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Canada

GENOMICS R&D INITIATIVE

ANNUAL PERFORMANCE REPORT

2013-2014




Through the Genomics Research and Development Initiative, federal science departments and agencies collaborate in the field of genomics research to address biological issues that are important to Canadians, focusing on the role of federal government research

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EXECUTIVE SUMMARY

The Genomics Research and Development (R&D) Initiative (GRDI) is a Government of Canada initiative that enables structured collaborations and common approaches in federal science departments and agencies in the field of genomics research to address issues that are important to Canadians. The GRDI has been funded for three-year cycles: Phase I (1999-2002), Phase II (2002-2005), Phase III (2005-2008), Phase IV (2008-2011), and Phase V (2011-2014).

The Initiative has advanced significantly in the delivery of its overarching goal to apply high quality, genomics-based R&D solutions in federal laboratories to support regulatory, public policy, and operational mandates of Canada's government in socially and economically 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. The section 'GRDI at work for Canadians' exemplifies how government policy makers and regulators used results obtained to date from GRDI research to support their decisions and how private and public stakeholders have adopted innovative or improved tools and processes using GRDI research results.

Fiscal year 2013-2014 was the third and last year of Phase V of the GRDI. During this phase, the Initiative continued to support mandated research in participating departments and implemented a new model of structured collaboration supporting 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.

Considerable progress was achieved in 2013-2014, exemplified by the following highlights:

- A microfluidic-based detection platform for food and water-borne pathogens was deployed in a front-line Canadian Food Inspection Agency (CFIA) regulatory testing laboratory for performance assessment;
- A bioinformatics system for storing, managing and sharing whole genome sequence data of *E. coli* and *Salmonella* is complete and under end-user testing;
- Using molecular methods developed under the GRDI, a mollusc of Japanese origin found on tsunami debris in British Columbia was identified authoritatively as not being harmful;

- Downy mildew found in spore traps that were flagged as pathogens were identified to be a common weed pathogen;
- Research has contributed to the identification of Atlantic salmon escapees in wild populations; to our understanding of salmonid responses to the salmon louse; to the conservation of beluga whales in the Western Canadian Arctic; to the identification of aquatic invasive species; and to the characterization of key microorganisms in marine environments around offshore oil and gas production platforms;
- Infectious bacteria were detected and characterized with increased precision and greater informative power. These tools will make the control and surveillance of disease-causing bacteria more effective by decreasing response times, and enabling the trace back of more pathogens to their sources, while simultaneously characterising antimicrobial resistance and virulence properties of the pathogens.
- Significant progress was made in developing knowledge and tools to mitigate the effects of biotic and abiotic stresses that cause millions of dollars in yield losses to Canadian farmers on an annual basis. For example, using genomics tools, new sources of genetic diversity in cultivated, progenitor and wild species of Brassica crops that control a plant's ability to acclimate to adverse conditions were discovered that will be used to ensure that canola, Canada's most valuable crop contributing $19 billion dollars annually to the Canadian economy, remains highly productive in the face of climate change impacts.

This Annual Performance Report for 2013-2014 follows the Performance Measurement Framework that was developed for the GRDI in 2011. It presents the GRDI profile and planned results, its links to departmental objectives and program alignment architecture, and its governance, coordination and accountability structures. It then reports on performance for 2013-2014 in terms of governance, R&D, and maintenance of capacity. Appendix A presents summary statistics as well as a summary narrative account of R&D achievements for 2013-2014.

GRDI AT WORK FOR CANADIANS SINCE 1999

Since the implementation of the GRDI in 1999, participating departments and agencies have built a solid genomics research capacity and have gone a long way to deliver on the Initiative's stated objectives, as confirmed by two independent evaluations (2006 and 2010) and an audit by the Office of the Comptroller General (2012). Examples of practical applications that have resulted from GRDI research follow.

Government policy makers and regulators have used GRDI research results for evidence-based regulatory, policy, and resource management decisions

- The GRDI is building a database of Deoxyribonucleic Acid (DNA) sequences from the thousands of pests and pathogens that can damage food crops, including from old collection specimens. Accurate identification is essential: different species can look remarkably alike and even experts can have difficulty saying which is which. While a lot more work is required to complete this database, it is already making an important contribution to the diagnostics function at the CFIA to protect crops and trade.
- Even with import requirements in place aimed at keeping it out, soybean cyst nematode was detected in Ontario in 1987. At that time, soybean producers in affected areas became subject to regulations to prevent the movement of soil and plants that could be infested. With early detection in mind, GRDI scientists developed a test for the presence of this nematode in soil that is faster and more accurate than anything available in the past. In 2013, the test was used to confirm the presence of soybean cyst nematodes in Quebec for the first time, a finding that played a part in the CFIA decision to lift the regulations that had been imposed on soybean growers in Ontario and Manitoba.
- To remain competitive in the global marketplace, Canadian fruit growers work constantly to improve both the quality and the size of their harvest. Innovation often involves importing new varieties from other countries, creating a risk of also importing diseases that could have a serious impact on the industry, such as the plum pox virus. Testing for disease is a major, slow, and labour-intensive undertaking. At the CFIA Sidney Laboratory in British Columbia, up to 1,500 samples of grapevines alone are tested every year. With funding from the GRDI, scientists developed a technology that reduces the cost of testing by as much as 90 percent and are working to harmonize Canadian and US standards.
- Downey mildew of soybean is a quarantine species in very few countries. Still, Canada was recently challenged by Malaysia through the World Trade Organization to export soybeans that are free of the disease (a $50M annual market). Data assembled under the GRDI enabled scientists to very rapidly answer specific questions regarding hosts and distribution to help address the challenge.
- Genomics datasets developed by GRDI scientists are used operationally by federal regulators at Fisheries and Oceans Canada (DFO) 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 sustainably harvesting more abundant stocks.
- A method developed and validated by GRDI scientists to identify chemical agents based on their potential to damage DNA is in the process of being formally qualified by the US Food and Drug Administration.
- GRDI funded research supported risk assessments at Environment Canada and HC by using DNA fingerprinting to rapidly identify microbial

species in substances outlined in the Domestic Substances List. This supported compliance with the *Canadian Environmental Protection Act's* New Substance Notification Regulations for Living Modified Organisms.

- GRDI scientists developed a method to test the impact of chemicals on different species with much greater accuracy than conventional methods. In acknowledgement of this achievement, GRDI scientists were invited by the Organization for Economic Cooperation and Development (OECD) to join a group that sets international standards for the use of toxicogenomics in regulatory policy.
- A genomics method that uses biomarkers associated with chronic stress to investigate the effects of environmental disturbances on wildlife health was developed and validated by GRDI scientists. So far, this technique has been used to examine the effect of large scale environmental disturbances on the immune functions, reproductive activities, and survival of wild birds. Information collected through this work was disseminated to provincial decision-makers to support related risk mitigation efforts.
- GRDI scientists applied genomics methods to study the effects of contaminants, including organophosphate flame retardants on wild bird cells. By conducting exposure studies of priority chemicals in wild bird egg extracts, researchers were able to establish a link between contaminant levels detected in particular areas of the Great Lakes and their effect on wild bird species. Findings from this research are assisting Environment Canada's risk assessors develop regulatory criteria that will help protect the health of wildlife and humans from priority chemicals.
- To support the management of shellfish harvesting in New Brunswick and Prince Edward Island, GRDI scientists developed and validated DNA markers to identify pathogen sources in water that affect shellfish populations. This will provide data and insight on the sources of fecal pollution for risk assessments and inform potential options to improve water quality in shellfish areas.
- Campylobacter is responsible for over 400,000 cases of food poisoning every year and the leading cause of bacterial gastroenteritis in Canada. GRDI scientists developed an innovative generic fingerprinting method for rapid identification of Campylobacter strains, and transferred it to the British Columbia Centre for Disease Control and the CFIA. This approach provides results in a matter of hours rather than days; it enables front-line regulators to pinpoint where specific strains originates, and from there, look for ways to reduce their transmission.
- Sudden oak death is a fungal disease that could pose a significant economic risk to Canada if it entered the country and attacked hardwood forests. Canada exports some $5.5 billion worth of lumber and hundreds of millions of dollars in ornamental plants every year and major trading partners restrict imports of wood and plant materials from countries where the disease has been found. Because plants can be infected long before they show any symptoms, CFIA inspectors who survey the disease have relied on laboratory tests that can take as long as a month to produce results. Today, a new test developed by GRDI scientists that is much more sensitive and provides results in as little as 24 hours is used operationally by the CFIA, as well as by the US Department of Agriculture. Agencies in the United Kingdom and France are taking steps to adopt the test as well.
- Genomics data has allowed GRDI scientists to distinguish the subspecies and populations of northern Dolly Varden char as distinct groups. This research has resulted in the listing of northern Dolly Varden as a 'species of concern' in Canada, re-opening of the Big Fish River fishery, and partnerships with the Fisheries Joint Management Committee and Gwich'in Renewable Resources Board for genetic analysis to assist them with assessing the stability of their fisheries.
- Knowledge generated from genomics research on redfish provided new scientific advice for fisheries managers, recommending the Acadian redfish and deep water redfish be managed as separate resources. The research also helped play a role in the Committee on the Status of Endangered Wildlife in Canada's assessment of the status of deep water redfish as threatened in the Northwest Atlantic (2010), and facilitated a collaborative partnership with redfish harvesters to identify the redfish species being caught in the Laurentian Channel in the Gulf of St. Lawrence, where a moratorium on the redfish fishery has been in effect since 1995.
- The conservation of threatened Atlantic salmon populations around Newfoundland and Labrador is a major goal for DFO. Genetic data on wild

Atlantic salmon in Newfoundland and Labrador generated through a GRDI project contributed to support science advice included in the "*Southern Newfoundland Atlantic Salmon Recovery Potential Assessment*" and in the evaluation of the "*Potential Effects Surrounding the Importation of European-Origin Cultured Atlantic Salmon to Atlantic Salmon Populations and Habitats in Newfoundland*" to protect Canada's wild Atlantic salmon populations.

- The establishment of protocols and the collection of genetic baseline data on Atlantic salmon collected through GRDI were instrumental in enabling government enforcement officers in forensic analysis to identify confiscated fish products and trace them to their species or stock of origin.

Private and public stakeholders involved in the innovation continuum in Canada have adopted innovative or improved tools and processes using GRDI research results

- The balsam fir sawfly has been a problem for decades in Eastern Canada, reaching epidemic proportions since the early 1990s and posing a significant threat to the forest industry of the province. Based on research conducted by GRDI scientists, a baculovirus that specifically attacks the balsam fir sawfly was registered and licensed to Forest Protection Limited of New Brunswick for commercial use. More than 50 000 hectares of infested forest have since been treated with the virus as part of operational forest insect pest control programs by the Newfoundland and Labrador Department of Natural Resources and by the New Brunswick Department of Natural Resources. A new company, Sylvar Technologies, was formed to produce and commercialize the virus under the trade name Abietiv. Recognizing the value of its technology and research capabilities, Andermatt BioControl, a major biotechnology company based in Switzerland, acquired majority ownership of Sylvar in 2011.
- GRDI scientists found a new and unique bacterial marker that distinguishes fecal contamination from seagulls, a serious source of pollution around the Great Lakes. This marker has changed how Canadian municipalities manage their beaches, as it allows more targeted and cost-effective solutions for the cleanup of pollutions sources, and is now being used around the world. The US Environmental Protection Agency presented its Scientific and Technical Achievement Award in 2010 to the scientists for this breakthrough work.
- Fusarium head blight, a fungal disease that has caused Canadian wheat producers more than $1.5 billion in lost income since the mid-1990s, produces mycotoxins causing serious illness in people or animals who consume infected wheat. With support from the GRDI, scientists developed a library of genes identifying those that are used by the fungus to produce a number of mycotoxins, as well as when they are produced, and under what conditions. This is part of a global research effort that now provides the most complete and accurate sequencing of the fungus accessed by the international research community to explore how to block infection.
- Canada's forest industry plants an estimated 650 million trees every year. Long-term tree breeding programs help companies choose the best seedlings for planting. GRDI scientists are identifying genetic markers associated with the most valuable traits. With them, breeders will be able to tell at the seedling stage whether a tree has inherited desired traits that could otherwise be measured only when the tree has reached maturity, decades later. This research is already contributing to tree breeding programs of provincial governments in Quebec and New Brunswick, and has been recognized by a forest industry representative as 'some of the most positive developments we have seen in the field'.
- Marker-assisted breeding techniques developed by GRDI scientists for wheat have become integrated into a large-scale research alliance established with the common goal of improving the yield, sustainability, and profitability of Canadian wheat for the benefits of Canadian farmers and the economy. The Canadian Wheat Alliance includes major contributions by the National Research Council of Canada (NRC), AAFC, the University of Saskatchewan, and the Province of Saskatchewan, as per a formal agreement signed in 2012.

- Working under the umbrella of the North American Collaborative Oat Research Enterprise, which brings together the entire oat research community and stakeholders from Canada, the US and beyond, GRDI scientists have been instrumental in developing detailed knowledge of the genetic variation in thousands of different oat varieties. A dozen top oat breeders from around the world were engaged to grow a broad range of oat lines in different environments and the data generated provide breeders with a new tool for directed breeding of superior oat varieties.
- With support from the GRDI, scientists developed a new generation of targeted therapy for cancers – antibody-drug conjugates – and actively collaborate with Canadian companies. NRC and Zymeworks Inc., a Canadian biotherapeutics company and a world leader in antibody therapeutics, announced in 2014 a new strategic collaborative agreement for the development of biotherapeutics. This three-year multi-million dollar agreement will focus on developing ground-breaking therapies for the fight against cancer, as well as inflammatory and autoimmune diseases.
- The soil-borne root and stem rot of soybean causes widespread damage in soybean crops and can result in annual production losses of $40-$50 million a year in Canada, and as much as $2 billion globally. With support from the GRDI, scientists have elucidated resistance mechanisms that can be exploited to control the pathogen. New, quick and inexpensive diagnostic tests are being developed and commercialized to identify which strains are present in the fields of soybean producers so they can select a variety that carries resistance genes to these particular strains.
- Although antiretroviral therapy has dramatically increased survival and quality of life for people living with Human Immunodeficiency Virus (HIV), drug resistance continues to be a major limitation to maximising the benefit of treatment. Current methods to detect the emergence of drug resistant viruses are costly, laborious, lack sensitivity, and do not include coverage for newer antiretroviral drugs. GRDI scientists used next generation sequencing technology to develop a new method to detect HIV drug resistance that increases the speed and throughput of the test. This test has been developed in collaboration with clinical research partners and is contributing to the enhanced clinical management of HIV patients.

ACRONYMS

AAFC	Agriculture and Agri-Food Canada
ADM	Assistant Deputy Minister
ADM CC	ADM Coordinating Committee
BAW	Bertha Army Worm
CFIA	Canadian Food Inspection Agency
CFS	Canadian Forest Service
CIMMYT	International Maize and Wheat Improvement Centre
DFO	Fisheries and Oceans Canada
DNA	Deoxyribonucleic Acid
EAB	Emerald Ash Borer
EC	Environment Canada
FWS	Food and Water Safety
GRDI	Genomics Research and Development Initiative
HC	Health Canada
HIV	Human Immunodeficiency Virus
miRNA	MicroRNA
MSCs	Mesenchymal stem cells
NGS	Next Generation Sequencing
NRC	National Research Council Canada
NRCan	Natural Resources Canada
PCR	Polymerase Chain Reaction
PHAC	Public Health Agency of Canada
PMF	Performance Measurement Strategy Framework
QIS	Quarantine and Invasive Species
qPCR	Quantitative PCR
R&D	Research and development
RNA	Ribonucleic Acid
SNP	Single Nucleotide Polymorphism
STAGE	Strategic Technology Applications of Genomics in the Environment
STEC	Shiga-toxin Producing
US	United States of America
VTEC	Verotoxigenic *Escherichia coli*
WG	Working Group

GENOMICS R&D INITIATIVE - 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 5th 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 inter-departmental 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 CFIA, are eligible 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	2,550
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 funds with allocations from their A-base resources and from successful collaborations. Table 2 provides an overview of resources invested in 2013-2014 in support of GRDI projects, and demonstrates that non-GRDI funds represented almost twice the GRDI investments. Additional in kind investments 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 2013-2014 ($000)

DEPARTMENT/AGENCY	GRDI	NON-GRDI*	TOTAL
National Research Council	4,800	9,798	14,598
Agriculture and Agri-Food Canada	4,800	9,249	14,049
Health Canada	1,600	1,433	3,033
Public Health Agency Canada	1,600	4,165	5,765
Natural Resources Canada	1,600	2,853	4,453
Environmental Canada	800	1,867	2,667
Fisheries and Oceans Canada	720	1,273	1,993
SHARED PRIORITY PROJECT	**GRDI**	**NON-GRDI**	**TOTAL**
Quarantine and Invasive Species	1,856	3,062	4,918
Food and Water Safety	1,810	4,015	5,825
Coordination and Common Functions	314	40	354
Total	**19,900**	**37,755**	**57,655**

* includes funds from departmental A-base and other sources

Planned Results

As part of NRC's 2013-2014 Report on Plans and Priorities supplementary tables for the GRDI, the participating departments established a collective set of planned results:

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

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

Agriculture and Agri-Food Canada

Projects 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, oilseeds and legumes, 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

GRDI funded work will continue to be delivered through EC's *Strategic Technology Applications of Genomics in the Environment* (STAGE) program. STAGE will be guided by the following four research priorities: 1) strengthen predictive models to help understand and address the effects of existing and emerging stressors on organisms and their ecosystem functions; 2) understand and monitor aquatic and land-based ecosystems; 3) understand cumulative risks and impacts; and 4) manage the environmental risks of chemical, biological, and physical pollutants. Advancing genomics knowledge, tools, and technologies through the STAGE program will support policy making, regulatory development, and enforcement efforts essential for the delivery of EC's obligations under various environmental legislations and initiatives, including the *Canadian Environmental Protection Act* and the Chemicals Management Plan.

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 foodborne 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

Investments from the GRDI at NRC will support programs requiring genomics-related activities to help industry and government tackle strategic national priorities through mission-oriented research and technology deployment. In 2013-2014, these will be: 1) NRC's contribution to the Canadian Wheat Alliance, the goal of which is to improve the yield, sustainability, and profitability of wheat for the benefit of Canadian farmers and the economy. This will be achieved by improving breeding efficiency and reducing losses from drought, heat, cold and diseases, and improving nutrient use efficiency; and 2) the Biologics and Subsequent Entry Biologics program, the main objective of which is to cover all aspects of biologic development from discovery up to pre-clinical testing in collaboration with industrial partners.

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 selected research projects that target high priority issues in the areas of infectious and chronic diseases. Projects related to infectious diseases will address priority issues such as increasing our knowledge related to the emergence of antimicrobial-resistant bacterial pathogens, and related to emerging and re-emerging pathogens such as *Mycobacterium tuberculosis*. PHAC will also direct 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 detection and response to food-borne pathogens. In addition, PHAC researchers are creating automated bioinformatics 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 will also be investigated. In particular, researchers will investigate 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 use 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 (QIS) project) will develop 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 (FWS) project) will increase the speed and reduce the cost of genomics-based methods for pathogen isolation, detection and characterization; and develop 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 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, agriculture and the environment.

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

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 that focus on improving the sustainability and competitiveness of Canada's agriculture sector.

The CFIA participates in both shared priority projects and in the overall governance of the Initiative to support its regulatory mandate.

National coordination for genomics research at DFO is provided by the Biotechnology and Genomics Program. The Biotechnology and Genomics Program supports genomics research for Economically Prosperous Maritime Sectors and Fisheries and Sustainable Aquatic Ecosystems, two of the three Strategic Outcomes of the Department's Program Alignment Architecture. Genomics research is building the scientific knowledge base and expertise necessary to support priorities for fisheries and oceans management.

All GRDI-funded R&D activities undertaken at EC align with Departmental priorities including, conserving and restoring Canada's natural environment for present and future generations, and minimizing threats to Canadians and their environment from pollution. To this end, GRDI-funded activities at EC: contribute to the monitoring and understanding of Canada's ecosystem; help to assess risks posed by chemical pollutants to wildlife and migratory birds; and deliver practical applications that support regulatory compliance as well as evidence-based decision making related to risk mitigation and conservation efforts.

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 support-

ing 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.

During 2013-2014, NRC completed a major update of its Program Alignment Architecture to reflect NRC's new industry-focus, Government of Canada's Strategic Outcomes and federal priorities, and NRC's business processes. NRC's performance reporting is aligned accordingly. The GRDI at NRC supports the Strategic Outcome: *Canadian businesses prosper from innovative technologies*, the Program *Technology Development and Advancement*, and the Sub-Programs *Aquatic and Crop Resource Development and Human Health Therapeutics*. This is accomplished by contributing to research programs that focus on improving Canadian wheat and developing new biologics and subsequent entry biologics.

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 harmful consequences of chronic diseases. 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. Directly in line with the Program Activity of *Public Health Infrastructure*, the GRDI develops and applies 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.

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 continued to oversee the collective coordination of the GRDI. The governance structure for GRDI includes three main elements: an Assistant Deputy Minister (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 is 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, and 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 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, and more often when warranted by specific needs for recommendations and advice.

GRDI Coordination Function

The Coordination Function for the GRDI is housed at NRC. It provides GRDI-wide 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 help establish GRDI-wide research priorities, providing management and administration support, as well as support for performance management, reporting, evaluation, and communications. It is funded through the shared priorities portion of 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 participating departments and agencies 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, key public policy priorities, and private sector innovation.

PERFORMANCE

Governance

GRDI Interdepartmental Coordination

Ongoing coordination was provided by NRC for 2013-2014, the third and last year of Phase V, including timely secretariat support to GRDI departments and agencies and the implementation of the GRDI governance framework, management and operating processes put in place for Phase V. Four meetings of the ADM CC and eight meetings of the GRDI WG were held to allow for collaborative decisions. A client satisfaction survey was completed, indicating a satisfaction level rated at 97% by WG and ADM CC members. Leadership was provided to establish future strategic directions for Phase VI of the Initiative, for which the Government of Canada allocated $99.5M over 5 years (2014-19). Phase VI will follow the model pioneered under Phase V and in addition, will provide funding to support mandated research at the CFIA.

The implementation of shared priority projects was supported: funding was made available to participating departments based on the approved Project Charters; mid-term review report recommendations and responses from the teams were presented to and approved by the ADM CC in May 2013; and bi-annual progress reports were presented to the ADM CC (May and October 2013). Plans to develop an integrated Innovation Management Strategy for shared priority projects were prepared in response to recommendations received by the mid-term review expert panels in March 2013 and endorsed by the ADM CC.

The GRDI Performance Measurement Strategy was implemented with the finalization and approval by the ADM CC of the Annual Performance Report for 2012-2013, input into NRC's Departmental Performance Report and Report on Plans and Priorities, as well as the continued implementation of the Management Response and Action Plan to finalize implementation of all recommendations from the 2010 evaluation.

Mandated Research

Departments and agencies manage their GRDI activities within the scope of existing program areas aligned with their respective Strategic Outcomes, Activities, and Sub-Activities defined in their Program Alignment Architecture. Continued GRDI support was provided to Phase V projects based on adequate performance. These projects were selected based on their contribution to identified priorities where federal scientists had distinct expertise, using balanced portfolio approaches, and following formal approval processes.

Shared Priorities

Both shared priority projects have detailed governance structures in their Project Charters to ensure seamless integration and clear roles and responsibilities. These include Management Advisory Committees, comprising senior managers from each of the participating departments and agencies, a Science Advisory Board with members representing academia, government and industry, theme leaders, dedicated project managers, and overall leadership by Scientific Project Coordinators. Ongoing open communication was established through conference calls, emails, presentations, and regularly scheduled meetings, to share updates and provide decision-making fora. Web-based SharePoint sites were used in both projects to host the most current versions of all the project related documents for access by all project participants and Advisory Boards. Both projects will continue to be supported in the first two years of Phase VI of the GRDI (2014-2016).

Research and Development

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 impacts, and are thus included in the GRDI Performance Measurement Framework.

Direct scientific outputs for 2013-2014 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 2013-2014 against planned results are provided in Annex 3, and Annex 4 presents a list of research tools and processes developed under the GRDI.

Awards and prizes were awarded to several GRDI scientists to recognize the excellence of their research:

- Sylvie Cloutier (AAFC) received the Farm Credit Canada Rosemary Davis award for leadership in agriculture through innovation, creativity and a passion for the success of the industry;
- Mark Jordan (AAFC) received the Appreciation of Associate Editorship award from the journal of In Vitro Cell Development and Biology;
- Mathew Links (AAFC) received the 2013-2014 University of Saskatchewan Graduate thesis award for top PhD in the Life Sciences and Governor General's academic gold medal for top PhD;
- Scott Redhead (AAFC) was elected as a Fellow of the Mycological Society of America;
- Karen Dunmall (DFO) received the Natural Science and Engineering Research Council Graduate Scholarship, the W. Garfield Weston Scholarship and the J. Frances Allen Scholarship;
- Carole Yauk (HC) received the Healthy Environments and Consumer Safety Branch Assistant Deputy Minister's Award for Excellence in the category of "Leadership" and the 2013 HC, Deputy Minister's Award for Excellence in the category of "Leadership";
- Carole Yauk's (HC) team posters were voted: top 10 Toxicity Risk Assessment Abstracts by the Society of Toxicology (Phoenix AZ, March 2014); best poster at HC Research Forum (Ottawa, Dec. 2013); and best poster at the International Conference on Environmental Mutagens (Brazil, Nov. 2013).
- Richard Hamelin (NRCan) received the IUFRO Scientific Achievement Award in recognition of his scientific achievements in the field of forest pathology.

Maintenance of Capacity

Highly Qualified Personnel

The number of highly qualified personnel engaged in GRDI projects is much larger than the number of persons whose salary is covered by GRDI funds. In 2013-2014, more than 850 persons were engaged in GRDI projects, representing 370 full time equivalents. These comprised 668 scientific and technical staff, 59 post-doctoral fellows, 122 students (PhD, MSc, BSc, and Co-op) and 7 administrative officers.

Facilities

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

At AAFC several of pieces of equipment were purchased in a number of genomics laboratories to support GRDI funded mandated projects including: a Samsung SUR40 - multiuser / multi-touch device

(table format), a Perceptive Pixel display 55" - multiuser / multi-touch device, a dissecting microscope, a Polymerase Chain Reaction (PCR) machine, an Illumina MiSeq, a Qiagen QiaCube, an Agilent BioAnalyser, a spectrophotometer, a freeze drier, and 2 droplet digital PCR machines. For the Quarantine and Invasive Species project, AAFC purchased new hardware infrastructure to support computation and storage and leveraged contributions from different projects, laboratories and centres to make a larger purchase for the benefit of the interdepartmental team. New software was installed on the compute cluster and new infrastructure included a 27 terabyte Isilon Storage Node, a 200 terabyte Storage Appliance, and 4 compute nodes (purchased by CFIA).

Infrastructure acquisition for DFO projects consisted of a Molecular Imager® Gel Doc™ XR+ System from Bio-Rad; a Veriti® Thermal Cycler from Life Technologies, a Qubit® 2.0 Fluorometer from Life Technologies; a E-Gel® SizeSelect™ Agarose Gels from Invitrogen; DNA size select system (E-gel; Invitrogen) and an Airclean® System 600 PCR workstation from Airclean. Additionally DFO ensured maintenance of capacity through an extension to service agreement for Dnastar Lasergene software and a software upgrade for the QIAxcel from Qiagen.

The HC core genomics laboratory maintains a state-of-the-science DNA microarray facility including: Agilent DNA microarray scanner and associated labware and software; Agilent Bionalyzer; Nanodrop spectrophotometer; two CFX real-time PCR machines; GeneSpring Gx microarray analysis software; Ingenuity Pathway Analysis; NextBio and Metacore Pathway Analysis software; and a core informatics platform including two high-end workstations (T7500) and three Dell R-900 servers. Support from the GRDI has allowed the leverage of internal funds to expand the facility and include next generation sequencing capabilities. The laboratory is now equipped with the Life Technologies Ion Proton and all required bioinformatics infrastructure (servers, operating systems, back-up and software) that will enable the evolution of genomics analyses from DNA microarrays to RNA sequencing, ChIP-seq and full genome sequencing. International recognition of the high caliber of experiments conducted in the facility has also led to invited involvement in validation exercises for RNA sequencing through the International Life Science Institute. The laboratory also acquired a tissue dissociator.

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

At EC, GRDI funding contributed to the acquisition of laboratory equipment including a 454-sequencer, two large growth chambers for algal/cyanobacteria culture collection, an Algal Online Analyzer Profiler, and a confocal laser microscope. Bioinformatics capacity was also increased by the implementation of a bioinformatics work station and programs for the analysis of Ribonucleic Acid (RNA) sequences.

Infrastructure acquisitions for PHAC projects consisted of an automated DNA extractor, the KingFisher Flex, to facilitate high throughput extraction of DNA for use with genomic assays, as well as computing infrastructure and data analysis capacity. GRDI funds were used to directly support ongoing maintenance and support of over 1 million dollars of PHAC funded capital equipment, including flow cytometers, quantitative real-time polymerase chain reaction machines, and diagnostic equipment. In addition, the FWS project, as well as other GRDI projects leveraged in kind use of PHAC funded capital equipment including state-of-the art computing infrastructure largely housed at the National Microbiology Laboratory, massively parallel sequencing infrastructure, and the proteomics core facility.

APPENDIX A– SUPPLEMENTAL PERFORMANCE DETAILS

Annex 1 – GRDI Projects and funding allocations from GRDI

GRDI FUNDS ($)	PROJECT TITLE
QUARANTINE AND INVASIVE SPECIES	
1,856,000	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	
1,810,000	Strengthening food and water safety in Canada through an integrated federal genomics initiative
AGRICULTURE AND AGRI-FOOD CANADA*	
	1) Biodiversity, gene mining and functional analysis for the identification and extraction of genes for desirable traits, including mechanisms of plant resistance to biotic and abiotic stress and insect and pathogen virulence
258,308	Bertha armyworm (*Mamestra configurata*): genomics, population dynamics and biodiversity of pest and pathogens
200,717	Camelina - an integrated industrial oilseed crop platform for Canada
234,008	Defining molecular virulence in fusarium and unique resistance mechanisms in wheat and maize towards reducing fusarium mycotoxins in Canadian cereals
73,578	Exploitation and characterization of carbohydrate active enzymes from metagenomic and metatranscriptomic rumen samples
112,223	Exploiting wheat leaf rust fungus molecular resources to combat cereal rust diseases
208,931	Exploiting the biodiversity within the Brassica crops and exotic Brassicaceae
30,404	Fine mapping of the Sr9 stem rust resistance locus in wheat
22,793	Functional analysis of durable wheat rust resistance.
74,786	Genetic determinants of cultivar-specific virulence in the root rot pathogen *Phytophthora sojae*
4,614	Genetic characterization of the orange wheat blossom midge resistance gene Sm1
86,587	Genetics and genomics of symbiotic nitrogen fixation: all in the name of entry
197,221	Genomic-assisted strategies for evaluating and utilizing potato genetic resources
115,102	Genomics of multi-toxin synergies and interactions of fusarium species in Canadian cereals to guide the development of resistant crops, mycotoxin monitoring, and hazard characterization
67,412	Next-generation genomics for oat improvement
82,494	Toward development of next generation resistance to soybean mosaic virus: genomics and genetics of soybean-virus interactions

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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	
21,323	Prototyping the Microsoft surface for bioinformatics
3) Enhanced efficiency of plant breeding	
181,865	Cell penetrating peptide transfection technology validation and deployment in Research Branch - Enabling functional genomics programs
272,017	Identifying and modulating determinants of DNA recombination to accelerate genetic improvement of crops
42,869	Managing crop reproduction
ENVIRONMENT CANADA	
100,440	Genomics research in support of *Canadian Environmental Protection Act* risk assessment of existing and new microbial substances
52,650	Metagenomic and DNA microarray characterization of water quality in shellfish areas monitored by Environment Canada
60,750	Development and validation of a crustacean microarray and correlation of gene expression profiles with traditional toxicological end-points for contaminant exposure
115,020	Avian toxicogenomics and adverse outcome pathways - New tools for risk assessment
90,720	Metagenomic tools for assessment and monitoring in aquatic ecosystems
17,820	Determining breeding source populations of purple sandpipers (*Calidris maritima*) wintering along eastern Canada and the northeastern United States
102,060	Use of high throughput genomics to predict the potential health effects of oil-sands contaminants on fish health
32,000	Genomic approach to toxic and harmful algal bloom prediction and management
51,030	Elucidating the relationship between toxicogenomic gene expression profiles and functional biological outcomes in underlying rainbow trout and neonate *Daphnia magna*
85,860	Evaluation of the toxicity of emerging contaminants in aquatic organisms using genomics
51,030	Using toxicogenomics in wood frogs and the adverse outcome pathway for environmental effects monitoring of oil sands industrial development
40,500	Novel stress biomarkers to study impacts of large-scale environmental changes on health of wildlife
FISHERIES AND OCEANS CANADA	
40,250	Stock delineation of redfish (*Sebastes mentella*) based on genetic analyses of archived otoliths
155,080	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
52,000	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
24,000	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
74,500	Characterization of infectious hematopoietic necrosis virus carrier state in sockeye salmon using genomic tools
115,000	Arctic fish genomics as ‘sentinels’ of ecosystem integrity and change
77,000	Low pathogenic infectious salmon anemia virus variant in vivo: a comparative genomic study

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HEALTH CANADA	
194,000	Genomic characterization of clinically important foodborne isolates of *Campylobacter* and *Listeria* impacting public health
228,000	Immunotoxicogenomics and food allergy: developing a genomics assay to assess chemical food contaminants that modulate pathways leading to food allergy
220,000	Genomic characterization of tissues from P53+/- transgenic mice exposed to genotoxic and non-genotoxic carcinogens for developing short term cancer bioassays
150,000	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
400,000	Integrating genomics endpoints into regulatory toxicology
258,000	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	
3,856,767	Wheat Improvement Flagship (Enhancing fusarium and rust tolerance; Genomics-assisted breeding; Abiotic stress; Seed development)
943,233	Biologics and Subsequent Entry Biologics: Development of support technology
NATURAL RESOURCES CANADA	
231,000	Applied genomics for tree breeding and forest health
198,900	Spruce budworm eco-genomics: from population dynamics to population suppression
192,000	Genomics-enhanced next generation forest disease diagnostic and monitoring
160,000	Genomics of tree-microbe interactions
189,400	H*Ap*lnomics: host, *Agrilus planipennis* integrative genomics
PUBLIC HEALTH AGENCY OF CANADA	
68,809	The modifying effect of genetic polymorphisms involved in folate and B12 metabolism on the relationship between folate/B12 intake and vitamin status
95,568	Prospect for proteomic biomarkers of inflammation to predict early risk of type II diabetes and to monitor response to nutritional intervention by vitamin D
93,845	New technology for HIV drug resistance testing – a model for integrating next generation sequencing and data analysis
71,676	Identification of targets to monitor the dissemination of carbapenem-resistance genes in enterobacteriaceae
143,352	The association of vitamin D insufficiency and related genetic variants with tuberculosis infection and disease in a Canadian cohort
152,908	Uncovering the signatures of *Mycobacterium tuberculosis* specific immune responses to distinguish active versus latent tuberculosis infection
86,011	Molecular characterization of *Salmonella* Enteritidis for surveillance and control of foodborne illness
95,568	Improving the accuracy of automated prokaryotic genome annotation
238,917	A rapid geno-serotyping tool for the classification of *Salmonella* serovars
286,703	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
143,352	Application of comparative genomics to the identification of shiga-toxin producing *Escherichia coli* subgroups and pan-genomic markers frequently associated with human disease

* Non-pay operating expenditures only

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, including but not exclusive to personnel financed through GRDI funds.

	NUMBER OF RESEARCH AND TECHNICAL PERSONNEL									
	AAFC	DFO	EC	HC	NRC	NRCan	PHAC	QIS	FWS	**TOTAL**
Research scientists	55	12	17	15	27	13	32	30	69	**270**
Research professionals	5	8	6	17	12	13	16	17	35	**129**
Research technicians	83	16	28	15	37	18	4	31	37	**269**
Post-doctoral/visiting fellows	11	1	9	6	10	13	3	6	0	**59**
Graduate students	12	5	10	2	0	4	3	2	6	**44**
Undergraduate students	14	0	15	0	5	2	9	32	1	**78**
Administrative officers	3	0	0	0	1	1	1	1	0	**7**
Total	**183**	**42**	**85**	**55**	**92**	**64**	**68**	**119**	**148**	**856**
Total Full Time Equivalents	**92.2**	**9.3**	**39.9**	**20.3**	**68.5**	**35.0**	**22.9**	**28.8**	**53.5**	**370.4**

Collaborations

Collaborations by department/agency, expressed in terms of number of individual research collaborators from an organization 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									
	AAFC	DFO	EC	HC	NRC	NRCAN	PHAC	QIS	FWS	**TOTAL**
Universities (Canadian)	13	8	47	6	8	16	14	19	3	**134**
Universities (international)	16	3	15	4	2	10	1	27	2	**80**
Other international research organizations	6	1	7	1	2	6	5	7	0	**35**
Other Canadian research institutions	4	0	1	0	0	4	0	7	0	**16**
Private sector	1	0	5	3	10	0	1	5	1	**26**
Other government departments	15	0	17	10	31	6	5	33	6	**123**
Other public sector organizations such as provinces and municipalities and NGOs	0	2	9	0	3	14	8	10	2	**48**
Participation in national or international genomics-related committees	8	0	4	5	3	21	1	4	5	**51**
National or international genomics research peer review committees served on	8	0	0	1	3	2	7	0	3	**24**
Total	**71**	**14**	**105**	**30**	**62**	**79**	**42**	**112**	**22**	**537**

Scientific Contributions

Scientific contributions include scientific information and publications produced, accepted, in press, or published (including online) in 2013-2014. They include contributions from any project team member as long as they relate to the GRDI project. They also include contributions deriving from a previous phase of the project, if produced in 2013-2014. They do not include submitted papers or publications in draft form, nor contributions that were reported in previous years.

	NUMBER OF R&D OUTPUTS									
	AAFC	DFO	EC	HC	NRC	NRCAN	PHAC	QIS	FWS	**TOTAL**
Publications in refereed journals	28	7	53	20	17	30	22	17	6	**200**
Publications in refereed conference proceedings	14	1	9	0	3	12	11	1	2	**53**
Technical reports	0	0	9	0	1	3	1	2	0	**16**
Books (edited, written)	0	0	0	0	0	0	0	0	2	**2**
Other publications (ex. book chapters, monographs, abstracts, notes, etc. industry magazines)	6	4	7	1	1	8	7	9	2	**45**
Poster presentations at conferences	12	4	15	15	8	19	14	4	2	**93**
Invited presentations	28	18	21	9	13	26	8	27	6	**156**
National conference presentations	8	4	6	4	2	14	7	2	2	**49**
International conference presentations	19	10	16	6	9	12	11	9	1	**93**
Active participations in national conferences (organizer, chair, panel discussion etc.)	5	0	5	1	2	4	2	0	0	**19**
Active participations in international conferences (organizer, chair, panel etc.)	4	0	3	5	0	3	4	3	2	**24**
Editorial posts for national and international journals (excludes peer reviewers)	6	2	4	0	3	6	2	4	0	**27**
Deposits in genomics related databases or libraries	3	0	8	3	1	35	635	15	0	**700**
New genomics related databases or libraries	2	2	4	0	1	1	3	2	0	**15**
Awards, prizes	3	3	1	6	0	1	0	0	0	**14**
Total	**138**	**55**	**161**	**70**	**61**	**174**	**727**	**95**	**25**	**1,506**

Communications products

	NUMBER OF COMMUNICATIONS PRODUCTS									
	AAFC	DFO	EC	HC	NRC	NRCAN	PHAC	QIS	FWS	**TOTAL**
Media interviews	8	1	0	0	15	0	0	1	0	**25**
Press releases and announcements	0	0	1	0	4	0	1	0	0	**6**
Newspaper and magazine articles	1	0	3	0	68	0	0	0	0	**72**
Community presentations	0	4	4	0	2	0	0	0	2	**12**
Brochures, fact sheets, web pages	1	1	2	0	21	1	3	0	0	**29**
Total	**10**	**6**	**10**	**0**	**110**	**1**	**4**	**1**	**2**	**144**

Knowledge/Technology Transfer

	NUMBER OF KNOWLEDGE/TECHNOLOGY TRANSFERS									
	AAFC	DFO	EC	HC	NRC	NRCAN	PHAC	QIS	FWS	**TOTAL**
Outreach activities	18	0	7	6	8	2	11	2	1	**55**
Material transfer agreements	21	0	4	0	12	0	1	0	3	**41**
Transfer of standard operating procedures	1	0	1	0	5	1	5	8	4	**25**
Disclosures	0	0	0	0	11	0	1	0	0	**12**
Active patents, patent applications, patents issued	18	0	1	0	4	0	1	2	6	**32**
Licenses issued	0	0	0	0	0	0	1	0	1	**2**
New formal collaborative agreements / standard operating protocols	0	1	3	0	3	0	1	0	1	**9**
Knowledge transfer workshops with stakeholders/end-users	0	0	3	0	1	0	1	4	0	**9**
Requests for research results, papers, collaborations	59	2	2	0	0	0	2	0	2	**67**
Total	**117**	**3**	**21**	**6**	**44**	**3**	**24**	**16**	**18**	**252**

Research tools and processes

Research tools and processes include those produced in 2013-2014, deriving from previous phases of the GRDI if produced in 2013-2014, 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	QIS	FWS	**TOTAL**
Research tools	20	5	15	11	6	4	6	7	5	**79**
Research processes	7	0	2	0	9	2	8	3	1	**32**
Total	**27**	**5**	**17**	**11**	**15**	**6**	**14**	**10**	**6**	**111**

APPENDIX A

Annex 3 – Highlights of Results Achieved in 2013-2014

Concerted interdepartmental research along shared priorities and common goals on issues that are relevant to the mandates of multiple departments

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

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

The QIS project is a collaborative effort by 28 Principal Investigators from six departments and agencies, divided into five sub-projects and focusing on the protection of Canadian biodiversity and trade from the impacts of global change through an improved ability to monitor invasive alien and quarantine species. These species can cause millions of dollars in economic losses, result in trade disputes and border closures, cause irreversible environmental damage, and require vigilance and rapid responses when such a species is detected in Canada.

Sub-Project 1: Optimization and standardization of nucleic acid extractions

The objectives are to optimize and standardize methods for nucleic acid extraction for 1) preserved and archived tissues originating from the various federal collections and 2) bulk samples collected in the field for use in sensitive direct detection. Significant progress was made this fiscal year. Protocols for DNA extraction from the various samples have been tested and/or developed, and PCR primers were optimized. A detection assay for DNA from bulk insect samples and from environmental water samples has been developed. An insect sequence library was used to rapidly confirm the presence of a regulated quarantine pest at multiple locations beyond quarantine area boundaries in British Columbia. The team selected commercial kits and published protocols for double stranded RNA extraction of plant viruses. A DNA extraction Standard Operating Procedure (SOP) for sampling plant material from herbaria was developed. A microfluidic device prototype for the concentration of fungi of sizes ranging from 25 to 40 um was developed and tested.

Sub-Project 2: Barcoding of aquatic invasive species of highest risk to Canadian native fauna and trade

The objectives are to generate research outputs and outcomes that will (1) enable enforcement by DFO of impending Aquatic Invasive Species regulations that will be part of a new or revised Fisheries Act; and (2) support EC's primary responsibility areas of Ecosystem Sustainability – Protecting National Capital, and Environment Protection – Understanding Cumulative Risks. Significant progress was made this fiscal year. Eight species were contributed to the Royal Ontario Museum (ROM) collection, and issues with the preservation of samples and with the loss of traceability between previously submitted barcodes and vouchers have been identified. A total of 56 locations in British Columbia have been sampled for species of molluscs, crustaceans, and tunicates. Several hundred individual planktonic samples have also been obtained from Pacific, Atlantic, and Arctic Canada through collaboration with the Canadian Aquatic Invasive Species Network (CAISN II). The team has established strategies and workflows for specimen processing and over one thousand parasites specimens have been sent for sequencing.

Sub-Project 3: Barcoding of quarantine and invasive species in terrestrial ecosystems

The objective is to generate DNA barcode libraries that will provide baseline identifiers for confirmation of identities, focusing on species found in terrestrial ecosystems in Canada that are of quarantine significance and of economic importance to Canada. Significant accomplishments include: laboratory protocols for the production of DNA barcodes were developed and tested; complete barcodes for 1796 specimens and partial barcodes for 211 specimens have been developed; analyses of the barcode for Downy Mildew (*Peronospora manshurica*) were used to rapidly generate highly relevant information, addressing a regulatory export issue, to confirm that it would be nearly impossible to certify soybean as free of the mildew, and the information was transferred to the Canadian Grain Commission and CFIA and

used to address the regulatory challenge; cultures of the ten most unwanted forest fungal pathogens were obtained and DNA was successfully extracted; the experimental conditions for rapidly determining *Phytoplasma* spp contamination using archived samples was optimized and novel sets of universal primers for the different target groups were designed and optimized; and a loop-mediated isothermal amplification (LAMP) assay was also developed that was applied to many Canadian agricultural samples to determine the sequence of major phytoplasma strains circulating in Western Canada and that will be used for the first time directly in the field during the growing season of 2014.

Sub-Project 4: Direct detection of quarantine and invasive species

The objective is to address real, practical needs to detect invasive species in matrices not previously considered useable or to radically improve and expand on current detection methods, using next generation sequencing. A protocol for generating libraries for beetles and their fungal associates has been developed. Next generation sequencing parameters such as sensitivity and accuracy of detection, development of workflows, cost and methods validation are all being assessed and compared to current methods. NGS workflow software is being developed to automate the analysis of the NGS data to facilitate access through a web browser for diagnosticians. New collaborations are underway to have extraction methods and NGS methods validated and recognized by both the Canadian and American governments.

Sub-Project 5: Bioinformatics

The objective is to create a cyber-infrastructure platform to manage and analyse data generated by the QIS project. The team leveraged in-kind support for informatics, including core informatics staff, infrastructure, and applications in biodiversity bioinformatics at AAFC. Work is ongoing with Shared Services Canada and AAFC Information Systems Branch to provide access to other government department collaborators. Standards required for the capture and management of specimen vouchers, DNA extraction and sequencing information were evaluated and implemented in a custom-made spreadsheet as an intermediate step until other federal collaborators are able to directly access the project database. The AAFC database, SeqDB, has been updated to capture data generated by the QIS project, capturing to date 32,174 sequences (167.5 plates). In addition, several thousand sequences have been generated in-house and are being imported into SeqDB. Protocols for preparation and processing of samples for sequencing have been disseminated to collaborators. The team also successfully ported the core content of the Canadian Biodiversity Information Facility portal to a newly-developed, government-compliant web environment that can be reused toward the creation of a GRDI portal.

Food and Water Safety (FWS) Project

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

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

The FWS is a collaborative effort by six departments and agencies, divided into three sub-projects to develop the tools and infrastructure needed to apply genomics-based methods for pathogen isolation, detection, characterization, and source attribution, focusing on two priority microbial pathogens: verotoxigenic *Escherichia coli* (VTEC) and *Salmonella* Enteritidis. It includes the development of an integrated federal system to manage, store and provide open access to genomic data, genomic-based methods to increase the discrimination of risk assessment criteria and improved identification of pathogen sources. Activities are organised under three major themes, (1) *Isolation and Detection*, (2) *Information Generation* and (3) *Bioinformatics*.

Sub-Project 1: Isolation and Detection

The main objective is to develop genomics-based tools for the rapid isolation and detection of: 1) O157 and 2) six priority non-O157 VTEC, from a variety of food, water and environmental matrices. The detection and identification of pathogens in foods is highly dependent on the ability to extract and isolate the contaminant from highly complex food and environmental water matrices. To this end, scientists have aimed at isolating these pathogens either as whole intact cells or by extracting their nucleic acids. A number of isolation approaches have been investigated: filtration devices based on size exclusion or positively-charged membrane captures; metabolic labelling; monoclonal antibodies; a microfluidic-based device designed to isolate whole bacterial cells

from food matrices; and comparison of DNA extraction methods from soil and water samples. Work on enhancing the rapidity and sensitivity of detection of targeted food and waterborne microbial agents has resulted in the development of novel technologies (quantitative PCR assay; metagenomics sequencing in leafy greens; array-based photonic wire evanescent field instrument; microfluidic-based platform) that will significantly strengthen Canada's capacity to address food contamination threats. The microfluidic-based platform has been automated and deployed in a front-line CFIA regulatory testing laboratory for a rigorous assessment of its performance.

Sub-Project 2: Information Generation

Data of sequenced genomes of 191 non-O157 VTEC strains were added to the FWS database for analysis, bringing the total to date to 334 strains (total of 525 VTEC genomes including in-kind contributions). The total number of strains of Salmonella sequenced under the FWS project has now reached 79. Environment and food surveillance activities for VTEC and *Salmonella* Enteritidis are also generating a pan-Canadian awareness of pathogen type, prevalence, and sources, as well as of the factors contributing to their presence and persistence. New genomic-based tools are being validated for microbial source attribution and tracking. Analyses are being performed for VTEC risk assessment and risk modelling. Comparative genomic analysis is expected to identify unique genetic markers and protein features relevant for pathogen detection, for attribution to potential sources of contamination, and to aid in the selection of the best methods for VTEC identification in various sample types.

Sub-Project 3: Bioinformatics

Deliverables are centered on 1) the design and development of a computational platform for the storage, management, analysis, and reporting of microbial genomes and associated metadata; and 2) bioinformatics training workshops focusing on genomic epidemiology. Several important milestones have been achieved for the development of the Integrated Rapid Infectious Disease Analysis platform. A system for storing, managing and sharing whole genome sequence data is complete and under end-user testing. The ontology development team is complete and underway. Tools for genomic epidemiology have been integrated into the Galaxy workflow engine. A common look and feel has been designed and mock ups of the overall web application have been designed and refined by end users. Four training workshops on Microbial Genomics and Bioinformatics were held, training over 100 persons on the application of whole genome sequencing in modern microbial genomics analysis. This will provide public health workers with the ability to analyze whole genome sequence data for infectious disease tracking, outbreak response, pathogenomics, and population dynamics. PHAC scientists are members and active participants in the Global Microbial Identifier, a consortium of over 200 scientists from over 30 different countries working together to build a roadmap for the implementation of a global genomic epidemiology platform and network.

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

With support from the GRDI, NRC scientists are developing a new generation of targeted therapy for cancers – antibody-drug conjugates – and are actively collaborating with several Canadian companies. NRC and Zymeworks Inc., a Canadian biotherapeutics company and a world leader in antibody therapeutics, announced a new strategic collaborative agreement for the development of biotherapeutics in March 2013. This three-year multi-million dollar agreement will focus on developing ground-breaking therapies for the fight against cancer, as well as inflammatory and autoimmune diseases. To date, NRC has produced and characterized over 6000 virtually-designed proteins to meet Zymeworks' needs and greatly accelerate its therapeutics and platform developments.

The partnership with AVIDBiologics, first announced in January 2013, continues for the development and preclinical validation of three novel antibody-drug conjugates for the treatment of cancer. The antibody-drug conjugates are directed at cell surface targets which are highly expressed by multiple cancers, exhibit tumor restricted expression, and are rapidly internalized. These targets were selected from a list of cancer antigens generated through NRC's chain of cutting edge genomic, proteomic and bioinformatics technology platforms. Several other Canadian partners are currently evaluating other targets from the list for potential therapeutic antibody development.

In May 2013, Alethia Biotherapeutics, a long time NRC collaborator, announced a global strategic alliance with the International Biotechnology Center Generium to jointly develop AB-16B5, a monoclonal antibody inhibitor of epithelial-to-mesenchymal transition. This antibody targets a specific epitope of the secreted Clusterin protein and inhibits the ability of the protein to induce epithelial-to-mesenchymal transition. This patented technology was developed at NRC with the support of GRDI and licensed to Alethia.

In March 2014, NRC held its highly regarded life science technology showcase event, BioTransfer, in Toronto for the first time. The event, held in conjunction with several academic partners from across the country, covered biotherapeutics, diagnostics and medical devices and included several technologies whose development was supported by the GRDI. Attendance was excellent, with representatives from academia, industry and venture capital and over 100 business-to-business meetings were scheduled by interested parties.

Genomic knowledge for the Canadian health regulatory system

Genomic characterization of foodborne isolates of *Campylobacter* and *Listeria*

In this project, HC researchers developed a rapid, automated method to sequence and analyse bacterial DNA. Applying this method, the research team sequenced the complete genomes of 150 different isolates of *Campylobacter jejuni* and more than 200 isolates of *Listeria monocytogenes* – two key foodborne pathogens. They identified several important genes and DNA markers associated with different bacteria strains, which will be incorporated into diagnostic tests to help enhance the safety and quality of our food system. For example, research data was used to identify DNA sequences associated with the geographic, temporal, environmental or animal origin of various bacteria strains, as well as biological properties such as the ability of pathogens to resist exposure to stress, infect humans or cause severe symptoms. Results from this project have potential applications in industry, health care, disease surveillance, regulations and health policy – they will enable the food industry, food inspectors and health risk assessors to address problems arising from the presence of important foodborne pathogens.

Genomic assessment of chemical food contaminants leading to food allergy

In recent decades, the incidence of food allergy in Canada has been increasing for unknown reasons. Health Canada researchers set out to develop genomics-based tools to screen specific chemicals for their effects on the development of food allergy. To do so, they produced a cell culture assay that measures the effects of chemicals on immune biomarkers that are related to food allergy risk. Overall, this project has yielded data of interest to toxicologists and regulators in the evaluation of novel food additives and contaminants, including colouring agents and nanomaterials. The success of this research provides toxicologists with a new tool to assess the ability of chemicals to alter immune responses, and to search for the underlying causes behind the increasing incidence of allergic disease.

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

The purpose of this project was to develop a more rapid approach than the standard 2-year cancer bioassay for assessing the potential carcinogenicity of fungal toxins. In the last fiscal year, HC researchers completed the microRNA (miRNA) profiling of target organs from transgenic mice exposed to four important fungal toxins. In addition, the team successfully detected and identified miRNA changes in the serum from mice exposed to fungal toxins. This work will enable the development of rapid methods for detecting toxicity in humans, and thereby enhance our ability to detect and respond to the presence of fungal toxins in food consumed by Canadians. The long term benefit is improved health for Canadians and improved food safety.

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

Stem cells have tremendous potential to treat diseases for which there are currently no cures – however, the use of stem cells is not without risk. In this project, HC researchers are developing diagnostic tools that allow thorough evaluation of the risks and benefits associated with the therapeutic use of human mesenchymal stem cells (MSCs), a type of adult stem cell. Data describing the team's progress in understanding the cancer risks associated with MSCs has been published in several peer-reviewed journals. In addition, the team has generated a list of potential biomarkers that identify MSCs that are

both safe and effective for treating diabetes. These biomarkers are now being validated to determine whether they distinguish between stem cells that can treat diabetes and those with the potential to form cancerous tumours.

Integrating genomics endpoints into regulatory toxicology

A cell culture methodology was developed and validated to screen chemical agents for potential genotoxic (DNA damaging) mechanisms of action. The system is able to differentiate between known genotoxic and non-genotoxic agents and can be applied in various cell culture systems. This project is one component 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.

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

In the first study of its kind, HC researchers systematically investigated the toxic effects of individual polyaromatic hydrocarbons, as well as synthetic and complex mixtures of polyaromatic hydrocarbons on specific tissues of exposure. The team exposed mice to simple mixtures of four and eight polyaromatic hydrocarbons, collected gene expression data from various mouse tissues, and prepared the results for publication. Preliminary data analyses show that their toxicity in a mixture is not additive. This suggests the need to rethink current methods for assessing the risk of complex mixtures, which are based largely on the assumption that individual components of a given mixture act via similar mechanisms in an additive fashion.

Genomics knowledge to strengthen public health programs and activities related to infectious and chronic disease

Development of rapid methods for molecular typing of *Salmonella*

Two complementary projects focused 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 first approach involved an international collaboration between the Animal Health and Veterinary Laboratories Agency in the United Kingdom, the Austrian Institute of Technology in Austria, and the Laboratory for Foodborne Zoonoses, PHAC. These partners developed and validated a molecular typing tool that rapidly and inexpensively identifies serotypes of *Salmonella* based on DNA sequences. The new assay reduces testing time over traditional methods from 7 to 1 day, thereby increasing diagnostic turnaround time, and reducing costs. This assay will now be transferred to several public health laboratories to take advantage of the technical advancement including the PHAC Reference Laboratory for Salmonellosis, the National Microbiology Laboratory (PHAC), and the Public Health Ontario Laboratory.

In an alternative approach, GRDI researchers developed a new method to characterise strains of *Salmonella* Enteritidis, which is responsible for 40% of Salmonellosis in Canada. Previously, subtyping methods for S. Enteritidis were limited, impairing the ability of public health labs to identify outbreaks and conduct effective traceback. The new genomics-based tool, will facilitate these public health responses, thereby improving the response capacity of the public health system, enhancing food safety and reduce the burden of illness.

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

GRDI researchers have developed laboratory and analytical techniques to support genomic epidemiology-based investigations of foodborne pathogens such as *E.coli*. These techniques include the development of custom genome databases, bioinformatics tools, and analytical pipelines, for the analysis of genome sequence data in support of rapid response to public health events. Shiga-toxin producing *Escherichia coli* (STEC) are associated with outbreaks of severe human disease characterized by bloody diarrhea and kidney failure. However, STEC vary considerably in the frequency and severity with which they are associated with human disease. GRDI researchers are developing genomic methods to differentiate strains of STEC that pose the greatest risk of causing severe human disease from those strains that are more likely to be restricted to animals or rarely associated with human disease. In addition, the genomic regions associated with human disease will also be of interest to investigate as targets for therapeutics such as vaccines and in designing/enhancing molecular typing methods for STEC. The data and

software tools generated by this work have been made publicly available to share with researchers from around the world. Work to further develop these tools will continue in Phase VI of the GRDI.

Other Infectious Pathogens

Tuberculosis is a re-emerging priority infectious disease in Canada and disproportionately affects immigrant and Canadian-born Aboriginal populations, however, the interplay between host and environmental factors that predispose humans to tuberculosis remains poorly understood. Emerging evidence suggests that the innate immune response to tuberculosis is dependent upon vitamin D, however, there is variation in how vitamin D modulates innate immunity and that variation is dependent upon host genetic make-up and environmental factors. Studies have focused on identifying the role of vitamin D in controlling the risk for tuberculosis infection. Variations among the genes involved in vitamin D biology have been characterised in large populations of infected and non-infected individuals. Strikingly, common variants were detected that were associated with resistance to becoming infected. These results will be followed up with further studies to study possible mechanisms through which vitamin D biology influence susceptibility to tuberculosis infection. In related studies, genomic analysis of rare variants in vitamin D related pathways were identified. Those findings are being confirmed through the study of other tuberculosis infected subpopulations. The results of these experiments identify vitamin D related pathways in the control risk of tuberculosis and its transmission. Further studies will be needed to determine how a modifiable risk factor of a common disease and the host genetic background can be used jointly in improved disease control.

Antiretroviral therapy has dramatically decreased the morbidity and mortality due to HIV. However, HIV drug resistance constitutes a major limitation to maximizing the clinical benefit of antiretroviral therapy. An up-to-date HIV drug resistance testing method that addresses these issues is urgently needed. By combining DNA sequencing, DNA barcoding and advanced bioinformatics technologies, PHAC researchers have created a testing method that covers all the viral genes targeted by antiretroviral therapy. In addition, an automated data analysis pipeline has been developed to support the technique. An internet-based HIV drug resistance analysis web server has been developed that takes the analyzed data and formats the results into reports that are accessible to clinicians. This web server will enable remote access to analytic results and allow users to upload data through internet, customize analysis settings, visualize and retrieve user-interpretable HIV drug resistance reports and related data sets. This final piece of the drug resistance platform is in the process of being implemented with clinician collaborators.

The rise in prevalence of infectious pathogens with resistance to antibiotics is a critical development that threatens our capacity to provide effective health care. GRDI researchers have developed genomic epidemiological tools to better understand the spread of the superbugs through whole genome sequencing and by using methods to determine the genetic sequence of transmissible genetic elements that spread resistance genes with bacterial populations and even between species. The application of these tools promises to lead to a better understanding of how these bacteria spread in our hospitals, and ultimately to the application of the new knowledge generated to reduce the infections and deaths caused by these superbugs.

Bioinformatics Tools

To facilitate the rapid analysis of genomic sequence data, an automated genome annotation system has been developed. In benchmark evaluations, the annotation system developed by PHAC researchers outperformed other tested genome annotation systems. This expert system will advance microbial genomics by increasing the reliability of genome annotations which are growing in importance as government policy makers increasingly are relying on the genomics and big data solutions to advance public health mandates and priorities. Examples of the benefits of this system include: increased ability to accurately detect virulence factors and antimicrobial resistance genes in a high throughput genomic screening for surveillance setting. Long term benefits of this work include increased food and water safety and security, and enhanced monitoring and control of nosocomial infections.

Other researchers have created open source software, termed Panseq, to compare the genes present among a collection of bacterial genomic sequences. This analysis is used to detect strain-specific virulence factors and to investigate pathogens of epidemic diseases by scanning

variations in essential genes. Panseq is publicly available on a website (http://lfz.corefacility.ca/panseq) and as a stand-alone version.

SuperPhy is another publicly available bioinformatics software application developed with GRDI support. It allows easy identification of: 1) virulence and antimicrobial resistance determinants 2) epidemiological associations between specific genotypes, biomarkers, geospatial distribution, host, source, and other meta-data; 3) statistically significant clade-specific genome markers (presence/ absence of specific genomic regions, and single-nucleotide polymorphisms) in bacterial populations; 4) *in silico* molecular type for traditional wet-lab typing methods including multi-locus sequence typing, comparative genomic fingerprinting, Shiga-toxin subtyping and serotyping. The SuperPhy platform will help inform researchers looking at large STEC collections, in assigning strains to phylogenetic lineages and sub-groups and in identifying virulence and antimicrobial resistance determinants.

The Panseq and SuperPhy platforms currently house over 1000 in-house and publicly available *E. coli* genomic sequences, as well as the analytical tools to perform epidemiological and comparative inquiries by users with and without bioinformatics training.

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

The Canadian Wheat Improvement flagship program, funded in part by GRDI, is NRC's contribution to a large-scale research alliance established to improve the yield, sustainability, and profitability of Canadian wheat for the benefits of Canadian farmers and the economy. The Canadian Wheat Alliance includes major contributions by NRC, AAFC, the University of Saskatchewan, and the Province of Saskatchewan. NRC continued to solidify existing collaborations and to develop additional collaborations with industry and other national and international institutions. For example, NRC and AAFC signed a collaboration agreement with the (CIMMYT) in the area of durum wheat diseases. CIMMYT is one of the largest wheat R&D institutions with significant resources and expertise in wheat breeding and the largest collection of wheat germplasm in the world.

This program has developed strong expertise in genomics and developmental aspects relevant to performance and yield in wheat. Highlights of scientific progress are as follows:

1) Genomics Assisted Breeding: Optimal Single Nucleotide Polymorphism (SNP) discovery was established for the hexaploid wheat genome and provided a deep allele inventory for Canadian wheat. Multiple genetic mapping populations have been characterized and candidate genes were identified for some target genes. The coding regions of 43 Canadian wheat lines were sequenced to provide an important inventory of genetic variations, and candidate genes were identified for some target traits. Half of chromosome (5RL) has been sequenced and assembled as part of the cold tolerance activity and half chromosome (7EL) of wheat fusarium resistant lines has been sequenced and assembled.

2) Enhancing Fusarium and Rust Resistance: Re-sequencing of rust isolates revealed a rapid evolution, highlighting the importance of finding new sources of resistance. Three fusarium head blight susceptibility genes were identified and validated, and mutations for at least one of these genes were identified for potential introduction to confer resistance to new varieties.

3) Improving Wheat Productivity under Conditions of Abiotic Stress: Drought related traits ready for genetic analysis and gene identification in durum populations as first step in developing molecular tools for water usage efficiency in spring wheat.

4) Targeting Developmental Pathways to improve Performance and Yield in Wheat: Detailed cellular and developmental analyses were completed for key stages of embryo and seed tissues in wheat. The genomic analysis revealed the expression of ~80,000 genes during grain development in hexaploid progenitor lines. Metabolite analyses revealed distinct early and late stage dominant biochemical pathways and also different metabolic activities in embryo and endosperm compartments, which provide knowledge for improving seed yield and performance.

Genomics has become an essential component of the agricultural research toolbox as the industry strives to develop new and innovative products and processes, and maximize production in the face of

increasing population and climate change. In 2013-2014, AAFC scientists continued to build on project results described in the 2012-2013 Annual Report under the three themes outlined below.

Biodiversity, gene mining and functional analysis for the identification and extraction of genes for desirable traits

Fifteen of AAFC's nineteen GRDI projects are focussed on the use of genomics to discover and employ genes for desirable traits to address major disease and insect challenges in wheat, canola, potatoes and soybeans, and to generate new value-added opportunities for the sector. Global crop losses due to diseases and insects are a major factor impacting food security, and cost producers billions of dollars annually in lost yields. New diseases and pests, and new more virulent strains of existing diseases and pests, continually threaten Canadian crops driving the need for sustained genomics research to identify new resistance genes, understand the genetics and biology of resistance and virulence, and deploy resistance genes into new cultivars. Canada is dependent on global trade of agricultural products and as markets change driving a need for new and innovative crops and agricultural products, genomics research is playing a key role in ensuring the continued profitability of the sector. Research highlights include:

Significant progress has been made towards understanding plant resistance/susceptibility to fusarium head blight and fungal infection mechanisms. New knowledge generated by this work will contribute significantly to the development of novel strategies to manage fusarium diseases of cereal crops, and to improve the stability and safety of grain production. This research has led to a number of national and international partnerships.

Since grain samples are often contaminated by multiple fusarium species, methods were established to detect and validate the production of and biological relevance of multiple mycotoxins produced by co-infecting fusarium species. Data collected on the effects of competition between fungal species co-inoculated on wheat demonstrate the need for further studies on multi-toxin synergistic effects.

A seventh allele associated with the stem rust resistance gene Sr9 has been discovered that confers resistance to the recently discovered and highly virulent stem rust race Ug99. An improved genetic map of the Sr9 region has been produced, flanking DNA markers have been identified, and DNA markers tightly linked to Sr9 identified. This progress will enable scientists to predict which genes will provide more durable resistance and support the development of allele-specific markers for marker-assisted breeding to develop new stem rust resistant varieties of wheat.

Using genomics tools, scientists have identified valuable biodiversity from germplasm collections of canola and Ethiopian mustard as well as the wider Brassica germplasm base (including progenitor and wild species). The genome structure of plants with varying ability to acclimate to adverse conditions has been further described and potential regions of the genome essential for controlling this ability have been identified. This knowledge will be used as a tool in breeding programs to rapidly address the ability of canola and other Brassica crops to remain highly productive under stressful conditions. Data generated from this GRDI project also supports a number of related industry-led and funded projects.

New knowledge regarding the mechanism by which the soybean mosaic virus infects the soybean plant at the molecular level has demonstrated the important role of small and micro RNAs in infection and breakdown of gene-mediated resistance. Further advancement of this knowledge will support breeding programs to develop soybean varieties with stronger resistance to soybean mosaic virus, currently one of the most serious disease organisms affecting soybean production in Canada.

Researchers have demonstrated that genotyping-by-sequencing is a rapid, cost effective, and genetically robust method for genetic improvement of oat varieties that can be applied directly in germplasm screening and molecular breeding efforts. The GRDI has enabled Canada to engage in international collaborations and it is largely through early reports from GRDI supported research that the oat community has quickly adopted genotyping-by-sequencing and applied it in their breeding programs.

The soil-borne plant pathogen *Phytophthora sojae* causes widespread damage in Canadian soybean crops and can result in annual production losses of $40-$50 million a year in Canada. Based on new knowledge surrounding the inheritance of the pathogen's ability to infect plants, new quick and

inexpensive diagnostic tests are being developed to identify which strains of *Phytophtora sojae* are present in soybean fields so that farmers can select a soybean variety that carries resistance genes for those strains.

The expression of the Lr34 gene, which confers resistance to leaf rust in wheat, is variable depending on the genetic background of the wheat cultivar into which it is incorporated. In addition, it is known to have a synergistic effect on other resistance genes. New genetic stocks have been created that will enable the Lr34 gene to be evaluated in different genetic backgrounds. This information will enable breeders to combine Lr34 and other resistance genes into appropriate wheat backgrounds in order to achieve enhanced durable rust resistance.

The generation of genomic and proteomic resources for obligate biotrophic pathogens, such as the cereal rust fungi, has tremendously accelerated research into their infection strategies. This allows scientists to better understand and address stem and leaf rust diseases in wheat. For example, genome-wide comparisons and association studies have pointed to candidate virulence factors that trigger resistance in certain wheat cultivars. Such avirulence effectors can be used to screen germplasm for novel sources of resistance.

Little is known about the underlying biodiversity of the Bertha Army Worm (BAW), a major pest of canola in Canada, and how this will impact the development of biologically-based control strategies. A draft genome for BAW has been produced, and genetic markers are being developed to explore the genetic diversity of geographic populations of this pest. Field populations of BAW were screened for epizootics of virus and fungal pathogens. Several novel strains of baculoviruses were identified which showed high virulence towards BAW and they will be used to investigate genes that may be exploited in novel insect control methods such as biopesticides.

Critical genomics resources for potato improvement have been established that will facilitate the development of a potato genomics-assisted breeding pipeline. Phenotypic characterization of a diverse range of potato genetic resources for late blight resistance and critical adaptation and quality traits was achieved and SNP data was generated using DNA from advanced breeding lines that will be used in a pilot genomic selection project.

A small number of plant families, primarily legumes like peas and soybeans, don't require industrial nitrogen because they have the ability to obtain their own nitrogen through a symbiotic relationship with nitrogen-fixing bacteria found in the soil. Researchers have discovered the genetic mechanism by which plants recognize the beneficial bacteria which in turn leads to the initiation of a process known as nodule formation, whereby root cells change to accommodate the bacteria and support symbiotic nitrogen fixation. This knowledge underpins further research that aims to transfer the symbiotic nitrogen fixation process to food crops, mostly cereals, which currently rely on industrial fertilization.

Using samples from animals that vary in their ability to efficiently digest lignocellulosic material in the rumen, researchers have identified the most important classes of glycoside hydrolases that contribute to the breakdown and digestion of fibre. Results pointed towards specific classes of carbohydrate active enzymes that are severely under-represented in all existing metagenome data sets, yet are highly expressed in the microbial population actively breaking down feedstuffs in the rumen. Also, based on the use of total RNA sequencing, first time information about the complete active microbial communities in the rumen, including anaerobic fungi, can be evaluated. This discovery will be used across many projects that evaluate microbial ecology and effects on animal performance and health.

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

There is a need to invest in developing novel ways to interact with genomics data that has been generated to date and that which is in-progress (e.g. genome sequences and metagenomic profiles). A number of platforms (Microsoft Surface, Samsung SUR40, and Perceptive Pixel) have been evaluated and software has been developed that can combine bioinformatic analysis with multi-touch interactions. Application areas that have been prototyped include phylogenetic

trees, genome browsing and the ability to develop collaborative storyboards in the analysis of complex data.

Enhanced efficiency of plant breeding

New knowledge and tools pertaining to pollen and stigma proteomes were generated. Triticeae pollen- and tapetum-specific promoters were introduced into *Brachypodium distachyon* and plants with these promoters were generated for use in future research to increase crop productivity by mitigating the impacts of temperature stress on pollination.

The use of the MutS system as a means to increase meiotic recombination in *Brassica napus* plants using the Arabidopsis model was validated with early phenotypic results supporting its functionality. Genetic tools were established to enable quantification of the effect of MutS in *B. napus* in subsequent research. Future application of the MutS technology combined with results from a related experiment regarding a native *B. napus* gene that controls the stringency of chromosome pairing and exchange during meiosis holds great promise to enable development of novel genetic diversity in *B. napus* for breeding improved varieties.

Genomic knowledge for forest generation and protection

Identification of genes controlling desirable attributes in economically important tree species

This project looks to understand how to efficiently build the forest of the future by using trees from today's forests that have the desired traits. The project is complimentary to a Genome Canada funded project, SMarTForests. The desired traits relate to fibre quality and forest sustainability, such as: phenology and growth; wood quality characteristics; resistance to biotic and abiotic factors; and adaptation to environmental change. Central to this project is the creation of genomics based markers that help identify and select trees at an early age that possess these desirable traits.

2013-2014 saw advances towards this goal by the development of models that provide accurate predictions of wood and growth traits in young trees. Transfer of these technologies to end users, who have tree breeding programs such as JD Irving, has begun. Research on other traits such as phenology, adaptation, resistance mechanisms to forest pests and wood chemistry continued.

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. Provincial governments rely on decision support systems (DSS) to inform their forest managers on how to proceed with the management of insect pests. CFS researchers have identified genetic markers that will assist pest management by their ability to identify and track migrant spruce budworm, thus potentially minimizing its spread.

Few control options exist for the spruce budworm. In an effort to add new tools for their management, the team examined genes involved in overwintering in an effort to disrupt the natural process. These genes are responsible for the creation of anti-freeze proteins, essential for budworm winter survival.

CFS researchers are using genomics to develop potential management tools for the emerald ash borer (EAB). The EAB is a wood boring beetle, originally from Asia, causing severe economic and ecological damage to native ash trees. Whereas the work on spruce budworm is looking to disrupt the pests' ability to survive the winter, scientists working with the EAB are investigating genes involved in molting (a process that allows the insect to grow). Interfering with the molting process kills the EAB.

A different avenue being examined toward the production of management tools for EAB involves searching for fungi that live on ash trees but are lethal to the pest. The same species of fungus may have many strains and the different strains may vary in their degree of lethalness. Genomic approaches used by

CFS scientists have allowed them to find candidate strains that can survive on ash trees and are lethal to EAB.

Future forests will benefit from having trees that are resistant to pests and pathogens, especially in this era of changing climate and increased global trade. Research by CFS scientists focused on identifying and understanding the genes in fungi that infect trees and the genes in trees that resist fungal attack. Work focused on two fungal diseases, white pine blister rust and poplar leaf rust. Genomic tests for resistance to white pine blister rust are ready to be transferred to breeding programs.

Prevention is the best strategy for forest health. Less than 10% of the world's estimated 1.5 million fungal species have been described, therefore the potential for unidentified emerging pathogens finding their way to Canada and establishing themselves could be overwhelming. The research on pathogens supported by GRDI funds is complementary to a Genome Canada funded project, TAIGA. The research is developing tools to detect potentially damaging fungi. By comparing the genomic sequences of various pathogens, CFS researchers examined genes that are related to pathogenicity, or the ability to kill, for the early detection of fungi with pathogenic potential. Detection is not the only application for genomics-based tools, they can also assist in monitoring appearance and spread. Sequencing the genomes of known disease causing pathogens (such as the causal agents of white pine blister rust, sudden oak death and poplar canker) allowed the scientists to better understand patterns of epidemics and identify pathways of introductions.

Genomics knowledge and advice for the management of fisheries and oceans

For Phase V of the GRDI, eight genomics research projects are underway at DFO 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 non-pathogenic infectious salmon anemia virus and subsequent exposures to pathogenic strains; and characterize the genomics of infectious hematopoietic necrosis virus carrier state in Sockeye salmon and physiologically compromised Pacific salmon.

Examples of the emerging results and outcomes of DFO's genomics research projects from the previous GRDI phase include the following:

Conservation genomics of Atlantic Salmon in Newfoundland and Labrador

Conservation of threatened Atlantic salmon populations around Newfoundland and Labrador is a major goal for DFO. Through sampling of wild Atlantic salmon from conservation units around Newfoundland and from aquaculture samples representative of all strains cultured on the South Coast of Newfoundland, researchers developed microsatellite-based marker systems for identifying aquaculture escapes in wild populations. Genetic data on wild Atlantic salmon in Newfoundland and Labrador contributed to science-based recommendations provided to protect Canada's wild populations of Atlantic salmon and became instrumental in enabling government enforcement officers in forensic analysis to identify confiscated fish products and trace them to their species or stock of origin.

Discriminating capelin populations in the Northwest Atlantic

Capelin is a commercially exploited, key forage-fish species found in the boreal waters of the North Pacific and North Atlantic, with four capelin stocks assumed to inhabit the northwest Atlantic based on meristic, morphometric, tag returns, and seasonal distribution patterns. Researchers examined the population structure of capelin in the Canadian northwest Atlantic using genetic-based methods results suggest groupings that are somewhat different than the contemporary stock structure used for fisheries management and indicate that some changes in management practices may be required.

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

This research was integrated into a Genome BC funded research project, Genomics in Lice and Salmon. The combined research has contributed to unprecedented advances in sea lice genomics. Genomics tools including a novel 38K microarray and

a suite of over 100 variable microsatellites as molecular markers for salmon louse were developed. These tools were applied to gene transcription analyses (microarray development and quantitative Polymerase Chain Reaction) and chemical interaction analyses which are fundamental to vaccine target identification, species and population analysis. Population-level analyses of salmon louse in British Columbia, and more widely within the Pacific and Atlantic Oceans, showed evidence of virtually unrestricted gene flow among populations within both Ocean basins, likely the result of parasitism on highly migratory salmonid hosts. Comparative infection experiments revealed evidence for a diversity of response mechanisms to salmon louse among salmon species and revealed insight into the early development of natural resistance.

Genetic monitoring and conservation of beluga whales in the Western Canadian Arctic

This project has investigated genetic stock structure in beluga aggregations in the Beaufort Sea to identify management units for monitoring the effects of human activity and the impacts of climate change. The areas used by summer aggregations of beluga in the Mackenzie River Delta have been designated as part of the Tarium Niryutait Marine Protected Area, with a conservation objective of maintaining the genetic fitness and integrity of beluga assemblages. Results suggest that there is a social structure within the Beaufort Sea stock of beluga whales. As belugas taken during the hunt in the Beaufort Sea have a very strong male bias, this dataset provides an opportunity to investigate the relatedness patterns in groups of male belugas.

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

Population genetic patterns can shed light on many aspects of natural populations that are relevant to conservation, resource, or ecosystem management. Genomics methods were used to identify species of tunicates that invade British Columbia and Oregon and to characterize their populations. Population structures will be compared to invasion vector maps to better understand how this species may be spreading in the Pacific Northwest and what intervention options exist to limit its spread to new locations.

Microbial characterization of produced water and its influence on the microbial community in the marine environment around offshore oil and gas production platforms

Microorganisms play essential roles in global processes ranging from the recycling of matter in our air, water and soil, to causing or preventing disease in plants, animals, and humans. Until recently, we have lacked the tools to address fundamental questions about natural microbial population structures. The purpose of this project was to characterize the natural populations of microorganisms in the ecosystem around the Hibernia platform and in the produced water of the oil and gas production platforms. Key microorganisms were identified and quantified that may be used as tracer microorganisms for produced water. With improvements to detection methods, these particular signature microorganisms may be useful as markers to monitor the dispersion of produced water in the surrounding ocean. Knowledge gained from this project will be useful for the development of future protocols for regulatory and policy development.

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

In 2013-2014, EC developed genomics tools and approaches to support regulatory compliance and enforcement, wildlife management, pollution prevention, and risk assessment of potentially toxic substances. This was achieved by building environmental genomics capacity based on the four priority research areas described below.

Strengthen predictive models

Efforts were undertaken to improve the efficiency and accuracy of models to predict the effects of chemical exposure by building a better understanding of the molecular mechanisms underlying the overt toxicological effects of chemicals in both wildlife and aquatic life. For instance, genomics tools and approaches were developed to examine the impact of existing and emerging chemicals (i.e., their transport, fate, effects, and associated risks) on the biology and physiology of organisms as well as biodiversity and ecosystem functions. In particular, related research focused on assessing microbial function, activity, and biodiversity in response to naturally occurring and anthropogenic contaminants in aquatic ecosystems.

Better understanding microbial characteristics significantly enhances the accuracy of the models which contribute to improved risk assessment.

Understand and monitor ecosystems

Environment Canada continued focus its R&D activities on understanding and monitoring aquatic and land-based ecosystems. Tools and approaches were developed to examine the movement and habitat requirements of populations at risk; and to monitor the toxicological impacts of substances released into priority ecosystems, such as the Great Lakes. The application of this work enables EC scientists to better understand changes in marine bird species, such as the Black legged Kittiwake and the Purple Sandpipers, and to better monitor the impacts of pollutants on aquatic life such as fish and wood frogs.

Understand cumulative risk and impacts

R&D activities focused on the development of tools to advance our understanding of cumulative environmental impacts and related risks associated with multiple stressors interacting over time. Genomic techniques were developed to investigate wildlife stress and its effects on immune functions, reproduction, and survival. For example, EC scientists developed and validated the use of feather corticosterone concentrations as a measure of stress in wild birds, as well as other techniques to identify biomarkers associated with chronic stress. This research will support conservation efforts by helping to identify the implications of large scale environmental changes on wildlife populations and biodiversity.

Manage environmental risks

Environment Canada's scientists developed various innovative methods and tools to support the management of environmental risks posed by chemical, biological, and physical pollutants. One method entailed exposing a crustacean microarray to varying levels of contaminants and examining their effects on specific genes. By using this method, scientists were able to demonstrate significant changes in gene expression in certain species due to contaminant exposure. These methods support regulations such as the 1999 Disposal at Sea Regulations under the *Canadian Environmental Protection Act* as well as the department role under the *Fisheries Act*.

APPENDIX A

Annex 4 – Research tools and processes produced by the GRDI

Research tools:

- Microbial In Silico Typer software to simulate/predict the results of multiple molecular sub-typing methods from draft-genome sequence data (FWS);
- GView software to view, interact, investigate, and markup bacterial genomic sequence data (FWS);
- GView Server, web site (https://server.gview.ca) hosting commonly applied comparative analysis tools (FWS);
- SNP Phylogenomics Pipeline software to extract phylogenetically informative SNPs from whole genome sequences, and use them to build a phylogenomic tree (FWS);
- Short Read Archive to allow storage of raw sequence reads with project data management and authenticated security (FWS);
- Protocols for the extraction of nucleic acids from marine vertebrates and invertebrates(QIS);
- Protocols for the extraction of nucleic acids from field and bulk samples (QIS);
- New set of degenerate PCR primers for amplifying and sequencing specific DNA regions in parasitic flatworms (digeneans and cestodes) (QIS);
- Novel PCR assay to detect the cpn60 gene of Phytoplasma spp (QIS);
- New set of primers for barcodes of several plant families (QIS);
- Canadian Biodiversity Information Facility web portal (QIS);
- SeqDB: GRDI project database(QIS);
- Novel candidate genes for resistance in FHB-resistant wheat line CS-7EL (AAFC);
- Eight sequenced *Fusarium graminearum* genomes (AAFC);
- Fusarium microarray data deposition #GSE56340 in NCBI GEO (AAFC);
- 43 fusarium strains identified, cultured and deposited in the Canadian Culture Fungal Collection (AAFC);
- Improved physical, genetic, and cytogenetic map of oat (AAFC);
- Genome sequence for *Camelina sativa* (AAFC);
- Lr34 transgene in genetic background lacking native Lr34 (AAFC);
- Lr34 promoter deletion series of wheat lines (AAFC);
- Genome sequences of two Canadian *Fusarium avenaceum* isolates (AAFC);
- Improved genetic map of the Sr9 gene that confers resistance to wheat rust, flanking and tightly linked DNA markers (AAFC);
- Knockout gene function mutants for three alleles of Sr9 (AAFC);
- RAD tag sequence database for BAW moths from 5 locations across Western Canada (AAFC);
- 200 SNPs identified and mapped on the draft BAW worm genome (AAFC);
- Genome sequences for 50 field strains of the baculovirus, *Mametra configurata nucleo-polyhedrovirus* from BAW populations across western Canada (AAFC);
- Novel cereal and oilseed anther-specific promoters to manipulate crop fertility (AAFC);
- Validation of use of MutS as a means to increase meiotic recombination in plants using the Arabidopsis model (AAFC);
- Genetic tools to enable quantifying the effect of MutS in *B. napus* (AAFC);

- Genetic platform and tools for assessing other strategies to modulate meiotic recombination frequency in *B. napus* (AAFC);
- Major locus controlling recombination between homoeologues mapped in *B. napus* (AAFC);
- Novel germplasm for use in research and breeding programs nationally and internationally (AAFC);
- DNA extraction protocols for archived Atlantic salmon (*Salmo* salar) scales (DFO);
- DNA markers for genotyping wild and farmed Atlantic salmon (*Salmo* salar) (DFO);
- Complete mitochondrial genome sequencing from each of the five beluga (*Delphinapterus leucas*) Canadian populations (DFO);
- Database of highly polymorphic region (HPR) types of Infectious Salmon Anaemia Virus (ISAV) from different strains of Atlantic salmon (*Salmo salar*) (DFO);
- High throughput methodology for monitoring 45 different microbes relevant to fisheries, aquaculture and salmon enhancement facilities (DFO);
- Reverse transcription quantitative polymerase chain reaction method for identification of contaminant exposure in crustaceans (EC);
- Agilent 44K Chicken Microarray for screening for potential toxic effects of priority environmental contaminants in birds (EC);
- In situ incubation device for growth and development of microbial communities (EC);
- Variable microsatellite loci for Purple Sandpiper for genetic studies of other related shorebirds (EC);
- Purple Sandpiper mtDNA sequences of cytochrome-b and ND2 for phylogeny and phylogeographic studies (EC);
- Sequencing of the retroviral element associated with clam leukemia (EC);
- Shotgun analysis methods for the analysis of fish plasma protein (EC);
- Rainbow Trout brain and white sucker liver transcriptome sequences (EC);
- Bioinformatics pipe-line for the analysis for RNA sequence data (EC);
- Denature gradient gel electrophoresis, clonal/restriction fragment length polymorphism and next generation sequencing for the detection of microbial species (EC);
- Luminex 200 system for the detection of microbial strains (EC);
- Cyanobacteria Blooms (cHAB) strain collection characterized for toxin and volatile organic compound producing gene sequences (EC);
- Single cell genomics and Fast Technology for Analysis Cards for cHABs for source tracking (EC);
- Chronic Daphnia magna exposure test using genomic and phenotypic anchoring (EC);
- qPCR procedures for detecting and quatifying DNA of Human Bacteriodales gut bacteria, ruminant (cow) Bacteriodales gut bacteria, and seagull Catellicoccus gut bacteria in water samples for microbial source tracking (EC);
- Genomic characterization of clinically important foodborne isolates of Campylobacter and Listeria impacting public health (HC);
- Standard operating procedures for generating and conducting whole genome sequences of two key foodborne pathogens, Listeria, and Campylobacter (HC);
- Genomic assessment of chemical food contaminants leading to food allergy (HC);
- Assay for regulators to screen chemical food additives and contaminants for their ability to activate the immune system and increase the risk of food allergies (HC);
- Genomic characterization of tissues from P53+/- transgenic mice exposed to genotoxic and non-genotoxic carcinogens for developing short term cancer bioassays (HC);
- Improved screening assay for regulators to more rapidly detect and identify miRNA changes in serum and tissue resulting from fungal toxin exposure (HC);

- 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 (HC);
- Scientific diagnostic tools for regulators to evaluate human mesenchymal stem cells' complex protein mixtures and their potential to form cancerous tumours (HC);
- Improved bioassay for regulators to cost effectively and more rapidly screen the toxicity of chemicals (HC);
- Toxicogenomics for mixture toxicology: Genomics-guided proteomic approach to identifying biomarkers of exposure and effect for carcinogenic complex mixtures in the environment (HC);
- Statistical protocols and bioinformatics analyses of complex multivariate genomics data for use in human health risk assessment of complex chemical mixtures (HC);
- Improved software tools (NRC);
- Plant Orthology Browser: *http://nrcmonsrv01.nrc.ca/pob/* (NRC);
- Orthology & gene order analytics: standalone scripts/programs (NRC);
- Molecular detection assays (qPCR) of key forest pathogens (NRCan);
- Fungal culture collection (NRCan);
- Bioinformatics pipeline for identification of secreted proteins (NRCan); and
- Bioinformatics pipeline for assay development workflow using genomic sequences (NRCan);
- A new SNP-based tool for subtyping of *S.* Enteritidis (PHAC);
- Automated prokaryotic genome annotation (PHAC);
- HyDRA- an internet-based HIV DR data processing web server (PHAC);
- Biorepository of 400 *Salmonella* isolates from a wide variety of serovars (PHAC);
- Panseq: (http://lfz.corefacility.ca/panseq) for the pan-genomic analyses of closed and draft genomic sequences (PHAC);
- SuperPhy: (http://lfz.corefacility.ca/) for epidemiological and comparative inquiries by users with and without bioinformatics training (PHAC).

Research processes

- Genomics-based framework, which couples *in silico* molecular subtyping to whole-genome phylogenetic analysis of genome-sequenced bacterial isolates, for the development and assessment of molecular subtyping methods (FWS);
- Standard Operating Procedure for the sequencing (barcoding) of plant DNA using one to four gene areas (QIS);
- Galaxy genomic workflow tool customized for use on the project HPC cluster (QIS);
- Standard Operating Procedure for the extraction of herbarium plant DNA (QIS);
- Systems to modulate meiotic recombination frequency from *E. coli* to yeast to plants (AAFC);
- Rapid 96-well plate test to screen Arabidopsis lines with specific deleted ABC transporters for responses to *F. graminearum* (AAFC);
- Optimized protocols for phenolic extraction to study the effects of *F. graminarium* infection in wheat (AAFC);
- High throughput genomic methods to screen the yeast gene deletion collections against both the purified mycotoxin DON and whole fungal filtrates from *F. graminearum* (AAFC);
- Safe and effective protocol for generating EMS-induced gene knock-out mutations in the Sr9 locus (AAFC);
- Collaborative Image sorter for Microsoft Multi-touch devices (AAFC);
- Net Bio version of Gnome surfer (AAFC);

- Metagenomic and transcriptomic analysis of river microbial communities using next generation sequencing (EC);
- Diagnostic markers for identification of reproductive impairment and acute toxicity of copper on *Daphnia magna* (EC);
- SNP discovery approaches (NRC);
- Parallel mate-pair library approach and assembly approaches (NRC);
- Data analysis pipeline that integrates quantitative trait locus and expression quantitative trait tolus mapping methods (NRC);
- Three RNA sequence processing pipelines (NRC);
- Viral Induced Gene Silencing for wheat (NRC);
- Optimized procedure for DNA extraction from environmental samples (NRCan);
- Optimized procedure for DNA extraction from herbarium specimens (NRCan);
- Improved annotation and assembly of whole genome sequences (PHAC);
- novel TPP-based HIV drug resistance testing platform (PHAC);
- An accurate draft genome assembly with high-confidence base calls (PHAC);
- Genome finishing using confirmatory Sanger sequencing to resolve all possible misassemblies within contigs and to close gaps within scaffolds (PHAC);
- High-quality SNP determination (PHAC);
- Data visualization tools of pathogen macro- and micro- diversity (PHAC);
- Statistical analysis of genomic data for molecular marker discovery and assessment framework for newly-developed molecular assays (PHAC);
- Rapid characterisation of STEC strain genotype and phenotype, to identify those belonging to a common source outbreak by public health laboratories, or those that contain particular virulence or AMR determinants (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 science-based 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 (other government departments; universities; international organizations; private sector; etc.)
- In-kind contributions by collaborators
- Stakeholders and end-users determined by all participating departments/agencies every three 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

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

AREA	INDICATOR	FREQUENCY	TARGET[1]	RESPONSIBILITY
Research tools and processes	# of research tools produced # of research processes produced	Annual	Within the range recorded for Phase IV (30)[1]	Departments
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 other government departments)	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

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

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.