concept for engineering synthetic DNA replication complexes (AAFC);
- Novel transient protein expression systems (AAFC);
- A novel multi-gene plant expression system (AAFC);
- A novel mechanism to generating recombinogenic lesions in plants (AAFC);
- A method suitable for extraction of large amounts of root pathogen DNA (AAFC);
- A high throughput assay for identifying disease resistance in Arabidopsis (AAFC);
- Optimized conditions for extracting triticale stigma proteins (AAFC);
- Microsatellite markers and methods adopted by international collaborators (DFO);
- Standard operating procedures for toxicogenomic testing of lobster larvae exposure to contaminants, for EC's Disposal at Sea program and available on request (EC);
- Shotgun analysis of the expressed proteome in plasma samples from wild fish for Great Lakes Risk assessors and managers (EC);
- A robust purification methodology for tagless growth factor traps (NRC);
- Improved pharmacodynamics of growth factor traps and recombinant protein therapeutic candidates (NRC);
- Functionalization protocol for bacteria serotyping sensors (NRC);
- Novel process for bio-conjugating antibodies to therapeutic microbubbles (NRC);
- Optimized DNA extraction of a fungal pathogen from cultures and leaf spots (NRCan);
- Optimized whole genome amplification of a fungal pathogen using Multiple Displacement Amplification (NRCan);
- Protocol for the pyrosequencing of amplicons (plant tissues) and their bioinformatics analyses (NRCan);
- Genomic analysis proves for foodborne pathogen outbreak tracking and source attribution (PHAC);
- Optimized multiplex PCR and hybridization protocols for use in the salmonella geno-serotyping assay (PHAC).

APPENDIX B -

GENOMICS R&D INITIATIVE: PERFORMANCE MEASUREMENT FRAMEWORK OVERVIEW

In fulfillment of the requirements and guidelines of the Treasury Board, a horizontal Performance Measurement Strategy Framework (PMF) was developed for the GRDI in 2011. The PMF formalizes the commitment of the eight departments and agencies involved in the GRDI regarding the common measurement and accountability requirements associated with this Initiative. The PMF is based on a previous Results-Based Management and Accountability Framework that was developed in 2007 to address relevant conclusions and recommendations resulting from the formative evaluation of the GRDI completed in 2006. It also considers recommendations resulting from the impact evaluation that was completed in 2010.

The logic model presented in Figure 1 reflects the overall objectives for the GRDI, recognizing that there are significant differences in particular needs and priorities of each department, recognizing also that a proportion of the funds will be mobilized for coordinated interdepartmental projects along shared priorities and common goals, while the balance of resources will be used by departments and agencies to support their mandates and priorities.

A number of activities will be conducted to reach these objectives, focused on R&D activities and including research support related to management, coordination, evaluation, reporting, training, access to world-class research infrastructure and networks, strong collaborations, dissemination and transfer of research results, and translation of knowledge into commercial and public good applications.

These activities will generate outputs such as rigorous management processes, scientific information and publications, research tools and products, and a highly skilled workforce. As an immediate outcome, these outputs will be made available to support governmental mandates as well as horizontal integration. Intermediate outcomes will consist in uptake and application of the knowledge and tools generated by the GRDI for policy and regulatory decisions, for addressing key public policy priorities, as well as for supporting private sector innovation. Ultimately, the GRDI would be one of the factors contributing solutions to issues that are important to Canadians, resulting in improved human health; improved food safety and security; enhanced sustainability and management of the environment, agriculture, forestry and fisheries; and growth of S&T innovation.

The GRDI comprises three important program elements:

Governance: While good management is an important aspect of any government program, it is particularly important to recognize for this initiative because of the number of departments involved. It is thus important that the practices in place support effective departmental and interdepartmental coordination. It is also critical that departmental and shared initiative priorities be well defined so that the projects are selected to ensure that government-wide priorities for genomics research information are addressed. Without this important program component, some of the outcomes and ensuing impacts may not occur or not be as successful. Future phases of the GRDI in particular seek to demonstrate the viability of a truly interdepartmental approach and the ability of GRDI participating departments/agencies to work together, show complementarities, add value to existing departmental resources, and build strong partnerships.

Research and Development: Research and development is the central component of this initiative to respond to priorities, support governmental mandates, inform policy and regulatory decisions, and foster innovation. All activities surrounding the actual conduct of R&D, the transfer of technologies and results to stakeholders for uptake and application, and the communication of these results are critical to ensuring progress towards all outcomes and ensuing impacts.

Maintenance of Capacity: Capacity building was the focus of earlier phases of this initiative and it is critical that this capacity continue to be maintained. The maintenance of a highly skilled workforce is essential for the federal labs to undertake the type of research projects required to ensure the success of the initiative as well as be credible participants in genomics research and applications. In order to continue to maintain the federal research capacity, it is also critical that the existing infrastructure be maintained and that new state-of-the-art infrastructure be acquired to ensure that federal labs can continue to play their role in genomics research to inform regulations, policies and other decisions. Without continued capacity maintenance, some of the outcomes and ensuing impacts may not occur or not be as successful.

Table 2 outlines the performance indicators, sources and responsibility for the outcomes outlined in the logic model presented in Figure 1 earlier which should be reported upon, either in the annual performance report or at the time of evaluation as appropriate. Evaluations will not attempt to measure the impact of GRDI against the long-term outcomes, as attribution becomes more tenuous. Rather, it will focus on the achievement of immediate and intermediate outcomes, and assess whether it is reasonable to expect that the achievement of intermediate outcomes would contribute to the achievement of the long-term outcomes.

As this is a horizontal Initiative including several departments and agencies, some descriptive information is also included in the Framework related to projects, financial support and stakeholders and end-users. This is intended to support consistent collection and reporting on GRDI activities within individual departments, and are not included as indicators of performance.

Descriptive information

- Project Information developed by all participating departments/agencies every 3 years
- Project titles and summary descriptions (key objectives and impact areas)
- Financial Information reported annually by all participating departments/agencies
- Internal $ leveraged from A-base resources
- Other funding by collaborators (OGDs; universities; international organizations; private sector; etc.)
- In-kind contributions by collaborators
- Stakeholders and end-users determined by all participating departments/agencies every 3 years
- List of stakeholders and end-users available for each research project (including contact information)

Figure 1 – Logic Model for the interdepartmental Genomics R&D Initiative

Research supported by the GRDI seeks to uphold regulatory, public policy, and operational mandates in important areas such as health care, food safety, sound management of natural resources, a sustainable and competitive agriculture sector, and environmental protection, with strong collaborations with university and private sectors

	OUTPUTS	IMMEDIATE OUTCOMES	INTERMEDIATE OUTCOMES	LONG-TERM OUTCOMES
Governance	Project selection and performance management guidelines Planning meeting and workshop reports Project charters and plans Annual Performance Reports at Initiative and department/agency levels Forward-looking plans for future phases of the Initiative	Participating departments/agencies are working together to plan, set priorities, and implement coordinated management approaches	Government policy makers and regulators have used research results for evidence-based regulatory, policy, and resource management decisions Private and public stakeholders involved in the innovation continuum in Canada have adopted innovative or improved tools and processes using research results	Improved human health in Canada Enhanced sustainability and management of Canada's environment, agriculture, forestry and fisheries sectors Improved food safety and security in Canada
Research & Development	For interdepartmental/agency shared priority research projects and departmental/agency mandate-driven research: Scientific information and publications Research tools and processes Collaborations with university, private-sector, and other levels of government Communication products	Government policy makers and regulators have access as appropriate to new knowledge, tools and advice generated by scientists for policy and regulatory decisions supporting government mandates and shared priorities Private and public stakeholders involved in the innovation continuum in Canada have access as appropriate to new knowledge generated by scientists for the development of innovative or improved tools and processes		
Maintenance of Capacity	Highly skilled workforce			

Table 1: Program Performance Measurement Strategy Framework

AREA	INDICATOR	FREQUENCY	TARGET[1]	RESPONSIBILITY
Project selection and performance management guidelines	Templates and guidelines for priority setting, project selection and management processes produced for interdepartmental pilot projects	Once per phase	100% templates and guidelines approved	NRC secretariat
	Templates and guidelines for priority setting, project selection and management processes produced for department/agency mandated research projects	Once per phase	100% templates and guidelines developed and shared with GRDI WG	Departments
Planning meeting and workshop reports	Percent of meeting and workshop reports completed and approved	At time of meetings and workshops	100%	NRC secretariat Departments
Project charters	Percent of project charters produced for approved interdepartmental pilot projects following appropriate templates and guidelines	Once per phase, revised annually	100%	NRC secretariat
Annual Performance Reports at Initiative and department/ agency levels	GRDI-level performance report produced Departmental performance reports produced for the GRDI	Annual	100%	NRC secretariat Departments
Forward-looking plans for future phases of the Initiative	Next Phase plan produced based on updated environmental scans and needs assessment	Once per phase	Plan approved by ADM CC	NRC secretariat
Scientific information and publications	# of scientific contributions: - publications in refereed journals - publications in refereed conference proceedings - technical reports - book chapters - other publications - poster presentations at conferences - invited presentations - national conference presentations - international conference presentations - participations in national conferences - participations in international conferences - editorial posts for national and international journals - genomics related databases or libraries	Annual	Within the range recorded for Phase IV (1,871)[1]	Departments
Research tools and processes	# of research tools produced # of research processes produced	Annual	Within the range recorded for Phase IV (30)[1]	Departments

AREA	INDICATOR	FREQUENCY	TARGET[1]	RESPONSIBILITY
Collaborations with university, private sector, and other levels of government	# of participations in national or international genomics-related committees # of national or international genomics research peer review committees served on	Annual	Within the range recorded for Phase IV (97)[1]	Departments
	# of formal research collaborations (i.e. established in funded project workplans) by organization type: -universities (Canadian and international) -other international research organizations -other Canadian research institutions -private sector -other public sector organizations such as provinces and municipalities (excluding OGDs)	Annual	Within the range recorded for Phase IV (792)[1]	Departments
Communications products	# of communications products, including: -media interviews -press releases -community presentations (science fairs and events, schools) -brochures, fact sheets, web pages	Annual	Within the range recorded for Phase IV (151)[1]	Departments
Highly skilled workforce	# of research and technical personnel: -research scientists -research officers -technical officers -research professionals (biologists, physicists, chemists, IT specialists) -post-doctoral fellows -visiting scientists -graduate students -undergraduate students	Annual	Within the range recorded for Phase IV (1,690)[1]	Departments
Participating departments/agencies are working together to plan, set priorities, and implement coordinated management approaches	Projects funded were selected based on agreed upon selection criteria	Once per phase	100%	NRC Secretariat Departments
	% of resources allocated to interdepartmental collaborations established along shared priorities	Annual	Twenty percent of total GRDI resources allocated to collaborative projects for 2012-2013 and 2013-2014	NRC secretariat
	# of research projects involving three or more GRDI departments to address federal priorities	Once per phase	At least two	Departments

AREA	INDICATOR	FREQUENCY	TARGET[1]	RESPONSIBILITY
Government policy makers and regulators have access as appropriate to new knowledge, tools and advice generated by scientists for policy and regulatory decisions supporting government mandates and shared priorities	# of outreach activities for disseminating results to end-users	Annual	Within the range recorded for Phase IV (27)[1]	Departments
Private and public stakeholders involved in the innovation continuum in Canada have access as appropriate to new knowledge generated by scientists for the development of innovative or improved tools and processes	# of transfer activities: - outward material transfer agreements - transfer of standard operating procedures - disclosures - active patents, patent applications, patents issued - licenses issued - formal collaborative agreements / standard operating protocols - knowledge transfer workshops with stakeholders / end-users - requests for research results, papers, collaborations	Annual	Within the range recorded for Phase IV (339)[1]	Departments
Government policy makers and regulators have used research results for evidence-based regulatory, policy, and resource management decisions	# of regulatory, policy, and resource management decisions informed by GRDI research	Every 5 years	At least ten regulatory, policy and resource management decisions informed by the last 5 years of GRDI research	Evaluators
Private and public stakeholders involved in the innovation continuum in Canada have adopted innovative or improved tools and processes using research results	# of examples where innovative tools and processes have been adopted in Canada based upon GRDI research	Every 5 years	At least seven innovative or improved tools and processes adopted in Canada based upon the last five years of GRDI research	Evaluators

[1] Quantitative targets have been established based on GRDI Phase IV Annual Performance Reports between 2008 and 2011.