



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

**FOI to Environment and Climate Change Canada re: avian influenza virus evidence**

**Christine, an unincorporated woman** <cmssyc@gmail.com>  
 To: "AIPRP / ATIP (ECCC)" <ecatip-ecaiprp@ec.gc.ca>

Thu, Apr 10, 2025 at 11:26 AM

April 10, 2025

To:  
 the man or woman responsible for responding to ATIP requests  
 ATIP Coordinator Environment and Climate Change Canada  
 Place Vincent Massey - Annex  
 351 Saint-Joseph Blvd, 9th floor  
 Gatineau (Québec) K1A 0H3

via email to: [ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca)

Good day,

Your offer of access to general records per the terms and conditions in the Access to Information Act is hereby accepted.  
 The order is below.

**Ordered Records:**

All studies in the possession/custody/control of "Environment and Climate Change Canada", **authored by anyone, anywhere:**

1. - that **scientifically prove/provide evidence of the existence of the alleged "avian influenza virus"** (showing that the alleged particles exist, invade and replicate in "host" cells and cause the illness/symptoms that they are alleged to cause), or
2. - (if no records exist for #1) that at least describe the **purification of particles that are alleged to be "avian influenza virus"** directly from bodily fluid/tissue/excrement of so-called "hosts", with purification confirmed via EM imaging, or
3. - **wherein the purported "genome" of any alleged "avian influenza virus" was found intact** in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or
4. - that **scientifically demonstrate contagion of the illness / symptoms** that are allegedly caused by purported "avian influenza viruses", or
5. - wherein **any test that purportedly relates to the alleged "avian influenza virus" was validated** (logically, this would require the alleged virus to first be proven to exist).

**Urgency & Danger to Animal Life and Well-being**

This is an urgent issue: farmers are being harassed to "dispose of" their animals and take other disruptive measures under the premise of a never-shown-to-exist virus.

**Publicly Available Records**

If any records match the above description of requested records and are currently available to "the public" elsewhere, please assist me by providing enough information about each record so that I may identify and access each one with certainty (i.e. title, author(s), date, journal, location). Please provide URLs and/or DOIs where possible.

**Timeframe:**

If a timeframe is necessary, please use January 1, 1955 - the date of the search.

**Format and conveyance:**

Searchable pdf documents sent to me via email; please don't ship anything to me.

**Fee:**

The \$5 is in the mail.

**Privacy:**

I do not agree or assent to this order or "personal information" being shared with any 3rd parties including those that provide FOIA services, without my explicit written consent.

I am not providing a phone number or address in order to protect my privacy, since they are not required in order to carry out the search or to convey the response to me. I am on the land known as Canada and have lived here my entire life; birth certificate (scanned) is attached.

**Contact Information:**

email: [cmssyc@gmail.com](mailto:cmssyc@gmail.com)

Christine, agent (not surety or trustee)  
for Massey, Christine [REDACTED] and all derivatives  
All rights reserved.



BC.jpg  
161K



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

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## ECCC: FOI to Environment and Climate Change Canada re: avian influenza virus evidence

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AIPRP / ATIP (ECCC) &lt;ecatip-ecaiprp@ec.gc.ca&gt;

Wed, Apr 23, 2025 at 4:13 PM

To: "cmssyc@gmail.com" &lt;cmssyc@gmail.com&gt;

Good afternoon,

Please be advised that this type of request falls under the Access to Information Act, a prescribed fee of \$5.00 is required.

- FYI – Click on this link: <https://ouvert.canada.ca/en>
  - Click on « Request information »
  - Make a request and continue
  - None of the above - I am looking for general government records; next
  - Got it, I have all these things prepared; next
  - Select our institution « *Environment and Climate Change Canada* »
  - Proceed as a guest

We will begin processing your request as soon as the payment is received.

Should you have any questions, please do not hesitate to contact us.

Sincerely,

Accès à l'information et protection des renseignements personnels | Secrétariat de l'AIPRP

Access to Information and Privacy | ATIP Secretariat

9<sup>e</sup> étage, Place Vincent Massey Annexe | 9<sup>th</sup> floor, Place Vincent Massey Annex

[351 Boulevard St. Joseph](#) | [351 St. Joseph Boulevard](#)

Gatineau, Québec K1A 0H3

[ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca)



Environment and  
Climate Change Canada

Environnement et  
Changement climatique Canada





Christine, an unincorporated woman <cmssyc@gmail.com>

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## **ECCC: FOI to Environment and Climate Change Canada re: avian influenza virus evidence**

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**Christine, an unincorporated woman** <cmssyc@gmail.com>

Wed, Apr 23, 2025 at 4:21 PM

To: "AIPRP / ATIP (ECCC)" <ecatip-ecaiprp@ec.gc.ca>

The fee was sent in the mail long ago.

[Quoted text hidden]



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## Access to Information Request | Acknowledgement receipt (ECCC File: A-2025-00030) Avian Influenza Virus

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AIPRP / ATIP (ECCC) <ecatip-ecaiprp@ec.gc.ca>  
To: "cmssyc@gmail.com" <cmssyc@gmail.com>

Thu, May 1, 2025 at 3:34 PM

ECCC File: A-2025-00030

Ms. Christine [REDACTED] Massey,

■

Please find attached the acknowledgement receipt for your *Access to Information request*.

If you have any questions, please contact us by email at [ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca)

Lyne Séguin

Accès à l'information et protection des renseignements personnels | Secrétariat de l'AIPRP

Access to Information and Privacy | ATIP Secretariat

9<sup>e</sup> étage, Place Vincent Massey Annexe | 9<sup>th</sup> floor, Place Vincent Massey Annex

351 Boulevard St. Joseph | 351 St. Joseph Boulevard

Gatineau, Québec K1A 0H3

[ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca)



Environment and  
Climate Change Canada

Environnement et  
Changement climatique Canada

Canada



A-2025-00030.pdf  
159K



Environment and  
Climate Change Canada      Environnement et  
Changement climatique Canada

9<sup>th</sup> Floor, Place Vincent Massey Annex  
351 Saint-Joseph Blvd.  
Gatineau, Québec K1A 0H3

Your File    Votre référence  
Avian Influenza Virus  
Our File    Notre référence  
A-2025-00030

May 1, 2025

Ms. Christine [REDACTED] Massey  
[REDACTED]

Dear Ms. Massey,

This is to acknowledge receipt on May 1, 2025 of your request under the *Access to Information Act* for:

"All studies in the possession/custody/control of "Environment and Climate Change Canada", authored by anyone, anywhere:

1) that scientifically prove/provide evidence of the existence of the alleged "avian influenza virus" (showing that the alleged particles exist, invade and replicate in "host" cells and cause the illness/symptoms that they are alleged to cause), or;

2) (if no records exist for #1) that at least describe the purification of particles that are alleged to be "avian influenza virus" directly from bodily fluid/tissue/excrement of so-called "hosts", with purification confirmed via EM imaging, or;

3) wherein the purported "genome" of any alleged "avian influenza virus" was found intact in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or;

4) that scientifically demonstrate contagion of the illness / symptoms that are allegedly caused by purported "avian influenza viruses", or;

5) wherein any test that purportedly relates to the alleged "avian influenza virus" was validated (logically, this would require the alleged virus to first be proven to exist).

• Urgency & Danger to Animal Life and Well-being

This is an urgent issue: farmers are being harassed to "dispose of" their animals and take other disruptive measures under the premise of a never-shown-to-exist virus.

.../2

Canada

- **Publicly Available Records**

If any records match the above description of requested records and are currently available to "the public" elsewhere, please assist me by providing enough information about each record so that I may identify and access each one with certainty (i.e. title, author(s), date, journal, location). Please provide URLs and/or DOIs where possible.

- **Timeframe:** If a timeframe is necessary, please use January 1, 1955 - the date of the search."

*Please note that this also serves as a receipt for the \$5.00 application fee.*

We have started processing your request and will contact you as soon as possible. Please find enclosed our principles for assisting your request.

If you have any questions regarding this request, do not hesitate to contact us by email at [ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca). Please quote the above file number on all future correspondence concerning this request.

Yours sincerely,

*(Signed)*

Access to Information and Privacy | ATIP Secretariat  
Environment and Climate Change Canada | Government of Canada  
[ecatip-ecaiprp@ec.gc.ca](mailto:ecatip-ecaiprp@ec.gc.ca)

Enclosure

# Our principles for assisting your request

In processing your request under the *Access to Information Act* or *Privacy Act*, we will:

1. Process your request without regard to your identity.
2. Offer reasonable assistance throughout the request process.
3. Provide information on the *Access to Information Act* or *Privacy Act*, including information on the processing of your request and your right to complain to the Information Commissioner of Canada or Privacy Commissioner of Canada.
4. Inform you as appropriate and without undue delay when your request needs to be clarified.
5. Make every reasonable effort to locate and retrieve the requested records/personal information under the control of Environment and Climate Change Canada.
6. Apply limited and specific exemptions to the requested records/personal information.
7. Provide accurate and complete responses.
8. Provide timely access to the requested information/personal information.
9. Provide records/personal information in the format and official language requested, as appropriate.
10. Provide an appropriate location to examine the requested information/personal information.



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

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**ECCC Extension Notice for Access to Information Request A-2025-00030**

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**AIPRP / ATIP (ECCC)** <ecatip-ecaiprp@ec.gc.ca>

Thu, May 29, 2025 at 11:37 AM

To: "cmssyc@gmail.com" &lt;cmssyc@gmail.com&gt;

Cc: "general@oic-ci.gc.ca" &lt;general@ci-oic.gc.ca&gt;

Good afternoon,

Please see the attached extension notice for your access to information request.

Thank you,

Alana Lachance

*(she, her, elle)*

Accès à l'Information et Protection des Renseignements Personnels | Access to Information and Privacy

Secrétariat Ministériel | Corporate Secretariat

Environnement et Changements climatiques Canada | Environment and Climate Change Canada

Place Vincent Massey Annexe | Place Vincent Massey Annex

[ECATIP-ECAIPRP@ec.gc.ca](mailto:ECATIP-ECAIPRP@ec.gc.ca)

**A-2025-00030 - Extension.pdf**

234K



Environment and  
Climate Change Canada

Environnement et  
Changement climatique Canada

9th floor Place Vincent Massey Annex  
351 St. Joseph Boulevard  
Gatineau, Quebec  
K1A 0H3

Your File    Votre référence

Avian Influenza Virus

Our File    Notre référence

A-2025-00030 / AL

May 29, 2025

Ms. Christine [REDACTED] Massey  
[REDACTED]

Dear Ms. Massey,

This is further to your request under the *Access to Information Act* (the Act) for:

**"All studies in the possession/custody/control of "Environment and Climate Change Canada", authored by anyone, anywhere:**

**1) that scientifically prove/provide evidence of the existence of the alleged "avian influenza virus" (showing that the alleged particles exist, invade and replicate in "host" cells and cause the illness/symptoms that they are alleged to cause), or;**

**2) (if no records exist for #1) that at least describe the purification of particles that are alleged to be "avian influenza virus" directly from bodily fluid/tissue/excrement of so-called "hosts", with purification confirmed via EM imaging, or;**

**3) wherein the purported "genome" of any alleged "avian influenza virus" was found intact in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or;**

**4) that scientifically demonstrate contagion of the illness / symptoms that are allegedly caused by purported "avian influenza viruses", or;**

**5) wherein any test that purportedly relates to the alleged "avian influenza virus" was validated (logically, this would require the alleged virus to first be proven to exist).**

**• Urgency & Danger to Animal Life and Well-being**

**This is an urgent issue: farmers are being harassed to "dispose of" their animals and take other disruptive measures under the premise of a never-shown-to-exist virus.**

.../2

Canada

- **Publicly Available Records**

If any records match the above description of requested records and are currently available to "the public" elsewhere, please assist me by providing enough information about each record so that I may identify and access each one with certainty (i.e. title, author(s), date, journal, location). Please provide URLs and/or DOIs where possible.

- **Timeframe: If a timeframe is necessary, please use January 1, 1955 - the date of the search."**

Pursuant to paragraphs 9(1)(a), (b) and (c) of the Act (copy attached), an extension of 90 days is required beyond the statutory 30-day limit allowed for the processing of your request as meeting the original time limit would unreasonably interfere with the operations of the Department. Consultations with other government institutions and notifications to third parties pursuant to subsection 27(1) of the Act are also required and cannot reasonably be completed within the original time limit.

Please note that the notification process pursuant to paragraph 9(1)(c) of the Act normally takes approximately 60 days but it could be much more if a third party challenges the release of the records in court.

Please be advised that you are entitled to complain to the Information Commissioner concerning the processing of your request within sixty days of the receipt of this notice. In the event you decide to avail yourself of this right, your notice of complaint should be addressed to:

Information Commissioner of Canada  
30 Victoria Street  
Gatineau, Québec K1A 1H3

If you have any questions regarding this request, please contact Alana Lachance by email at [Alana.Lachance@ec.gc.ca](mailto:Alana.Lachance@ec.gc.ca).

Yours sincerely,

Original signed by,

Susan Drysdale  
Director, Access to Information and Privacy

c.c. Information Commissioner of Canada

## ***Access to Information Act***

### EXTENSION OF TIME LIMITS

9.(1) The head of a government institution may extend the time limit set out in section 7 or subsection 8(1) in respect of a request under this Act for a reasonable period of time, having regard to the circumstances, if

(a) the request is for a large number of records or necessitates a search through a large number of records and meeting the original time limit would unreasonably interfere with the operations of the government institution,

(b) consultations are necessary to comply with the request that cannot reasonably be completed within the original time limit, or

(c) notice of the request is given pursuant to subsection 27(1)

by giving notice of the extension and, in the circumstances set out in paragraph (a) or (b), the length of the extension, to the person who made the request within thirty days after the request is received, which notice shall contain a statement that the person has a right to make a complaint to the Information Commissioner about the extension.

#### Notice of extension to Information Commissioner

(2) Where the head of a government institution extends a time limit under subsection (1) for more than thirty days, the head of the institution shall give notice of the extension to the Information Commissioner at the same time as notice is given under subsection (1).



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**Notice: Breach of Contract A-2025-00030**

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Christine, an unincorporated woman <cmssyc@gmail.com>  
To: "AIPRP / ATIP (ECCC)" <ecatip-ecaiprp@ec.gc.ca>, Susan.Drysdale@ec.gc.ca  
Cc: "general@oic-ci.gc.ca" <general@ci-oic.gc.ca>, Alana.Lachance@ec.gc.ca

Thu, Oct 9, 2025 at 2:07 PM

Good day Susan Drysdale who acts as Director, Access to Information and Privacy, Environment and Climate Change Canada.

Thank you for your letter dated May 29, 2025 advising of an extension of 90 days beyond the statutory 30-day limit allowed for the processing of the order.

I hope that searching for studies that scientifically prove/provide evidence of the existence of the imagined "avian influenza virus", or that scientifically demonstrate contagion of the non-specific "bird flu" illness / symptoms, or that at least show the claimed "viral genome" being found intact in the bodily fluid/tissue/excrement of a "host", or that at minimum describe particles suspected of being said alleged virus being found and purified from a "host" (so that valid sequencing, characterization and controlled experiments could later take place) - which the "experts" at Canadian Food Inspection Agency, Agriculture and Agri-Food Canada, Public Health Agency of Canada, the U.S. Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, the U.S. Department of Agriculture and many other institutions were officially unable to provide or cite (as shown here: <https://christinemasseypoies.substack.com/p/dont-fall-for-the-avian-influenza>) - has not been too distressing or embarrassing for you and your colleagues.

This purpose of this message is to point out that the 90 days have long since passed and you are in breach of contract.

However I am pleased to advise that you have been granted an additional 24 hours from the sending of this email (October 9, 2025, 2:07 pm) to respond, at which time I will go public with your response or non-response, as the case may be.

Respectfully,

Christine, agent (not surety or trustee)  
for Massey, Christine [REDACTED] and all derivatives  
All rights reserved.



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

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**A-2025-00030**

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**Carle, Yves (ECCC)** <Yves.Carle@ec.gc.ca>  
To: "cmssyc@gmail.com" <cmssyc@gmail.com>  
Cc: "Carle, Yves (ECCC)" <Yves.Carle@ec.gc.ca>

Tue, Oct 21, 2025 at 3:17 PM

Dear Ms. Massey,

We have completed processing your request under the *Access to Information Act*.

Please find the complete release package in response to this request. Also note that we have attached a word document with a list of publications as per your request.

Thank you,

Yves

Yves Carle

ATIP Consultant, Corporate Secretariat

Environment and Climate Change Canada | Government of Canada

[yves.carle@ec.gc.ca](mailto:yves.carle@ec.gc.ca)

Consultant de l'AIPRP, Secrétariat Ministériel

Environnement et Changements climatiques Canada | Gouvernement du Canada

[yves.carle@ec.gc.ca](mailto:yves.carle@ec.gc.ca)

---

**3 attachments**

**A-2025-00030 response letter 21-10-2025.pdf**  
279K



**A-2025-00030 Release Package .pdf**  
10539K



**List of publications provided by WLSD-2025-00030 .docx**

23K



Environment and  
Climate Change Canada

Environnement et  
Changement climatique Canada

9th floor Place Vincent Massey Annex  
351 St. Joseph Boulevard  
Gatineau, Quebec  
K1A 0H3

Your File    Votre référence

Avian Influenza Virus

Our File    Notre référence

A-2025-00030 / YC

October 21, 2025

Ms. Christine Anne Massey



Dear Ms. Massey,

We have completed processing your request under the *Access to Information Act* for:

"All studies in the possession/custody/control of "Environment and Climate Change Canada", authored by anyone, anywhere:

1) that scientifically prove/provide evidence of the existence of the alleged "avian influenza virus" (showing that the alleged particles exist, invade and replicate in "host" cells and cause the illness/symptoms that they are alleged to cause), or;

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3) wherein the purported "genome" of any alleged "avian influenza virus" was found intact in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or;

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5) wherein any test that purportedly relates to the alleged "avian influenza virus" was validated (logically, this would require the alleged virus to first be proven to exist).

• Urgency & Danger to Animal Life and Well-being

This is an urgent issue: farmers are being harassed to "dispose of" their animals and take other disruptive measures under the premise of a never-shown-to-exist virus.

• Publicly Available Records

If any records match the above description of requested records and are currently available to "the public" elsewhere, please assist me by providing enough information

Canada

about each record so that I may identify and access each one with certainty (i.e. title, author(s), date, journal, location). Please provide URLs and/or DOIs where possible.

- Timeframe: If a timeframe is necessary, please use January 1, 1955 - the date of the search.”

Attached please find the complete release package in response to this request. Also note that we have attached a word document with a list of publications as per your request.

Please be advised that you are entitled to file a complaint with the Information Commissioner concerning the processing of your request within sixty days of the receipt of this notice. In the event you decide to avail yourself of this right, your notice of complaint should be addressed to:

Information Commissioner of Canada  
30 Victoria Street  
Gatineau, Québec K1A 1H3

If you have any questions regarding this request, please do not hesitate to contact Yves Carle by email at [yves.carle@ec.gc.ca](mailto:yves.carle@ec.gc.ca).

Yours sincerely,

Susan Drysdale  
Director, Access to Information and Privacy

Enclosures





Government  
of Canada

Gouvernement  
du Canada

Document Released Under the Access to  
Information Act / Document divulgué en vertu  
de la Loi sur l'accès à l'information

Canada

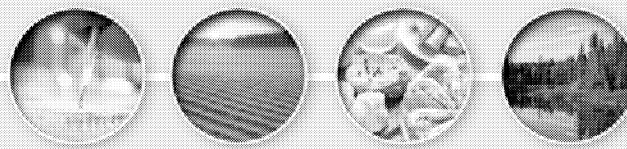
# GENOMICS R&D INITIATIVE

ANNUAL PERFORMANCE REPORT

2016-2017



*Through the Genomics Research and Development Initiative, federal science departments and agencies collaborate in the field of genomics research to address 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). It was renewed in 2014 for five years (Phase VI, 2014-2019).

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 fiscal year 2016-2017 was the third year of Phase VI of the GRDI. The Initiative continued to support mandated research in participating departments as well as a model of structured collaboration supporting two new highly coordinated interdepartmental projects along shared priorities and common goals: 1) Antimicrobial Resistance (the AMR project); and 2) Metagenomics Based Ecosystem Biomonitoring (the EcoBiomics project).

Considerable progress was achieved in 2016-2017, exemplified by the following highlights:

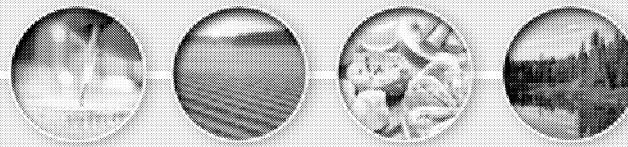
- A refined biomarker to identify genotoxic chemicals and a related software application were submitted to the US Food and Drug Administration biomarker qualification program;
- Incorporation of toxicogenomics data in the annual training session for regulators (Applied Genetic Toxicology for Regulatory Decision-Making);
- The new sequence typing for antibiotic resistance in *Neisseria gonorrhoea* (NG-STAR) enabled researchers to track the international spread of drug resistant

isolates of *N. gonorrhoeae*, and to identify AMR isolates that had not previously been characterised in Canada;

- A suite of bioinformatics tools to analyse bacterial whole genome sequences has been developed for more rapid and effective outbreak identification of foodborne pathogens such as *Salmonella*, *E. coli*, and *Campylobacter*;
- Next generation sequencing procedures and analytical tools to monitor the emergence of drug resistant variants of HIV have been transferred to public health laboratories in eight Latin American and Caribbean countries;
- More sensitive procedures were developed for public health investigators who track measles transmissions;
- Using whole genome sequencing, scientists were able to determine that the *Mycobacterium bovis* strain affiliated with the 2016 bovine tuberculosis outbreak in Alberta was not linked to earlier strains in Canada. This finding directed investigation and surveillance activities that aided the federal bovine tuberculosis eradication program;
- Scientists developed a web-based Genomics Portal that enables access to CFIA's database of bacterial genomes;
- Whole genome sequencing technology was successfully deployed in the CFIA's six food microbiology testing laboratories.

This Annual Performance Report for 2016-2017 follows the Performance Measurement Framework that was developed for Phase VI in 2015. 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 2016-2017 in terms of interdepartmental governance, R&D, and knowledge and networks. Appendix A presents summary statistics as well as a summary narrative account of R&D achievements for 2016-2017.





# ACRONYMS

|                |                                                                       |
|----------------|-----------------------------------------------------------------------|
| <b>AAFC</b>    | Agriculture and Agri-Food Canada                                      |
| <b>ADM</b>     | Assistant Deputy Minister                                             |
| <b>ADM CC</b>  | ADM Coordinating Committee                                            |
| <b>AMR</b>     | Antimicrobial resistance                                              |
| <b>CABIN</b>   | Canadian Aquatic Biomonitoring Network                                |
| <b>CFIA</b>    | Canadian Food Inspection Agency                                       |
| <b>CFS</b>     | Canadian Forest Service                                               |
| <b>CIPARS</b>  | Canadian Integrated Program for Antimicrobial Resistance Surveillance |
| <b>CITES</b>   | Convention on the International Trade of Endangered Species           |
| <b>CNISP</b>   | Canadian Nosocomial Infection Surveillance Program                    |
| <b>CNPHI</b>   | Canadian Network for Public Health Intelligence                       |
| <b>COSEWIC</b> | Committee on the Status of Endangered Wildlife in Canada              |
| <b>CRISPR</b>  | Clustered Regularly Interspaced Short Palindromic Repeats             |
| <b>DFO</b>     | Fisheries and Oceans Canada                                           |
| <b>DNA</b>     | Deoxyribonucleic Acid                                                 |
| <b>ECCC</b>    | Environment and Climate Change Canada                                 |
| <b>eDNA</b>    | environmental DNA                                                     |
| <b>FTE</b>     | Full Time Equivalent                                                  |
| <b>GRDI</b>    | Genomics Research and Development Initiative                          |
| <b>HC</b>      | Health Canada                                                         |

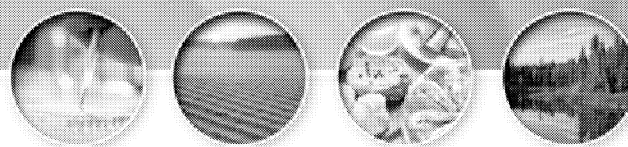
|                |                                                                    |
|----------------|--------------------------------------------------------------------|
| <b>HIV</b>     | Human Immunodeficiency Virus                                       |
| <b>IRIDA</b>   | Integrated Rapid Infectious Disease Analysis                       |
| <b>MALDI</b>   | Matrix-Assisted Laser Desorption/Ionization                        |
| <b>NGS</b>     | Next Generation Sequencing                                         |
| <b>NG-STAR</b> | Neisseria gonorrhoeae Sequence Typing for Antimicrobial Resistance |
| <b>NSERC</b>   | National Science and Engineering Research Council                  |
| <b>NRC</b>     | National Research Council of Canada                                |
| <b>NRCan</b>   | Natural Resources Canada                                           |
| <b>PCR</b>     | Polymerase Chain Reaction                                          |
| <b>PHAC</b>    | Public Health Agency of Canada                                     |
| <b>qPCR</b>    | Quantitative PCR                                                   |
| <b>R&amp;D</b> | Research and Development                                           |
| <b>RNA</b>     | Ribonucleic Acid                                                   |
| <b>S&amp;T</b> | Science and Technology                                             |
| <b>SGSA</b>    | Salmonella Genoserotyping Array                                    |
| <b>SNP</b>     | Single Nucleotide Polymorphism                                     |
| <b>SOPs</b>    | Standard Operating Procedures                                      |
| <b>SSC</b>     | Shared Services Canada                                             |
| <b>STAGE</b>   | Strategic Technology Applications of Genomics in the Environment   |
| <b>WG</b>      | Working Group                                                      |

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# 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 to:

- Agriculture and Agri-Food Canada (AAFC);
- Canadian Food Inspection Agency (CFIA);
- Environment and Climate Change Canada (ECCC);
- Fisheries and Oceans Canada (DFO);
- Health Canada (HC);
- Public Health Agency of Canada (PHAC);
- National Research Council of 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 depart-

ments. 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.

The federal government has allocated \$393.3M to the GRDI between 1999 and 2019: \$55M for Phase I (1999-2002); \$59.7M each for Phases II (2002-2005), III (2005-2008), IV (2008-2011), and V (2011-2014); and \$99.5M for Phase VI (2014-2019). Phase V of the GRDI (2011-2014) introduced a model that mobilized resources for concerted research on issues that are beyond the mandates of single departments, supporting highly coordinated interdepartmental projects along shared priorities and common goals. Two new projects were launched in April 2016: 1) Antimicrobial Resistance; and 2) Metagenomics-Based Ecosystem Biomonitoring.

## Resources

**Table 1: Funding Allocations (\$000)**

| DEPARTMENT/AGENCY                              | PHASE I<br>1999–2002 | PHASE II<br>2002–2005 | PHASE III<br>2005–2008 | PHASE IV<br>2008–2011 | PHASE V<br>2011–2014 | PHASE VI<br>2014–2019 |
|------------------------------------------------|----------------------|-----------------------|------------------------|-----------------------|----------------------|-----------------------|
| Agriculture and Agri-Food Canada               | 17,000               | 18,000                | 18,000                 | 18,000                | 15,300               | 22,200                |
| Canadian Food Inspection Agency                | –                    | –                     | –                      | –                     | –                    | 3,600                 |
| Environment and Climate Change Canada          | 3,000                | 3,000                 | 3,000                  | 3,000                 | 2,550                | 4,000                 |
| Fisheries and Oceans Canada                    | 2,500                | 2,700                 | 2,700                  | 2,700                 | 2,295                | 3,600                 |
| Health Canada / Public Health Agency of Canada | 10,000               | 12,000                | 12,000                 | 12,000                | 10,200               | 16,000                |
| National Research Council Canada               | 17,000               | 18,000                | 18,000                 | 18,000                | 15,300               | 22,200                |
| Natural Resources Canada                       | 5,000                | 6,000                 | 6,000                  | 6,000                 | 5,100                | 8,000                 |
| Shared Priorities                              | –                    | –                     | –                      | –                     | 8,955                | 19,900                |
| Medical Research Council <sup>1</sup>          | 500                  | –                     | –                      | –                     | –                    | –                     |
| <b>Total</b>                                   | <b>55,000</b>        | <b>59,700</b>         | <b>59,700</b>          | <b>59,700</b>         | <b>59,700</b>        | <b>99,500</b>         |

<sup>1</sup> Precursor to the Canadian Institutes of Health Research – 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 2016-2017 in support of GRDI projects, and demonstrates that non-GRDI funds

represented more than 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 2016-2017 (\$000)**

| DEPARTMENT/AGENCY                          | GRDI          | NON-GRDI*     | TOTAL         |
|--------------------------------------------|---------------|---------------|---------------|
| National Research Council Canada           | 4,440         | 12,204        | 16,644        |
| Agriculture and Agri-Food Canada           | 4,440         | 9,249         | 13,689        |
| Health Canada                              | 1,600         | 3,062         | 4,662         |
| Public Health Agency of Canada             | 1,466         | 1,280         | 2,746         |
| Natural Resources Canada                   | 1,600         | 3,904         | 5,504         |
| Environment and Climate Change Canada      | 800           | 1,575         | 2,375         |
| Fisheries and Oceans Canada                | 720           | 1,386         | 2,106         |
| Canadian Food Inspection Agency            | 720           | 3,437         | 4,157         |
| SHARED PRIORITY PROJECT                    | GRDI          | NON-GRDI      | TOTAL         |
| Antimicrobial Resistance                   | 1,799         | 2,880         | 4,679         |
| Metagenomics Based Ecosystem Biomonitoring | 1,811         | 1,981         | 3,792         |
| Coordination and Common Functions          | 370           | 16            | 386           |
| <b>Total</b>                               | <b>19,766</b> | <b>42,852</b> | <b>62,618</b> |

\* includes estimated funds from departmental A-base and other sources

## Planned Results

As reported in the NRC Departmental Report on Plans and Priorities Supplementary Table for the GRDI, the participating departments established a collective set of planned results for 2016-2017.

- Using genomics to significantly increase Canada's share of global wheat production;
- Using genomics to improve the value of Canadian crops and agri-products;
- Using genomics for food safety, animal health and plant protection;
- Genomics knowledge and advice for the management of fisheries and oceans;
- Genomics-based tools and technologies for responsible environmental decision-making;
- Genomic knowledge for the Canadian health regulatory system;
- Commercially-relevant advances in genomics R&D related to human health;

- Concerted interdepartmental research along shared priorities and common goals on issues that are beyond the mandates of single departments;
- Genomic knowledge for forest generation and protection;
- Genomics knowledge to strengthen public health programs and activities related to the prevention and control of infectious disease.

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

### Agriculture and Agri-Food Canada

GRDI investments at AAFC will focus on the priorities outlined in the Canadian Crop Genomics Initiative, and will be leveraged to enable industry to take advantage of new innovative opportunities. Activities will fall under three broad themes: 1) Biodiversity, gene mining and functional analysis; to develop value-added traits (e.g. seed quality) for the highly competitive marketplace.

Enhance the resiliency of Canada's crop production in the face of potentially catastrophic abiotic and biotic stresses to maximize profitability of the sector; 2) Bioinformatics and physical tools: ensuring that scientists can maximize the opportunities presented by genomics-based research such as identification and characterization of genes coding for desirable traits related to seed quality or disease resistance; and 3) Improved access to biological materials and data sets: to enhance the efficiency of plant breeding to lay the scientific foundation for major advances in the development and delivery of priority traits identified by industry.

### **Canadian Food Inspection Agency**

At the CFIA, genomics research is focused on two thematic areas to enhance genomics capacity and capability to regulate pests and pathogens: "Detection and Isolation" and "Identification and Characterization." Under these themes, the CFIA's genomics research is aligned to its three business lines: animal health, food safety, and plant health. In animal health, genomics research activities are targeted to support management of public health risks associated with the transmission of zoonotic diseases as well as reportable and emerging animal diseases. For food safety, the genomic activities will enhance the CFIA in the areas of compliance testing, source attribution and risk profiling, while also enabling the enforcement of HC standards contributing to health risk assessment. Plant health genomics is focusing on further enabling early detection and rapid response, and informing regulatory decision-making for regulated plant pests and plant commodities within the agricultural and forestry sectors. Additionally, research is conducted horizontally to harmonize genomics activities across CFIA's three business lines with a focus to contribute to the improved transfer of technology and tools between CFIA business lines and to increase the accessibility to genomics tools for CFIA scientists.

### **Fisheries and Oceans Canada**

Genomics-enabled research within DFO will continue to be aligned within the following themes: 1) Protecting fish species and enabling sustainable harvesting: to develop and apply leading-edge genomics tools to accurately identify species, populations and stocks for fisheries management and the conservation of vulnerable stocks, species at risk and aquatic biodiversity; 2) Safeguarding Canadian fish and seafood products: to develop innovative genomics techniques to detect, monitor and minimize the impact of pathogens (e.g. Infectious Salmon Anemia virus) to safeguard the health of Canada's aquatic resources and Canada's export markets for fish and seafood products; and 3) Maintaining healthy and productive aquatic ecosystems: to develop and apply new genomics tools to monitor, mitigate and restore aquatic ecosystems.

### **Environment and Climate Change Canada**

ECCC will continue to deliver its GRDI funding under the Strategic Technology Applications of Genomics in the Environment (STAGE) program, with the following priorities for genomics research: 1) Ecotoxicology: to establish toxicology end points for microorganisms, chemicals of concern, and emerging stressors; and to predict the mode of action of chemicals of concern and their effects on organisms; 2) Wildlife conservation: to understand how genes are interacting in flora and fauna in response to environmental conditions and to track disease in wildlife; 3) Environmental monitoring: to develop indicators (e.g., gene expression profiles for key species) of ecosystem health in priority ecosystems (e.g., Great Lakes and St. Lawrence) and to track pathogen sources; and 4) Compliance and Enforcement: to analyze flora and fauna for individual species identification, parentage determination and ascertaining geographic origin. This work will enable the delivery of ECCC's obligation under the *Fisheries Act and the Canadian Environmental Protection Act*, and programs including the Chemicals Management Plan.



## Health Canada

Genomics research will continue to focus on four priority investment areas to strengthen HC's regulatory role:

- 1) Supporting regulatory knowledge on therapeutics and biologics: to inform and support regulatory decisions throughout the biotherapeutic product life-cycle;
- 2) Supporting regulatory knowledge on food safety and nutrition: enabling detection and characterization of food-borne micro-organisms; characterization of health effects of food contaminants (e.g. fungal toxins, anthropogenic contaminants seafood toxins), food allergens, nutrients, novel foods/food ingredients, and pre- and pro-biotics; and development of markers of health status and disease (e.g. cancer, diabetes, obesity, allergies and cardiovascular disease) in the context of nutrition, micro-organisms, allergens, and food contaminant exposure;
- 3) Protecting human health from potential adverse effects of environmental contaminants, radiation, consumer products and pesticides; and
- 4) Research on socio-ethical impacts of genomics technologies, outputs and products: approaches for responsible integration of genomics for societal benefit, taking into account ethical, legal and socio-economic considerations.

## National Research Council Canada

Investments from the GRDI at the 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 2016-2017, these will be:

- 1) the NRC 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 Biomanufacturing 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. These programs were approved for implementation by the NRC Senior Executive Committee after undergoing a rigorous program approval and implementation process.

## Natural Resources Canada

The Canadian Forest Service of NRCan will focus on accelerating the translation of accumulated genomics knowledge into applications in support of Canada's forest sector competitiveness, including:

- 1) Forest generation: the development of innovative genomic applications will result in accelerated production of higher quality fibre, translating into economic and environmental benefits for Canada; and
- 2) Forest protection: the development of innovative genomic diagnostic tools will enable rapid detection and management of invasive insects and diseases which threaten the health and ecological integrity of Canadian forests, the forest sector and forest communities.

## Public Health Agency of Canada

GRDI research activities at PHAC apply "-omics" technologies to generate new knowledge to support public health decision making, and to create new tools to enhance disease prevention and control. These technologies are providing methods to enhance:

- 1) the prevention and control of priority pathogens;
- 2) the response to antimicrobial resistant pathogens;
- 3) infectious disease surveillance; and
- 4) public health security measures.

The knowledge generated from genomic approaches is supporting more detailed risk analyses, as well as the identification and development of new intervention points for the control and prevention of infectious diseases.

## Shared Priorities

The Antimicrobial Resistance project will develop a greater understanding of the critical activities that contribute to the development of antimicrobial resistance and critical exposure pathways by which antimicrobial bacteria reach humans, which could then be used to help validate economically sustainable technologies, practices, and policies to mitigate the development of antimicrobial resistance; it is a key component of the Federal Action Plan for Antimicrobial Resistance and Use in Canada. It is coordinated by AAFC and involves CFIA, HC, NRC, and PHAC.



## Alignment with Government Priorities

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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 participating departments and agencies.

All research and innovation activities at AAFC (including those of the GRDI) directly support the achievement of prioritized research outcomes. The GRDI specifically contributes to the department's Strategic Outcome: An Innovative and Sustainable Agriculture, Agri-Food and Agri-Based Products Sector. Funding from the GRDI enables 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.

Activities of the CFIA under the GRDI support the agency's Strategic Outcome to Maintain a Safe and Accessible Food Supply and Plant and Animal Resource Base. Commodities and resources regulated under CFIA's Program Activities including the Food Safety program, Animal Health and Zoonotic program, and the Plant Resources program are all supported by genomics research outcomes. The GRDI program at the CFIA targets the development and application of genomics tools for the rapid detection of food pathogens, plant

pests, and animal disease agents. This enables the CFIA to respond effectively to regulatory needs in food safety, ensure compliance, maintain consumer confidence, and minimize animal and plant disease incursions.

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 ECCC align with two of the three Strategic Outcomes: Canada's Natural Environment is Conserved and Restored for Present and Future Generations, and Threats to Canadians and their Environment from Pollution are Minimized. To this end, the STAGE genomic research priorities at ECCC 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.

Research funded by the GRDI at HC contributes to the generation of regulatory knowledge required for the appropriate management and communication of health risks and benefits associated with food, products, substances, and environmental factors. The knowledge and tools generated by genomics research ultimately support departmental efforts to respond to current and emerging health issues under the Program Activity: Canadian Health System Policy, and Strategic Outcome: A Health System Responsive to the Needs of Canadians.

The Program Alignment Architecture of the NRC was updated to reflect the NRC new industry-focus. It is aligned with Government of Canada's Strategic Outcomes and federal priorities and to the NRC business processes. The NRC performance reporting is aligned accordingly. The GRDI at the 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 on developing new biologics.

At the Canadian Forest Service of NRCan, the GRDI has developed the foundation for contributing to the Strategic Outcome Canada's Natural Resource Sectors are Globally Competitive and to the Program Activity Innovation for New Products and Processes. It contributes to the 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 overarching strategic outcomes of promoting health, reducing health inequalities, as well as preventing and mitigating harmful consequences of infectious and chronic diseases. Researchers create innovative tools that apply genomic and bioinformatic technologies for more effective public health interventions. In addition, the GRDI generates leading edge scientific knowledge

to support public health decision-making and program development. By driving collaboration and knowledge exchange among public health professionals working in federal, provincial, territorial, municipal and non-government organisations, the GRDI facilitates the integration of reliable and current information into public health decision-making and interventions at all levels across Canada. The development and application of leading-edge public health science and of tools to provide specialized laboratory testing and reference services that will contribute to better public health and improved responses to emerging health risks, fall directly within the Program Activity of Public Health Infrastructure.

The federal science policy framework is currently provided by *Seizing Canada's Moment: Moving Forward in Science, Technology and Innovation* (hereafter referred to as the S&T Strategy), a strategy released by the federal government in December 2014 "as a commitment to keep science, technology and innovation at the forefront of government policy for years to come." This new strategy builds on the 2007 federal S&T Strategy, *Mobilizing Science and Technology to Canada's Advantage*. The GRDI contributes to the three pillars for Canada outlined in the S&T Strategy (people, knowledge, innovation) and supports the priorities of natural resources, health and life sciences, environment and agriculture. It informs good and sound decisions on public policy, regulatory responsibilities, and government priorities, congruent with the inherent value of federal research. It also supports technology commercialization efforts.

## 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 the NRC for previous phases of the GRDI continued to oversee the collective coordination of the GRDI. The governance structure for the 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, 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, and Industry Canada. The WG mandate 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.

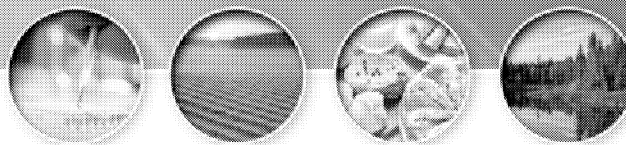
### **GRDI Coordination Function**

The Coordination Function for the GRDI is housed at the NRC. It provides GRDI-wide program coordination, communication, networking and outreach support, including support to the ADM CC and the GRDI WG, transparent and effective communication to departments regarding the planning cycle, process requirements, financial administration and other project management requirements, and support for SPP planning and implementation. This function also helps establish GRDI-wide research priorities; facilitates interdepartmental project development and peer reviews; ensures SPP Project Management Plans and funding agreements are in place; and supports performance management, reporting, evaluation, and communications. It is funded through the funding envelopes set aside for shared priority activities.

### **Performance Measurement Strategy Framework**

In fulfillment of the Policy on Evaluation (2009) and associated Guide to Developing Performance Measurement Strategies (May 2010), as well as the Policy and the associated Instructions to Departments for Developing a Management, Resources and Results Structure (March 2013), the Horizontal Performance Measurement Strategy that was developed for Phase V of the interdepartmental GRDI was updated for Phase VI. The updated version covers fiscal years 2014-2015 to 2018-2019 and formalizes the roles and responsibilities of the eight departments and agencies involved in the Initiative to support effective monitoring and evaluation activities. 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



## Interdepartmental Governance

### Coordinated Management Approaches

Ongoing coordination was provided by the NRC for 2016-2017, the third year of Phase VI, including timely secretariat support to GRDI departments and agencies and the implementation of updated GRDI governance, management and operating processes for Phase VI. Three meetings of the ADM CC and six meetings of the GRDI WG were held to allow for collaborative decisions. The launch of Phase VI shared priority projects was supported and funding was made available to participating departments based on the approved Project Management Plans. The GRDI Performance Measurement Strategy was implemented with the finalization and approval by the ADM CC of the Annual Performance Report for 2015-2016, and input into the NRC Departmental Results Report and Departmental Results Plan. The GRDI evaluation was completed under the leadership of the NRC Audit and Evaluation group and the interdepartmental GRDI Evaluation Working

Group. The Evaluation Report and a Management Response and Action Plan were approved by the ADM CC.

### 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. Annex 1 lists the mandated research projects funded in 2016-2017.

### Shared Priorities

Phase VI shared priority projects were launched, following approval by the ADM CC of formal Project Management Plans that describe detailed governance structures to ensure seamless integration and clear roles and responsibilities, and Science Plans that define study plans and deliverables for all project components at a more technical level.

## 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 2016-2017 and quantitative indicators for performance evaluation are enumerated in Annex 2 by department/agency for: scientific contributions (key scientific contributions demonstrating leadership; other scientific contributions; research tools and processes); knowledge translation and mobilization (contributions to scientific networks; collaborations; communications products; end-user engagement and knowledge transfer activities); and research and technical personnel. Highlights of the results achieved in

2016-2017 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:

- The leadership teams of the GRDI shared priority projects were awarded the Public Service Award of Excellence for 2016 in the category of Scientific Contribution: Cathryn L. Abbott, DFO; Sabah Bidawid, HC; Guillaume Bilodeau, CFIA; Patrice Bouchard, AAFC; Nathalie Corneau, HC; Robert Footitt, AAFC; Morag Graham, PHAC; Siegfried Janz, NRC; André Lévesque, AAFC; James Macklin, AAFC; Franco Pagotto, HC; Michael Rott, CFIA; Edward Topp, AAFC; Gary Van Domselaar, PHAC; Teodor Veres, NRC;

- Guillaume Bilodeau, Marie-José Côté, Cheryl Dollard, Eliane Guillemette, and Steve Jones (CFIA) were awarded the 2016 International Seed Testing Association (ISTA) Seed Science Advisory Group Prize at the ISTA Seed Symposium in recognition for their poster presentation;
- Guillaume Bilodeau, Brittany Day, Cheryl Dollard, Vasily Grebennikov, Delano James, Wendy Laviolette, Philip Macdonald, Michael Rott, Donna Smith, and Graham Thurston (CFIA) were awarded the CFIA President's Award – Dr. Evans Award for Partnership and Teamwork for their contribution to the Barcode of Life with the University of Guelph;
- Guillaume Bilodeau, Marie-José Côté, Delano James, Margaret Neuspiel and Michael Rott (CFIA) were awarded the Science Branch Recognition Program 2016, in the category of Collaboration/Partnership for contribution to the Invasive Alien and Quarantine Species Genomics Research and Development Initiative project;
- Ian Bradbury (DFO) was the recipient of a Cox Fisheries Scientist in Residence Award from Dalhousie University;
- Alex Leclerc, an Honours student in Vimal Balakrishnan (ECCC)'s laboratory, was awarded the "Best Presentation Award" at the Gananoque Environmental Science Conference;
- Matthew Meier (HC) received 2nd place prize for Best Poster by a New Investigator at the 47th Annual Meeting of the Environmental Mutagenesis and Genomics Society;
- Sabina Halappanavar (HC) received the 2016 Assistant Deputy Minister's Award in the Category of Science for her work in nanotoxicology;
- Sabina Halappanavar (HC) received the 2016 Deputy Minister's Award for Excellence in Science for her work in nanotoxicology;
- Steve Brooks (HC) received Assistant Deputy Minister Award for Science;
- Steve Brooks (HC) received Deputy Minister Award for Science;
- Roger Johnson's (PHAC) coop student Ray De Villa received first prize in research poster competition at the Ontario Ministry of Agriculture, Food and Rural Affairs 2016 Food Safety Research Forum, Guelph, Ontario, on May 24, 2016.

## Knowledge and Networks

To maximize the value of the GRDI and move that value to users for commercial and public good applications as the Initiative matures, knowledge translation and mobilization activities are required. These include the development of scientific networks, communications products, end-user engagement activities, science policy integration, science advice, transfer of protocols, field trials, outreach activities, etc. They ensure that research remains relevant to solve specific problems by maximizing opportunities to understand the needs of targeted end-users and active dissemination of GRDI results to them. Examples of knowledge and networks activities completed in 2016-2017 follow.

Scientists from CFIA established a reference genomic database of Canadian *Mycobacterium bovis* strains that played an important role in epidemiological investigations of the latest bovine tuberculosis outbreak (Alberta, 2016). These investigations demonstrated that the Alberta bovine *M. bovis* isolates were genetically different from *M. bovis* isolates recovered from Canadian domestic animals and wildlife between 1985 and 2015, and that they were recent introductions to Canada with a common ancestor from Mexico. A bioinformatics algorithm developed in collaboration with the United States Department of Agriculture was implemented at the Ontario Animal Health Laboratory for the *M. bovis*



genome data analysis. This promoted a harmonised approach for molecular epidemiological investigations of bovine tuberculosis outbreaks.

Through the GRDI-EcoBiomics project, Donald Baird (ECCC) participated in the European Union COST Action project: DNA AquaNet, which explores metabarcoding approaches to inform European legislation, including the Water Framework Directive and the Habitats Directive. He also collaborated on the UK Natural Environment Research Council Large Grant Project: Impacts of global warming in sentinel systems: from genes to ecosystems (Imperial College, London, UK).

Through the GRDI-AMR project, a material transfer agreement was signed with Les Aliments Breton Inc. to obtain swine fecal samples from diverse husbandry conditions. The project was also leveraged with funding from the National Science and Engineering Research Council (NSERC) to study the use of cranberries as an alternative to antibiotics in swine.

The NRC Wheat Flagship researchers contributed to: 1) the International Wheat Yield Partnership for research of photosynthetic efficiency in wheat; 2) the Wheat Initiative led by the Institut National de Recherche en Agronomie as part of an expert working group on adaptation of wheat to abiotic stress; and 3) the FusResis Consortium to develop enhanced Fusarium resistance in wheat.

Scientists funded by the GRDI at DFO focused on improving science advice to manage various fish stocks and aquatic resources, and disseminated scientific knowledge directly to managers, international partners, and communities whose livelihoods depend on the fisheries. They led or were involved in thirteen community meetings, three government advisory panels, three international and national genomics-related committees, and gave twenty-one media interviews to share the results of their research, and highlight the impacts of these results on long-term fisheries and aquatic resource management.

Scientists funded by the GRDI at ECCC participated in several international projects: 1) the DNA AquaNet project of the European Union Co-operation in Science and Technology Action, to explore the application of metabarcoding approaches within European legislation; 2) the 'Impacts of global warming in sentinel systems: from genes to ecosystems' Large Grant Project of the United Kingdom Natural Environmental Research Council; and 3) the international Daphnia Genomics Consortium. A scientist participated in the Organization for Economic Co-Operation and Development technical committee on Molecular Screening and Toxicogenomics, and in the Society of Environmental Toxicology and Chemistry Pellston Workshop for Advancing the Adverse Outcome Pathway Framework.

A lead HC scientist chaired an expert panel of the US National Institute of Environmental Health Sciences mandated to evaluate the use of genomics data in benchmark toxic dose modeling. A lead HC scientist also chaired the plenary session of the International Workshops on Genetox Testing (held every four years) in Tokyo on genetic toxicology assessments. These activities are expected to have major impacts on the procedures and strategies used for regulatory toxicology testing and risk assessment.

Data, signatures and algorithms produced by toxicogenomics research funded by the GRDI at HC were deposited in the National Institute of Environmental Health Sciences' Chemical Effects in Biological Systems Database, thus providing public access to gene toxicity prediction tools.

Several HC scientists serve as advisors for applying genomics technology to the risk assessment of chemicals for several international organizations, including the Organisation for Economic Cooperation and Development, the World Health Organization's International Programme on Chemical Safety, the Sustainable Nanotechnologies Project (SUN) Consortium, the International Life Sciences Institute's Genetic Toxicology Technical Committee, and the Horizon 2020 project consortium in the European Union.



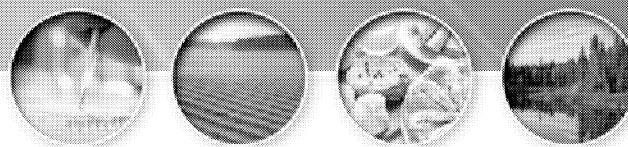
In the area of food nutrition, a lead HC scientist provided expert advice and guidance based on GRDI results to companies wishing to add fermentable carbohydrates to infant formula.

Researchers at NRCan continued to develop tools to map and monitor the spread of forest invasive alien species, and transfer these tools to partners. They collaborated with CFIA and provided them with fully validated tools for the detection of Asian gypsy moth, and are building on this collaboration to develop detection tools for another important threat to Canadian forests, the Siberian moth.

Research projects at PHAC are well networked to facilitate the translation of results into practice and to enhance the exchange of knowledge with partners nationally and internationally. At the national level, PHAC projects are collaborating with colleagues in almost all provincial and territorial public health laboratories. These relationships provide for the exchange of samples, data, and knowledge, and provide the mechanism to support the validation and adoption of newly developed assays by front line clinical laboratories. Projects of the GRDI that are developing enhanced tools to prevent foodborne pathogens are also working in conjunction with established national surveillance networks, FoodNet Canada, and PulseNet Canada. Similarly, projects developing genomics-based tools for the control and reduction of antimicrobial resistance are working closely with national antimicrobial resistance (AMR) surveillance networks, the Canadian Nosocomial Infection Surveillance Program and the Canadian Integrated Program for Antimicrobial Resistance Surveillance.

The relationships developed between genomics researchers and the surveillance epidemiologists strengthen GRDI projects through the exchange of samples and knowledge; they also facilitate the transfer of research outputs into practice. Internationally, PHAC GRDI projects are engaged with the World Health Organisation and the Pan-America Health Organisation to share knowledge and technological approaches for the eradication of measles virus, and for the detection and response to drug resistant human immunodeficiency virus. Work to enhance global surveillance of measles virus and antibiotic resistant *Gonorrhoea* is also on-going with partners from the World Health Organisation.

# APPENDIX A – SUPPLEMENTAL PERFORMANCE DETAILS



## Annex 1 – 2016-2017 GRDI Projects and Allocations from GRDI Funds

| GRDI FUNDS (\$)                                                                                                                                                                                                                                 | PROJECT TITLE                                                                                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| <b>SHARED PRIORITY PROJECTS</b>                                                                                                                                                                                                                 |                                                                                                                                  |
| 1,799,316                                                                                                                                                                                                                                       | Antimicrobial resistance (AMR)                                                                                                   |
| 1,810,860                                                                                                                                                                                                                                       | Metagenomics Based Environmental Biomonitoring (EcoBiomics)                                                                      |
| <b>AGRICULTURE AND AGRI-FOOD CANADA</b>                                                                                                                                                                                                         |                                                                                                                                  |
| <b>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</b>        |                                                                                                                                  |
| 274,578                                                                                                                                                                                                                                         | Accessing adaptive ancestral avena alleles                                                                                       |
| 410,915                                                                                                                                                                                                                                         | Advanced genetic technologies for improvement of camelina and canola                                                             |
| 115,207                                                                                                                                                                                                                                         | Cell-type specific chromatin dynamics in soybean hairy roots responding to water stress                                          |
| 245,776                                                                                                                                                                                                                                         | Effectors of Canadian <i>Puccinia striiformis</i> isolates                                                                       |
| 163,211                                                                                                                                                                                                                                         | Ethylene signalling and Fusarium head blight resistance in wheat                                                                 |
| 202,573                                                                                                                                                                                                                                         | Exploiting genomics to decipher hybrid vigour in <i>Brassica napus</i>                                                           |
| 232,335                                                                                                                                                                                                                                         | Genome-wide mining and mapping of disease resistance genes – novel strategies to enhance wheat disease resistance breeding       |
| 195,853                                                                                                                                                                                                                                         | Mining legume genomes for attributes of sustainable nutrient (nitrogen) acquisition through symbiosis                            |
| 49,214                                                                                                                                                                                                                                          | Molecular tools for identification of stored-product insects and their symbionts for use in pest control                         |
| 572,199                                                                                                                                                                                                                                         | Using genomics to reduce fusarium diseases and mycotoxin hazards in Canadian grain                                               |
| 138,249                                                                                                                                                                                                                                         | Using CRISPR to elucidate gene associated traits in wheat: Fusarium head blight resistance and yield capacity                    |
| 100,192                                                                                                                                                                                                                                         | Verification of plant defense genes against <i>Sclerotinia sclerotiorum</i>                                                      |
| <b>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</b> |                                                                                                                                  |
| 182,412                                                                                                                                                                                                                                         | Development of genomics and bioinformatics tools enabling epigenetic analyses in oilseed crops                                   |
| 251,537                                                                                                                                                                                                                                         | Development of identification and analysis tools for amplicon-based metagenomics, focussing on high risk and regulated pathogens |
| 233,626                                                                                                                                                                                                                                         | Exploring the applicability of new technologies and processes to the management and analysis of next generation sequencing data  |
| <b>3) Enhanced efficiency of plant breeding</b>                                                                                                                                                                                                 |                                                                                                                                  |
| 162,443                                                                                                                                                                                                                                         | Development of genome editing technology in crop somatic cells using cell penetrating peptides                                   |

|                                              |                                                                                                                                                                                                                                                    |
|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 341,783                                      | Effector-based breeding tools and Quantitative Trait Locus discovery for management of root rot in soybean caused by <i>Phytophthora sojae</i>                                                                                                     |
| 222,735                                      | Genomics and genetics of Soybean Mosaic Virus - soybean interactions: next generation viral resistance                                                                                                                                             |
| 305,153                                      | Process for making transplastomic cell and plant lines - tool for new trait development                                                                                                                                                            |
| <b>CANADIAN FOOD INSPECTION AGENCY</b>       |                                                                                                                                                                                                                                                    |
| 70,000                                       | Application of whole genome sequencing for molecular epidemiological investigations of bovine tuberculosis in Canada and for the high throughput discovery of novel diagnostic antigens for <i>Mycobacterium bovis</i> and <i>Brucella abortus</i> |
| 130,000                                      | Enhancing the CFIA's genomic capabilities for detection and characterization of high consequence known and unknown/unexpected animal viruses and their vectors/reservoirs                                                                          |
| 200,000                                      | Whole genome sequencing technologies as tools for the detection, isolation, identification and characterization of pathogens in support of Canadian food inspection objectives                                                                     |
| 200,000                                      | Detection and identification of plant pests and plants with novel traits using next generation sequencing                                                                                                                                          |
| 50,000                                       | Development of diagnostic sequencing methods to monitor, detect and characterize RNA viruses of food, animals and plants, following viral contamination or infection                                                                               |
| 70,000                                       | Development of infrastructure and bioinformatics tools to support genomics activities in CFIA's food, plant and animal business lines                                                                                                              |
| <b>ENVIRONMENT AND CLIMATE CHANGE CANADA</b> |                                                                                                                                                                                                                                                    |
| 55,000                                       | Analysis of Norovirus in Wastewaters and Environmental Samples                                                                                                                                                                                     |
| 13,000                                       | Application of genomics to assess the impact of harvest and other mortality sources on vulnerable populations of North Atlantic murre                                                                                                              |
| 52,535                                       | Development and validation of metabolomic techniques to evaluate impacts of large-scale environmental changes on stress responses in wildlife                                                                                                      |
| 95,960                                       | Development of next-generation genomic tools to investigate cumulative effects of urban pollution and pathogens in two sentinel fish species                                                                                                       |
| 42,985                                       | Environmental DNA - improving inference through validation studies                                                                                                                                                                                 |
| 33,250                                       | Genomics in support of effects based research                                                                                                                                                                                                      |
| 80,230                                       | Hybrid data generation from traditional and DNA-based biomonitoring                                                                                                                                                                                |
| 43,665                                       | Measuring Genome Health in Wildlife Populations                                                                                                                                                                                                    |
| 81,185                                       | Metabolomics for predicting the mode of action of chemicals of concern in aquatic organisms                                                                                                                                                        |
| 38,210                                       | Metagenomic Profiling of River Water Quality for Watershed Protection                                                                                                                                                                              |
| 47,258                                       | Rapid assessment of algal community composition and harmful blooms using DNA barcoding and remote sensing                                                                                                                                          |
| 57,310                                       | Toxicogenomic solutions for assessing exposure and effects of environmental contaminants in wildlife                                                                                                                                               |
| 52,535                                       | Transcriptomic analysis of the ecotoxicological effects of nanomaterials on microorganisms                                                                                                                                                         |
| 66,860                                       | Viable pathogen identification using DNA sequencing technology in microbial risk assessment                                                                                                                                                        |
| <b>FISHERIES AND OCEANS CANADA</b>           |                                                                                                                                                                                                                                                    |

|                                         |                                                                                                                                                                                                                                                                                         |
|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 176,000                                 | A range wide single nucleotide polymorphism (SNP) baseline for improved genetic mixed stock analysis in Atlantic salmon in the northwest Atlantic: application to domestic and international fisheries                                                                                  |
| 98,900                                  | Assessing the spatial scale of dispersal and connectivity in non-indigenous green crab ( <i>Carcinus maenas</i> ) and commercial sea scallop ( <i>Placopecten magellanicus</i> ) in Canadian waters using Restriction Site Associated DNA Sequencing and high throughput SNP genotyping |
| 144,200                                 | Bioinformatic support to develop "FIT-CHIP" for industry and salmon management applications                                                                                                                                                                                             |
| 42,500                                  | Development and evaluation of environmental DNA (eDNA) based detection and biosurveillance tools for aquatic invasive species to inform management and policy decision making associated with shellfish                                                                                 |
| 10,615                                  | eDNA analysis of aquatic invasive species and species-at-risk field programs                                                                                                                                                                                                            |
| 70,000                                  | Integrating neutral and adaptive genetic information for addressing knowledge gap in redfish ( <i>Sebastes</i> spp) population structure and its underlying mechanisms in Atlantic Canada: a genomic genotyping-by-sequencing approach of SNPs polymorphism                             |
| 145,450                                 | Rapid genomic screening for Atlantic salmon aquaculture escapees and hybrids using Restriction Site Associated DNA Sequencing and a high throughput nanofluidic dynamic array                                                                                                           |
| 32,250                                  | Stock delineation of narwhals ( <i>Monodon monceros</i> ) from Baffin Bay and adjacent areas using novel genetic markers developed from genomic techniques                                                                                                                              |
| <b>HEALTH CANADA</b>                    |                                                                                                                                                                                                                                                                                         |
| 185,000                                 | An integrated systems biology approach to investigate immunopotentiality induced by Respiratory Syncytial Virus vaccines                                                                                                                                                                |
| 225,000                                 | Development of genomics biomarker to provide mechanistic context and data in support of human relevance for chemicals inducing cellular stress responses                                                                                                                                |
| 240,000                                 | Identification of biomarkers for the standardization and risk assessment analysis of mesenchymal stem cell based health products                                                                                                                                                        |
| 100,000                                 | MicroRNA profiling of serum and milk from toxicological studies of natural and anthropogenic chemicals as an endpoint for comparative assessment with apical endpoints within the Benchmark dosing framework                                                                            |
| 134,000                                 | Safety of prebiotics in infants                                                                                                                                                                                                                                                         |
| 206,000                                 | Systems biology informed structure-activity-relationships to predict pulmonary pathology induced by nanomaterials                                                                                                                                                                       |
| 360,000                                 | The coming revolution: next generation sequencing detection of de novo mutations in the offspring to identify germ cell hazards                                                                                                                                                         |
| <b>NATIONAL RESEARCH COUNCIL CANADA</b> |                                                                                                                                                                                                                                                                                         |
| 888,000                                 | Biologics and Biomanufacturing program: development of support technology                                                                                                                                                                                                               |
| 3,552,000                               | Wheat improvement flagship (enhancing Fusarium and rust tolerance; genomics-assisted breeding; abiotic stress; seed development)                                                                                                                                                        |
| <b>NATURAL RESOURCES CANADA</b>         |                                                                                                                                                                                                                                                                                         |



|                                       |                                                                                                                                                                                                                                |
|---------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 56,870                                | Accelerating the discovery of insect volatile attractant molecules with genomics                                                                                                                                               |
| 77,284                                | An early detection tool for emerald ash borer and ash resource protection                                                                                                                                                      |
| 181,173                               | Applied genomics for tree breeding                                                                                                                                                                                             |
| 64,647                                | Development of metagenomic and bioinformatics tools to facilitate processing of trap captures                                                                                                                                  |
| 95,269                                | Developing molecular and environmental genomic approaches for microbial and invertebrate communities to assess ecosystem integrity in forest management                                                                        |
| 154,569                               | Developing the next generation biosurveillance tools for tracking and preventing forest pest invasions                                                                                                                         |
| 53,467                                | Development of molecular tools to detect living fungi and fungus-like organisms of phytosanitary concern in wood                                                                                                               |
| 66,105                                | Genomics-assisted tree breeding for improving remediation of disturbed forest ecosystems                                                                                                                                       |
| 123,946                               | Innovative land reclamation approaches following oil sand mining: Improving phytoremediation tree-soil microbes interactions                                                                                                   |
| 69,507                                | Spruce budworm eco-genomics: from population dynamics to population suppression                                                                                                                                                |
| 79,000                                | Tools for enhanced molecular detection of Asian gypsy moth and identification of their geographic origins                                                                                                                      |
| <b>PUBLIC HEALTH AGENCY OF CANADA</b> |                                                                                                                                                                                                                                |
| 137,255                               | BioTools for the predictive genomics of priority foodborne pathogens                                                                                                                                                           |
| 140,000                               | Closing the gaps in national surveillance of <i>Clostridium difficile</i> : epidemiologic and genomic characterisation of community-onset and recurrent <i>C. difficile</i> infections                                         |
| 27,377                                | Field trials of Oxford Nanopore minion sequencing technology                                                                                                                                                                   |
| 70,000                                | Implementation of a next generation sequencing testing platform to support Pan American Health Organization drug resistance surveillance                                                                                       |
| 50,000                                | Implementation of genome-based analyses to "One Health" surveillance of enteric disease                                                                                                                                        |
| 90,000                                | MALDI mass spectrometry identification of bacteria: the establishment of a national MALDI database to support diagnostic laboratories across Canada                                                                            |
| 50,000                                | <i>Neisseria gonorrhoeae</i> sequence typing for antimicrobial resistance: a novel sequence-based antimicrobial resistance typing scheme for tracking the global dissemination of <i>N. gonorrhoeae</i>                        |
| 70,000                                | Proposal for a whole genome sequence-based genotyping approach for tuberculosis in northern Canadian communities                                                                                                               |
| 60,000                                | PulseNet Canada: Model framework development for genomic technology delivery in a laboratory network                                                                                                                           |
| 146,322                               | Single nucleotide variant subtyping of <i>Salmonella</i> Enteritidis and <i>Salmonella</i> Heidelberg                                                                                                                          |
| 190,000                               | The use of whole genome sequence analysis to support healthcare-associated outbreaks of carbapenem-resistant <i>Enterobacteriaceae</i>                                                                                         |
| 124,652                               | Transfer of the validated <i>Salmonella</i> genosero-typing array into a PHAC reference laboratory and piloting the technology into the National Microbiology Reference Laboratory and targeted provincial health laboratories |
| 70,000                                | Translational analytic infrastructure for emerging pathogen discovery                                                                                                                                                          |
| 65,000                                | Validation of metagenomics as a <i>bona fide</i> laboratory approach for cost-effective enteric pathogen identification and subtyping                                                                                          |
| 50,000                                | Whole genome sequencing of measles virus of an effective molecular surveillance during measles elimination                                                                                                                     |
| 100,000                               | Whole genome sequencing of <i>Neisseria meningitidis</i> and its application to surveillance and understanding invasive meningococcal disease molecular epidemiology dynamics                                                  |

## Annex 2 – Quantitative Indicators for Performance Measurement

### Scientific Contributions

Scientific contributions include scientific information and publications produced, accepted, in press, or published (including online) in 2016-2017. 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 2016-2017. They do not include submitted papers or publications in draft form, nor contributions that were reported in previous years.

| NUMBER OF KEY SCIENTIFIC CONTRIBUTIONS                                        |            |           |           |           |           |           |           |            |           |             |            |
|-------------------------------------------------------------------------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|------------|-----------|-------------|------------|
|                                                                               | AAFC       | CFIA      | DFO       | ECCC      | HC        | NRC       | NRCan     | PHAC       | AMR       | Eco-Bionics | Total      |
| Publications in refereed journals                                             | 4          | 22        | 10        | 20        | 24        | 33        | 21        | 32         | 18        | 9           | <b>193</b> |
| Publications in refereed conference proceedings                               | 35         | 10        | 0         | 0         | 0         | 0         | 0         | 18         | 2         | 1           | <b>66</b>  |
| Books (edited, written) and book chapters                                     | 12         | 2         | 0         | 0         | 2         | 0         | 1         | 1          |           | 1           | <b>19</b>  |
| Invited presentations                                                         | 18         | 21        | 18        | 23        | 10        | 25        | 19        | 18         | 4         | 8           | <b>164</b> |
| International conference presentations                                        | 26         | 5         | 6         | 14        | 11        | 14        | 12        | 21         | 0         | 11          | <b>120</b> |
| Editorial posts for national/international journals (excludes peer reviewers) | 24         | 13        | 3         | 2         | 2         | 0         | 4         | 4          | 0         | 3           | <b>55</b>  |
| New genomics related databases or libraries                                   | 2          | 1         | 0         | 4         | 2         | 0         | 0         | 6          | 0         | 0           | <b>15</b>  |
| Awards, prizes                                                                | 6          | 4         | 1         | 1         | 5         | 1         | 0         | 1          | 2         | 1           | <b>22</b>  |
| <b>Total</b>                                                                  | <b>127</b> | <b>78</b> | <b>38</b> | <b>64</b> | <b>56</b> | <b>73</b> | <b>57</b> | <b>101</b> | <b>26</b> | <b>34</b>   | <b>654</b> |



| NUMBER OF OTHER SCIENTIFIC CONTRIBUTIONS                            |            |           |          |           |           |            |           |           |           |             |            |
|---------------------------------------------------------------------|------------|-----------|----------|-----------|-----------|------------|-----------|-----------|-----------|-------------|------------|
|                                                                     | AAFC       | CFIA      | DFO      | ECCC      | HC        | NRC        | NRCan     | PHAC      | AMR       | Eco-Bionics | Total      |
| Technical reports                                                   | 7          | 5         | 0        | 3         | 0         | 113        | 1         | 4         | 2         | 0           | <b>135</b> |
| Other publications (ex. abstracts, notes, industry magazines, etc.) | 22         | 2         | 0        | 1         | 2         | 3          | 1         | 3         | 0         | 2           | <b>36</b>  |
| Poster presentations at conferences                                 | 16         | 2         | 2        | 7         | 23        | 43         | 3         | 21        | 10        | 4           | <b>131</b> |
| National conference presentations                                   | 31         | 8         | 3        | 3         | 3         | 11         | 4         | 3         | 1         | 1           | <b>68</b>  |
| Deposits in genomics related databases or libraries                 | 165        | 0         | 0        | 1         | 2         | 0          | 20        | 44        | 3         | 0           | <b>235</b> |
| <b>Total</b>                                                        | <b>241</b> | <b>17</b> | <b>5</b> | <b>15</b> | <b>30</b> | <b>170</b> | <b>29</b> | <b>75</b> | <b>16</b> | <b>7</b>    | <b>605</b> |

### Research tools and processes

Research tools and processes include those produced in 2016-2017, deriving from previous phases of the GRDI

if produced in 2016-2017, as well as produced in previous years if they have been improved since last reported on.

| NUMBER OF RESEARCH TOOLS AND PROCESSES |          |           |           |           |           |           |           |           |          |             |            |
|----------------------------------------|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|-------------|------------|
|                                        | AAFC     | CFIA      | DFO       | ECCC      | HC        | NRC       | NRCan     | PHAC      | AMR      | Eco-Bionics | Total      |
| Research tools                         | 8        | 9         | 8         | 11        | 13        | 13        | 23        | 21        | 6        | 4           | <b>116</b> |
| Research processes                     | 1        | 2         | 11        | 5         | 6         | 5         | 8         | 12        | 2        | 0           | <b>52</b>  |
| <b>Total</b>                           | <b>9</b> | <b>11</b> | <b>19</b> | <b>16</b> | <b>19</b> | <b>18</b> | <b>31</b> | <b>33</b> | <b>8</b> | <b>4</b>    | <b>168</b> |

## Knowledge Translation and Mobilisation

Knowledge translation and mobilization activities include the development of scientific networks, communications products, end-user engagement activities, science policy integration, science advice, transfer of protocols,

field trials, outreach activities, etc. They ensure that research remains relevant to solve specific problems by maximizing opportunities to understand the needs of targeted end-users and active dissemination of GRDI results to them.

| NUMBER OF CONTRIBUTIONS TO SCIENTIFIC NETWORKS                                                                               |           |           |           |           |           |           |           |           |          |             |            |
|------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|-------------|------------|
|                                                                                                                              | AAFC      | CFIA      | DFO       | ECCC      | HC        | NRC       | NRCan     | PHAC      | AMR      | Eco-Biomics | Total      |
| Participation in government meetings/seminars/advisory panels related to regulations or policy in Canada and internationally | 15        | 18        | 9         | 13        | 20        | 4         | 2         | 21        | 0        | 0           | 102        |
| Participations in national or international genomics-related committees                                                      | 4         | 14        | 2         | 10        | 6         | 3         | 4         | 23        | 2        | 2           | 70         |
| National or international genomics research peer review committees served on                                                 | 7         | 3         | 1         | 2         | 2         | 2         | 4         | 0         | 0        | 0           | 21         |
| Participation in national conferences                                                                                        | 31        | 4         | 2         | 0         | 0         | 5         | 0         | 3         | 0        | 0           | 45         |
| Participation in international conferences                                                                                   | 32        | 1         | 0         | 3         | 6         | 45        | 1         | 2         | 1        | 0           | 91         |
| <b>Total</b>                                                                                                                 | <b>89</b> | <b>40</b> | <b>14</b> | <b>28</b> | <b>34</b> | <b>59</b> | <b>11</b> | <b>49</b> | <b>3</b> | <b>2</b>    | <b>329</b> |

## Collaborations

Collaborations by department/agency, expressed in terms of number of individual research collaborators in 2016-2017 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 RESEARCH COLLABORATORS                                                                        |           |           |           |           |           |           |            |           |           |             |            |
|---------------------------------------------------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|------------|-----------|-----------|-------------|------------|
|                                                                                                         | AAFC      | CFIA      | DFO       | ECCC      | HC        | NRC       | NRCan      | PHAC      | AMR       | Eco-Biomics | Total      |
| Canadian universities                                                                                   | 20        | 7         | 18        | 35        | 10        | 5         | 28         | 14        | 15        | 13          | <b>165</b> |
| International universities                                                                              | 31        | 1         | 6         | 10        | 6         | 5         | 16         | 11        | 3         | 1           | <b>90</b>  |
| Other international research organizations                                                              | 13        | 2         | 5         | 6         | 6         | 6         | 21         | 22        | 1         | 0           | <b>82</b>  |
| Other Canadian research institutions                                                                    | 6         | 0         | 0         | 0         | 0         | 8         | 1          | 0         | 2         | 0           | <b>17</b>  |
| Private sector                                                                                          | 7         | 0         | 2         | 3         | 3         | 10        | 5          | 0         | 2         | 2           | <b>34</b>  |
| Other government departments                                                                            | 8         | 22        | 3         | 26        | 8         | 3         | 9          | 5         | 5         | 9           | <b>98</b>  |
| Other public sector organizations such as provinces, municipalities, and Non-Governmental Organizations | 3         | 4         | 4         | 4         | 0         | 6         | 29         | 23        | 18        | 7           | <b>98</b>  |
| <b>Total</b>                                                                                            | <b>88</b> | <b>36</b> | <b>38</b> | <b>84</b> | <b>33</b> | <b>43</b> | <b>109</b> | <b>75</b> | <b>46</b> | <b>32</b>   | <b>584</b> |

| NUMBER OF COMMUNICATIONS PRODUCTS |          |          |           |           |          |           |          |           |           |             |            |
|-----------------------------------|----------|----------|-----------|-----------|----------|-----------|----------|-----------|-----------|-------------|------------|
|                                   | AAFC     | CFIA     | DFO       | ECCC      | HC       | NRC       | NRCan    | PHAC      | AMR       | Eco-Biomics | Total      |
| Media interviews                  | 1        | 0        | 7         | 1         | 0        | 3         | 0        | 0         | 19        | 1           | <b>32</b>  |
| Press releases                    | 0        | 0        | 1         | 6         | 0        | 6         | 0        | 4         | 1         | 1           | <b>19</b>  |
| Newspaper and magazine articles   | 1        | 0        | 18        | 20        | 0        | 4         | 0        | 1         | 0         | 0           | <b>44</b>  |
| Community presentations           | 3        | 0        | 9         | 13        | 0        | 3         | 0        | 0         | 0         | 0           | <b>28</b>  |
| Brochures, fact sheets, web pages | 0        | 0        | 0         | 3         | 0        | 8         | 3        | 10        | 0         | 2           | <b>26</b>  |
| <b>Total</b>                      | <b>5</b> | <b>0</b> | <b>35</b> | <b>43</b> | <b>0</b> | <b>24</b> | <b>3</b> | <b>15</b> | <b>20</b> | <b>4</b>    | <b>149</b> |

### End-user engagement and Knowledge transfer activities

| NUMBER OF OUTREACH ACTIVITIES                                      |           |           |           |           |           |           |           |           |          |             |            |
|--------------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|-------------|------------|
|                                                                    | AAFC      | CFIA      | DFO       | ECCC      | HC        | NRC       | NRCan     | PHAC      | AMR      | Eco-Bionics | Total      |
| End-user consultations                                             | 10        | 1         | 6         | 31        | 14        | 12        | 0         | 0         | 0        | 0           | 74         |
| Public meetings                                                    | 0         | 0         | 2         | 1         | 1         | 0         | 0         | 0         | 0        | 0           | 4          |
| Science advice, including to senior management                     | 7         | 18        | 3         | 15        | 7         | 2         | 4         | 21        | 0        | 0           | 77         |
| Outward material transfer agreements                               | 19        | 0         | 0         | 0         | 1         | 3         | 2         | 0         | 0        | 0           | 25         |
| Transfer of standard operating procedures                          | 2         | 13        | 0         | 3         | 1         | 22        | 4         | 7         | 0        | 0           | 52         |
| Disclosures                                                        | 0         | 0         | 0         | 0         | 0         | 4         | 0         | 0         | 0        | 0           | 4          |
| Active patents, patent applications, patents issued                | 0         | 0         | 0         | 0         | 0         | 8         | 0         | 0         | 0        | 0           | 8          |
| Licenses issued                                                    | 0         | 0         | 0         | 0         | 0         | 2         | 1         | 0         | 0        | 0           | 3          |
| New formal collaborative agreements / standard operating protocols | 2         | 0         | 0         | 1         | 0         | 6         | 1         | 4         | 0        | 0           | 14         |
| Knowledge transfer workshops with stakeholders/end-users           | 4         | 4         | 0         | 6         | 15        | 6         | 1         | 7         | 0        | 0           | 43         |
| Requests for research results, papers, collaborations              | 52        | 2         | 0         | 11        | 6         | 3         | 8         | 20        | 0        | 0           | 102        |
| <b>Total</b>                                                       | <b>96</b> | <b>38</b> | <b>11</b> | <b>68</b> | <b>45</b> | <b>68</b> | <b>21</b> | <b>59</b> | <b>0</b> | <b>0</b>    | <b>406</b> |

### 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 in 2016-2017, including but not exclusive to personnel financed through GRDI funds.

| NUMBER OF RESEARCH AND TECHNICAL PERSONNEL   |            |           |           |           |           |            |           |            |           |             |            |
|----------------------------------------------|------------|-----------|-----------|-----------|-----------|------------|-----------|------------|-----------|-------------|------------|
|                                              | AAFC       | CFIA      | DFO       | ECCC      | HC        | NRC        | NRCan     | PHAC       | AMR       | Eco-Bionics | Total      |
| Research scientists                          | 29         | 26        | 12        | 20        | 17        | 54         | 24        | 25         | 34        | 33          | 274        |
| Research professionals                       | 5          | 16        | 11        | 12        | 13        | 9          | 13        | 43         | 19        | 7           | 148        |
| Research technicians                         | 40         | 21        | 18        | 23        | 13        | 131        | 23        | 18         | 16        | 22          | 325        |
| Post-doctoral/ visiting fellows              | 15         | 2         | 6         | 7         | 6         | 21         | 5         | 7          | 3         | 4           | 76         |
| Graduate students                            | 20         | 3         | 2         | 8         | 3         | 0          | 5         | 7          | 12        | 1           | 61         |
| Undergraduate students                       | 20         | 7         | 2         | 6         | 8         | 9          | 5         | 5          | 6         | 4           | 72         |
| Administrative officers                      | 0          | 0         | 0         | 4         | 0         | 0          | 0         | 2          | 0         | 0           | 6          |
| <b>Total</b>                                 | <b>129</b> | <b>75</b> | <b>51</b> | <b>80</b> | <b>60</b> | <b>224</b> | <b>75</b> | <b>105</b> | <b>90</b> | <b>71</b>   | <b>962</b> |
| <b>Total Estimated Full Time Equivalents</b> | <b>61</b>  | <b>16</b> | <b>19</b> | <b>31</b> | <b>23</b> | <b>91</b>  | <b>38</b> | <b>31</b>  | <b>36</b> | <b>24</b>   | <b>370</b> |



## Annex 3 - Highlights of Results Achieved in 2016-2017

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

#### ***Metagenomics Based Ecosystem Biomonitoring (EcoBiomics) Project***

**Participating Departments/Agencies:** AAFC, CFIA, ECCC, DFO, NRC, NRCan, PHAC

**Scientific Coordination:** ECCC, AAFC

**Project Management:** AAFC

Biodiversity is paramount in water and soil to sustain diverse ecosystem services and economic activities across Canada. Genomics tools are the only tools available to characterize this complex biodiversity. The EcoBiomics project develops advanced genomics tools to assess freshwater ecosystem biodiversity and water quality in lakes and rivers; evaluate the health of soil essential to the productivity of agricultural and forestry

systems across Canada; and investigate soil remediation for the oil and mining sectors. This project will enable a more comprehensive perspective of water and soil as living systems.

A significant milestone was reached with the establishment of the Bioinformatics Platform that enables the coordination of metagenomics analyses across seven federal departments and agencies. The Platform was established through close collaboration with Shared Services Canada (SSC). It includes significant high performance computing and data storage capacity online at the Dorval computing centre, and enhanced bandwidth capacity for participating departments and agencies.

Common methods were selected for collecting soil, water and invertebrate samples, and for nucleic acid extraction. A standardized approach was established for soil, water, and invertebrate metadata. Over 1500 soil, water, and invertebrate samples were collected across Canada for DNA sequencing and candidate genomic observatories were identified in collaboration

with end-user groups such as ECCC's National Water Quality Monitoring Program, and the Canadian Aquatic Biomonitoring Network (CABIN). Optimal PCR primers were selected to amplify DNA from bacteria (16S), fungi (ITS2), algae (18S), and invertebrates (CO1) for metabarcoding studies, and a centralized amplicon library preparation approach was set up for soil, water and invertebrate samples. A centralized approach was also established for DNA sequencing using the NRC Illumina MiSeq (metabarcoding) and HiSeq (metagenomics) platforms. Bioinformatics training was provided to 70 project participants, including for the SeqDB genomic management system and other software tools. A Project workflow was developed to coordinate all research and data management. Collaborations were initiated with a similar new initiative in the European Union (DNAqua-Net) and with the new Genome Canada ATRAPP Project (Algal Blooms, Treatment, Risk Assessment, Prediction and Prevention through Genomics).

#### ***Antimicrobial Resistance (AMR) Project***

**Participating Departments/Agencies:** AAFC, CFIA, HC, PHAC and NRC

**Scientific Coordination:** AAFC

**Project Management:** AAFC

The development of resistance to antimicrobials by bacteria that were formerly sensitive is one of the most serious global health threats facing the world today. With no action, annual worldwide human deaths attributable to antimicrobial resistance could reach 10 million by 2050. The Antimicrobial Resistance project uses a genomics-based approach to understand how food production contributes to the development of antimicrobial resistance of human health concern, and explore strategies for reducing antimicrobial resistance in food production systems. It is a component of the Federal Action Plan for Antimicrobial Resistance and Use in Canada.



A description of strain collections has been compiled and a detailed plan for Whole Genome Sequencing (WGS) of bacterial isolates and metagenomes of targeted food and animal samples to understand the sources of clinical resistance. The metadata will initially be collected using available tools in the Canadian Network for Public Health Intelligence (CNPHI) while the sequence data is supplied directly to the Integrated Rapid Infectious Disease Analysis (IRIDA). Once a controlled vocabulary has been implemented for this metadata, it will be sanitized, transformed, and entered into the IRIDA system. Additional prospective sequence metadata will be entered directly into the IRIDA system. Training was provided to project participants for WGS data analysis. Over 1,500 human and non-human isolates have been sequenced to date.

For poultry, DNA from enterococci isolates was prepared and sent for sequencing, including from multi-antibiotic resistant *Escherichia coli* isolates and *Salmonella enterica* serovars (Enteritidis, Heidelberg, Kentucky, Typhimurium and Hadar). A formycin resistance gene (*fosA7*) was detected for the first time in Heidelberg. Feeding trials were conducted using feed supplemented with specific antibiotics, encapsulated essential oils (cinnamon and citral), pomaces from organic cranberry and wild blueberry and their ethanolic extracts to test their effectiveness against necrotic enteritis and coccidiosis in broiler chicken. A field experiment evaluating the persistence and transfer to crops of antibiotic resistance genes following application of poultry litter was undertaken on the AAFC London Research and Development Centre research farm.

For swine, an experimental study was conducted to compare the abundance of enteric bacteria showing resistance to antibiotics in feces from gilts and sows raised with or without antibiotics. From this study, 1910 bacterial isolates resistant to antibiotics were cultivated. The percentage of resistant Enterobacteriaceae was higher in gilts, but the abundance was similar among the groups. A total of 158 isolates were multi-resistant.

A total of 900 multi-drug resistant isolates of *Enterococcus faecalis* and *E. faecium* were isolated from beef cattle and their associated environment as well as from wastewater treatment plants and humans as part of

a "One Health" approach. Preliminary data suggests that there are distinct differences between isolates that are associated with cattle and their environment and those associated with humans.

The conceptual model for the AMR Integrated assessment model initially developed under a previous grant from the Ontario Ministry of Agriculture Food and Rural Affairs has been expanded to include data relevant to all of Canada. The model is being iteratively updated with new data and relationships as they are recognised or prioritised, and as additional pathways are populated.

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

Over several phases of GRDI support, the NRC has built an impressive target discovery and antibody development pipeline, primarily for oncology indications. Promising targets are identified based on their cancer-associated profiles. Hundreds of antibodies are then made against these targets and screened for specificity and function. NRC scientists are now adapting this pipeline to the latest immunotherapy modality: antibody-drug conjugates. The antibody components of these ADCs are being manufactured using the NRC Chinese Hamster Ovary cell production platform, creating a full development pipeline for therapeutic candidates. Combinations of genomic, proteomic, metabolomic and bioinformatic approaches are used for the following:

1. Target identification: To improve clinical efficacy and to overcome some limitations of first generation antibody-based therapeutics, the industry is currently shifting towards innovative and more powerful modalities such as antibody-drug conjugates, which offer the ability to deliver potent cytotoxic drugs specifically to tumor cells. The choice of therapeutic target is a critical success factor in this endeavor. The NRC continues to improve its target selection and prioritization approach, incorporating subtype classification, differential gene expression and subcellular localization data to the analysis of multiple types of cancer. Two rounds of antibody generation were carried out against over 40 new targets, yielding over 1000

clones, which are being functionally characterized. the NRC is partnering these assets with Canadian SMEs once they have completed *in vivo* validation.

2. Production platform: While improvements in Chinese Hamster Ovary-based recombinant protein titer and quality have been achieved by random cell-line mutagenesis and media optimization, efforts to engineer these cells greatly benefit from the application of a systems biology approach with an emphasis on genomics and metabolomics. This approach is accelerating our efforts in process intensification and is also providing a detailed molecular portrait of our proprietary cell line. This molecular characterization is being used in combination with metabolomic analysis to yield significant improvements in yield through optimization of media, especially in fed-batch mode. The composition of the media affects all aspects of metabolism, including key factors such as antibody production, cell density and cell viability that are critical for efficient production of high-quality biologics. Metabolomic analysis allows for the analysis of media composition during the different growth and production phases to understand nutrient utilization and inherent variations in metabolism. The NRC cell production platform is widely used for work with NRC clients and collaborators as well as for internal R&D.

## **Genomic knowledge for the Canadian health regulatory system**

### ***Safety of prebiotics in infants***

Maternal milk contains a wide variety of carbohydrates that are not digested in the small intestines of infants, but pass into the large intestines where they serve as an energy source for the developing bacterial community. Some infant formulas contain easily fermentable carbohydrates to mimic this function. It is important to assess the short-term and long-term effects of fermentable carbohydrates on the developing gut bacteria of young infants, given the large body of scientific literature linking these carbohydrates to gut bacteria composition, immunological function, and gastrointestinal disease.

In this project, HC researchers are studying the impact of dietary fermentable carbohydrates on the gut bacterial community of weaning rats, as well as the long term effects. Their goal is to use genomics-based methods to assess how these carbohydrates influence the composition of gut bacteria in growing infants and whether these changes can be related to changes in the metabolism and gene expression of the cells in the large intestine. They have found that the gene expression of intestinal cells varies depending on diet, sex and age. Interestingly, it appears that changes seen in the weaning rats are reversed after two months of feeding them regular food. Further analysis will be required to determine how these changes may impact later intestinal function.

This project is already increasing awareness among HC regulators of the physiological outcomes that are potentially associated with consuming fermentable materials, especially as they apply to infant formula.

### ***Identification and characterization of microRNA in serum and milk to measure the health effects of fungal toxins and chemical contaminants in food***

MicroRNA (small, non-coding RNA) is important in the regulation of gene expression and their translation into protein products. In this project, HC researchers set out to identify and characterize microRNA molecules found in rodent serum and milk that are associated with dietary exposure to fungal toxins and chemical contaminants currently detected in foods. So far, they have completed an analysis of the microRNA from isolated RNA in serum and liver samples of rodents exposed to several brominated flame retardants, as well as fungal toxin studies to determine the potential biomarkers of liver damage. The team has also completed benchmark dose-modeling of apical endpoints (e.g. toxicological effects involving body weight, liver lesions, organ weights, hematology endpoints, biochemistry endpoints) for specific types of flame retardant chemicals and fungal toxins.

This work will ultimately generate important regulatory toxicology data, thereby enhancing HC's ability to detect and respond to the presence of fungal toxins and chemical contaminants in food consumed by Canadians.

### ***Genomics approach to predict pulmonary pathology induced by nanomaterials***

Nanomaterials (tiny materials measuring less than 100 nanometres) can induce harmful effects in experimental animals. In a first study of its kind, HC researchers are combining toxicogenomics (the study of how genomes respond to toxic substances) and computational tools to identify and analyse the potential toxic effects of different classes of nanomaterials on lung cells and tissues. They conducted a comprehensive toxicogenomics analysis and compared the gene expression patterns in the lungs of mice exposed to different classes of nanomaterials, with the gene expression patterns from lungs showing respiratory diseases following exposures to infectious agents or chemicals. The researchers identified critical gene molecules responsible for lung pathology induced by nanomaterials. More recently, in a follow up study, they further demonstrated that carbon nanotubes-induced lung fibrosis involves a transcription factor that is also relevant for lung fibrosis in humans.

The results have been shared with HC's regulators and presented at international meetings and conferences involving the international regulatory community. The methods developed in the study can be used by HC to prioritize nanomaterials for further toxicological investigation and help in the rapid screening of nanomaterials that are potentially harmful. Future studies will test these methods on novel nanomaterials for which the toxicological data are scarce.

### ***Genomics approach to understand the respiratory syncytial virus vaccine***

A highly contagious virus that infects the respiratory tract of infants and young children, respiratory syncytial virus is the most common cause of bronchitis. To date, no vaccine has been approved for the prevention of infection although dozens of prototype vaccines have been under development for the last 50 years. The slow pace of respiratory syncytial virus vaccine development is largely due to a lack of both understanding of the disease and critical elements for evaluating the efficacy and safety of the vaccine.

This project aims to better understand candidate vaccines in relation to their safety and efficacy. Scientists are continuing Phase 1 animal studies on prototype vaccines; they have identified toxicity associated with certain forms of candidate vaccines and shed light on some of the underlying mechanisms. In addition, the researchers have developed methods to determine biomarkers pertinent to the safety and efficacy of candidate vaccines. The team has communicated its data to other government researchers and academics.

### ***Next generation sequencing detection of de novo mutations to identify germ cell hazards***

A *de novo* mutation is a genetic change that appears for the first time in a family member. De novo mutations are associated with a diverse array of genetic phenotypes or observable characteristics and they appear to contribute to a wide range of human diseases. Evidence suggests that many environmental agents cause DNA damage, thus increasing the risk of inherited mutations and genetic disease in offspring.

Scientists from HC are using genomics technologies to analyse chemically induced heritable mutations in animals and humans. The research team has applied advanced genomic technologies to measure heritable large scale genome changes in mice exposed to benzo(a)pyrene, a common environmental pollutant. The analysis of 300 samples has shown the presence of large scale duplications of DNA sequences in the offspring of exposed mice. Whole genome sequencing of six mouse families has shown a doubling of mutations in the offspring of exposed mice. The completed genome sequence of the MutaMouse transgenic model served as a frame of reference for identifying new mutations in the offspring of exposed males. The team has implemented a bioinformatics pipeline to establish the mutation spectrum in the sperm of exposed mice. This spectrum will be used for sperm-offspring comparisons and heritability assessments.

### ***Genomics approach for the standardization and risk assessment analysis of stem cell based health products***

Stem cells have tremendous potential to treat diseases for which there are currently no cures – however, their use can be risky. In this project, HC researchers are developing diagnostic tools to enable a thorough evaluation of the risks and benefits associated with the therapeutic use of human mesenchymal stem cells, a type of adult stem cell. In 2016-2017, the research team collaborated with three world-renowned scientists in the field of cancer stem cells and hematology. The team also searched for potential protein biomarkers with the Thermo Fisher Scientific Group.

These collaborative efforts have led to numerous presentations at national and international conferences as well as various publications – including one study providing the first evidence that human mesenchymal stem cells have a direct effect on the outcomes of leukemia patients following treatment, which could lead to improved treatments for aggressive forms of leukemia. In addition, the team has generated a list of potential biomarkers to identify mesenchymal stem cells that are both safe and effective for treating immune disorders. These biomarkers are currently being tested to determine their capacity to discriminate human adult stem cells that can suppress an over-active immune response. These successfully validated biomarkers will be used to develop diagnostic tests for evaluating stem cell-based health products.

### ***Development of practical toxicogenomics methods for hazard identification and risk assessment of environmental chemicals***

The traditional toxicology tests used to evaluate the health effects of chemicals are both time consuming and expensive. In this project, HC researchers are developing and validating genomics-based toxicology methods that promise to save time and money compared to traditional tests. The new methods can predict whether a chemical causes DNA damage or other adverse genetic effects.

In 2016-2017, the researchers advanced the application of genomics signatures (patterns of gene expression changes) to identify agents that cause various toxic effects. The team's major accomplishment was to complete the validation of a signature that predicts the ability of chemicals to cause DNA damage in cultured cells of relevance to humans. This work was submitted to the US Food and Drug Administration's Biomarker Qualification Program. The team also completed the development of a software tool that enables any laboratory in the world to apply the signature. Through several case studies, the team demonstrated how the signature can be integrated with both computational analysis of a chemical's structure and chromosome damage tests to predict the relevance of the chemical's responses to human health.

### ***Genomics knowledge to strengthen public health programs***

#### ***New methods to control and prevent food-borne illness***

As food safety is a national priority, PHAC research addresses the critical need for scientific and technical innovation in pathogen detection and characterisation to improve the identification of outbreaks, and accurate and timely source attribution. The international validation of Standard Operating Procedures and an open analytic infrastructure support cross border surveillance and response. The *Salmonella* Genosero-typing Array (SGSA) is being validated and integrated into the PHAC *Salmonella* reference laboratory for the World Organisation for Animal Health, located in Guelph, Ontario. A rapid molecular subtyping method is under development for *Salmonella* Enteritidis and *Salmonella* Heidelberg, types of *Salmonella* that cannot easily be resolved into outbreak clusters using current methods. The validation and certification of these innovative methods will enable their use by provincial and national reference laboratories.

The surveillance programs run by FoodNet Canada and the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) monitor foodborne pathogens and the use and resistance to antibiotics

in the food chain. These programs monitor different points along the 'farm-to-fork' continuum: farms, surface waters, food production, and public health laboratories. Genomic epidemiology approaches applied to food safety are in development to support these programs in the identification of risk factors, sources of exposure, virulence factors, determinants of antimicrobial resistance, and transmission dynamics along the food chain of *Escherichia coli*, *Salmonella*, and *Campylobacter*.

GRDI researchers are working on the successful transition of enteric disease surveillance by the PulseNet Canada network from traditional molecular methods to whole genome sequencing. This will enable all network members to apply whole genome sequencing to foodborne disease surveillance and food safety. A translation framework to encompass all aspects of genomics in the context of PulseNet Canada has been designed, and implementation across Canada is proceeding on schedule.

New metagenomics sequencing approaches are being developed to characterize multiple pathogens in a single isolate without costly and labour intensive culturing conditions. They allow the rapid identification and subtyping of bacterial pathogens directly from complex clinical samples, such as stool, to ultimately improve the speed and accuracy of public health response to infectious disease outbreaks.

### **Detection and genomic epidemiology of priority pathogens**

Researchers at PHAC continue to develop and apply modern technologies (e.g., genomics and mass spectroscopy) alongside advanced scientific computing to address the strategic need to advance the modernization and innovation of Canada's public health capacity for rapid identification of infectious pathogens.

Limited endemic outbreaks of measles are still occurring worldwide. The current genotyping marker used to indicate the absence of "Canadian" measles in circulation has become less effective to track increasingly identical isolates. A new method was developed to identify closely related isolates and track their occurrence to

support source attribution of emerging outbreaks. This will prepare Canada and the international community for the challenges of measles surveillance and elimination.

A national mass spectrometry database to support diagnostic laboratories across Canada has been established in collaboration with international colleagues in the United States and Europe. The mass spectroscopy identification of bacteria assists Canadian public health laboratories and hospitals in the identification of uncommon and rare bacterial pathogens and supports the implementation of new technology that is rapid, inexpensive and accurate for the identification of infectious disease pathogens.

Invasive meningococcal disease, caused by *Neisseria meningitidis*, has been endemic in Quebec for over 15 years. PHAC researchers have used whole genome sequencing to analyse the genetic epidemiology of 47 historical isolates. Their data demonstrates that a unique clone of this pathogen is circulating endemically within the province of Quebec. Notably, by characterising the presence of vaccine targets in the endemic clone, the data also predicts that an existing vaccine could be used to control the disease.

### **Antimicrobial resistance: supporting communities, hospitals and international response**

Reducing the growing threat posed by AMR is one of PHAC's highest priorities because of the risk of losing our ability to manage infectious diseases in humans and animals. To that end, GRDI supported research is developing genomic-based technologies and methods to promote appropriate antibiotic usage and effective infection control procedures. In addition, new tools and procedures are being developed that will enhance our capacity to detect and track AMR pathogens. Together, these activities are designed to reduce the risk posed by antibiotic-resistant infections while supporting the management and treatment of infectious diseases.

Examples include:

- **Human Immunodeficiency Virus (HIV) Drug Resistance:** PHAC researchers have developed a next generation sequencing-based HIV drug resis-



tance testing technology that offers significantly enhanced detection sensitivity, data throughput and cost reduction in comparison to conventional approaches. Canada's National Microbiology Laboratory is collaborating with eleven national/regional HIV reference laboratories in eight Latin America and Caribbean countries (Mexico, Brazil, Argentina, Chile, Colombia, Puerto Rico, Peru and Martinique) to transfer this drug resistance testing method activities to those labs. As a result, countries across Latin America will be able to independently and affordably perform enhanced HIV drug resistance surveillance and clinical monitoring. Better clinical management should in turn reduce HIV transmission by maintaining low viral loads in patients, and guiding the clinical response if drug resistant mutations emerge.

- ***Clostridium difficile***: Research is underway to minimize the burden of *C. difficile* in Canadian hospitals through the better understanding of transmission routes and recurrent cases in healthcare settings. Since infection and control prevention guidelines have focused mainly on patients within hospital settings, new information is needed on the emerging problem of community-onset infection and recurrent infections. Studies of risk factors for recurrent infection are directed at providing new clinical prediction tools to identify patients at highest risk of recurrent infection, which would allow for more targeted preventive and therapeutic interventions for patients with *C. difficile* infection.
- **Carbapenem resistance**: Carbapenem resistance has emerged in Enterobacteriaceae (a family of intestinal bacterial species) and is now causing large outbreaks at several Canadian hospitals. In collaboration with the provinces and hospitals, a standardized whole genome sequencing protocol is in development to support the control and prevention of healthcare-associated outbreaks of carbapenem-resistant Enterobacteriaceae. Single Nucleotide Variations between isolates and their relation to patient transmission patterns have been described. The development of this tool will inform strategies to apply a whole genome sequencing approach for

managing outbreak(s) on site; inform the Canadian Nosocomial Infection Surveillance Program (CNISP) and build capacity in provincial public health laboratories to assist in near real-time surveillance and control ongoing outbreaks.

- ***Neisseria gonorrhoeae***: A novel typing scheme has been developed to strengthen global surveillance of antibiotic resistance in *N. gonorrhoeae*. Known genetic mechanisms of resistance are being characterized to provide an internationally standardized nomenclature for *N. gonorrhoeae*. The standardization of molecular typing data associated with antibiotic resistance in *N. gonorrhoeae* allows public health practitioners around the globe to communicate in a common 'molecular language' enabling a more timely response to emerging drug-resistant strains of *N. gonorrhoeae*. Known as the Neisseria gonorrhoeae Sequence Typing for Antimicrobial Resistance (NG-STAR), this curated web-based user-friendly sequence typing tool based on antimicrobial resistance determinants in *Neisseria gonorrhoeae* is publicly accessible and will be available as a free online service for all scientists, enabling tracking and targeted responses.
- ***Mycobacterium tuberculosis***: Whole-genome sequencing of *M. tuberculosis* is being used to investigate highly homologous outbreak isolates found in Northern Manitoba and Nunavut. By developing an infrastructure for routine whole genome sequencing and genotyping, this study investigates the evolution of antibiotic resistance in previously sensitive strain populations and is leading to the identification of novel resistance mutations not detected by conventional methods. By increasing our knowledge of AMR determinants this study will assist public health officials in targeted surveillance, control and prevention.

## Using genomics to significantly increase Canada's share of global wheat production

The Canadian Wheat Improvement flagship program, funded in part by the GRDI, is the NRC 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 the NRC, AAFC, the University of Saskatchewan, and the Government of Saskatchewan.

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:** Work focuses on improving the necessary resources, including genomic sequences and annotation, large collections of genetic markers, high-throughput genotyping and the development of new populations for wheat breeding. A multiple genotyping and bioinformatics platform has been established to support Canadian wheat researchers and breeders for a range of applied genomic techniques including marker-assisted selection, gene pyramiding, association mapping, and the generation of high-density genetic maps. To maximise the utility of genetic diversity in wild relatives, significant progress has been made towards the development of genomic tools for enhancing the frequency of meiotic recombination and CRISPR/Cas9-based gene editing in wheat.
2. **Enhancing Fusarium and rust resistance:** Fusarium Head Blight and rusts are two major wheat diseases that together account for \$200 million in losses annually in Canada. Marker-assisted selection and rapid introgression methods developed at the NRC are being employed to produce germplasm with increased resistance to these diseases. Scientists at the NRC have identified a number of potential gene targets and markers that impart increased resistance with little yield penalty. To date, 45 genetic markers of resistance and 35 new lines of wheat showing increased resistance have been delivered to wheat breeders. Additionally, hundreds of novel gene and metabolite targets have been identified for future marker development. Several combinations of resistance genes were tested to identify novel combinations with synergistic ("booster") effects on rust resistance. Following multiple years of testing in disease nurseries, a few major effect quantitative trait

loci were detected on multiple chromosomes for various resistance component traits. Breeder-friendly markers were developed to facilitate the deployment of resistance into new Canadian varieties.

3. **Improving wheat productivity under conditions of abiotic stress:** Genetic markers and advanced wheat lines were developed for several abiotic stress related genes, including traits for drought, heat, or cold tolerance. A framework map of markers associated with physiological traits impacting drought tolerance, including root traits, photosynthesis and a number of yield-contributing traits was developed. A standardized whole phenology platform was established and used to discern genetic differences between wheat lines and identify superior lines with better root system and greater photosynthetic efficiency. Wax deposition is an important component of the complex mechanism responsible for performance under water deficit. A set of four key genes controlling the deposition of diketone waxes in reproductive-stages of wheat were identified. Promising biomarkers found to have correlation with increased cold hardiness and heat tolerance were implemented to select or develop valuable germplasm lines that offer unique molecular resources for winter hardiness and thermo-tolerance breeding.
4. **Targeting developmental pathways to improve performance and yield in wheat** Wheat as a crop is facing several challenges including yield gaps and low economic returns. To address these challenges, scientists at the NRC have significantly advanced the understanding of gene targets and regulatory networks influencing photosynthetic efficiency and grain development in wheat. A comprehensive gene expression atlas for grain development has been established. New wheat lines with more tillers, high vegetative biomass, upright leaf architecture, high photosynthetic efficiency and several desirable spike traits have been developed which provide a unique resource for wheat improvement breeding programs.

## Using genomics to improve the value of Canadian crops and agri-products

Genomics research is playing a key role in ensuring the continued profitability of the agriculture and agri-food sector. The GRDI at AAFC supports 19 GRDI mandated projects covering three overarching themes: 1) Biodiversity, gene mining and functional analysis for the identification of genes for desirable traits; 2) Delivery of genomics discoveries through bioinformatics and physical tools to improve access to biological materials and datasets, and to assist and accelerate the adoption and commercialization of new technologies; and, 3) Enhanced efficiency of plant breeding. Projects highlights follow.

### *Buried Treasure in our Oat Germplasm Collection: Accessing adaptive ancestral *avena* alleles*

Canada is the largest exporter of oats in the world. The oat industry brought \$430 million to the farm gate and exported \$620 million worth of high-quality oats in 2012. Wild oat species hold many secrets buried within their genetic makeup that can help improve cultivated oat. Oat breeders often go back to these ancestors and wild relatives to find useful traits such as disease resistance. Scientists are working on advanced methods to analyze the genetic variability that lies hidden in AAFC's collection of almost 30,000 varieties from 26 oat species. The research team grew, measured, and photographed 300 different seed samples from all available oat species and looked at their genetic information. This work has produced a major breakthrough in our understanding of the oat genome. Using genetic markers from a high-resolution map of oat chromosomes from cultivated oat, the team identified which wild oat species were the closest relatives of cultivated oat, and which specific oat chromosomes matched best with those from each wild species. These results provide important information about the evolution of oat, but they also have practical applications. The research helps to explain difficulties that breeders have experienced in crossing and recombining traits from different oat species. The new, high-resolution mapping results will provide guidance in choosing and selecting traits. The new information about oat's closest ancestors may even allow

us to create a new version of cultivated oat directly from its wild relatives. These results will provide new ways to access treasures that lie buried in our oat germplasm collections.

### *Next Generation Sequencing to Identify Pathogens: Development of identification and analysis tools for amplicon-based metagenomics, focussing on high risk and regulated pathogens*

Scientists at AAFC play a key role to accurately scan, analyze and document pests that have a detrimental impact on import and export commodities. Of particular concern are pathogens that can either cause significant yield loss (e.g. bunts and smuts of cereal crops) or impose health risks to livestock and humans (e.g. mycotoxin producing fungi). Over 1,200 fungal species are currently regulated by 15 countries / regions, and 38 species in Canada and over 50 in the United States are under quarantine surveillance. Next Generation Sequencing (NGS) technologies are used by AAFC scientists to detect regulated pathogens at low levels. However, it takes a trained expert to avoid misinterpretation of NGS data. Most "off the shelf" tools for automated classification and analysis of NGS are based on sequence similarity and are not useful in detecting very closely related species. For many of these species, when only sequencing information of targeted DNA regions are available, the accurate assessment of samples for the presence of a regulated pathogen or its close relative(s) requires additional or customized software and knowledge. As NGS technologies become readily available to many international users who may not have the required scientific expertise, misinterpretation of NGS data may generate "false positive" results and create barriers to trade. To prevent false positives and any potential trade issues, AAFC experts trained in taxonomy and genomics are developing bioinformatics tools to help scientists make the best and most accurate science-based decisions using NGS technologies. For example, tools are being developed to differentiate between pathogenic and non-pathogenic species amongst those that are closely related. Another tool in development profiles the biodiversity of microbes and monitors pathogens present in commodities and dif-

ferent environments of the agri-ecosystem. This work involves close collaboration with the CFIA and the Canadian Grain Commission.

***Genomic Tools for Pest Resistant Wheat: Genome-wide mining and mapping of disease-resistance genes - novel strategies to enhance wheat disease-resistance breeding***

Wheat midge pests and rust diseases (including Ug99, a highly destructive strain that is not yet in Canada) can cause significant yield losses for wheat producers. By working with DNA markers linked to rust and midge resistance genes, AAFC scientists can detect multiple pest resistance in a wheat line. Without the use of DNA markers, it is difficult or impossible to detect multiple pest resistance. DNA markers for rust resistant genes have already been provided to Canadian wheat breeding programs, the markers for midge resistance will follow shortly. Further improvements in DNA markers will be possible once they are sequenced and will enable the development of new pest resistant, higher quality wheat cultivars for the benefit of Canadian producers.

**Genomic knowledge for forest generation and protection**

***Identification of genes controlling desirable attributes in economically important tree species***

The GRDI funded research on genomic selection of trees with desirable traits is complementary to the projects funded by Genome Canada: Fast Tests for Rating and Amelioration of Conifers (FastTRAC), and SMarTForests. Genomics tools are essential to achieve economic benefits earlier than with conventional tree improvement programs. To identify cell lines with favourable breeding values early on and thus maximize economic benefits, scientists at the Canadian Forest Service (CFS) of NRCan are currently analyzing a new protocol of somatic embryogenesis initiation with ten families. They have also provided to end-users genomic selection models for productivity traits in Norway spruce.

***Increased knowledge of genomics-based pest diagnostics and mitigation***

Global trade and climate change are two factors that increase the risk of introduction and establishment of unwanted insects and pathogens into Canada's forests. Early detection and rapid responses are critical in mitigating this risk. Traps are commonly used to inventory forest insects. These traps are baited with special chemicals, often pheromones, to attract insects. Sorting and identifying insects captured in traps is a time consuming and costly process. Metagenomics and bio-informatics tools are being developed to identify insects caught in traps, both faster and at a lower cost. Pilot studies to demonstrate proof of concept and optimize metagenomics and bioinformatics tools are ongoing and ahead of schedule. To bait the traps for the brown spruce longhorned beetle and the emerald ash borer, two key economically important insect pests, scientists identified candidate 'attractive' proteins and have begun the design and engineering of a cell-based insect odorant volatile screening tool. The project uses functional genomics data for pest insect surveillance, a novel approach within the government of Canada.

The European gypsy moth is found in Canada and is a relative of the Asian gypsy moth, an unwanted insect. The CFIA conducts inspections of marine vessels and their cargo, especially those arriving from the Far East, to ensure that they are free of Asian gypsy moth. Vessels that are found to carry the insect, usually found as eggs, must leave port and remove all evidence of the insect. Scientists analyzed DNA from eight populations of Asian gypsy moth from across its range and developed markers that can identify their geographic origin. The team provided CFIA with fully validated detection tools, along with Standard Operating Protocols for the detection of Asian gypsy moth and closely related species, whose introduction would have important economic impact in Canada. The team has also developed tools for the detection of the pathogens responsible for butternut canker, Annosum root rot, and ash dieback. The work is complementary to the project funded by Genome Canada: BioSurveillance of Alien Forest Enemies

(BioSAFE), and is invaluable for negotiating agreements with Canada's trading partners and to lower the risks of detrimental introductions in North America.

A spruce budworm outbreak is currently affecting large stands of forests in Quebec and is poised to spread into Ontario. Models that forecast outbreak development will provide forest managers, specifically the Ontario Ministry of Natural Resources, with another tool to support management decisions for this pest. GRDI scientists have processed close to 1000 spruce budworm samples from 20 sites to estimate the spruce budworm population at time "0" for forecasting models.

Ash trees are at risk of disappearing from the landscape due to emerald ash borer attacks. Research continued to study the factors influencing Emerald Ash Borer larval performance in various ash species to help identify resistance mechanisms and to support the development of a diagnostic test, in collaboration with the cities of Montreal and Ottawa. The project is an example of citizen science in action: it is integrated with TreeTaggr, a user-friendly Twitter-based tool that allows Canadians to report on pest infestations and help protect urban forests.

Prevention is the best strategy for forest health. Scientists continue to collect genomic information on pathogens and insects that may have deleterious impacts on Canadian forests, developing tools that can be used to 1) certify plant and tree material as free of unwanted pathogens; and 2) monitor potential invasive species in Canada. Current work is focused on poplars and pines, some of the most important tree species in the northern hemisphere. The research is complementary to the project funded by Genome Canada: BioSurveillance of Alien Forest Enemies (BioSAFE).

Trees that are resistant to white pine blister rust are required to restore pines on the North American landscape. Scientists are studying resistance mechanisms in western white pine, limber pine, whitebark pine and eastern white pine. A selection tool based on SNP markers was used for screening of resistance in western white pine breeding programs, and a major gene resistance locus was discovered in Alberta limber pine. Resistant stocks and genomics knowledge are avail-

able to stakeholders to support restoration of white pine in forest ecosystems that are disturbed by blister rust in Canada and across North America.

The fungus-like pathogens known as *Phytophthora* are a *phytosanitary* concern for Canada and its trading partners. Current diagnostic methods that detect *Phytophthora* species cannot differentiate whether a positive result is coming from living or dead organisms. Building on the work started last year, a method was developed to detect living *Phytophthora* in both pure cultures and infected wood. The research team also gained valuable knowledge of the stability of *Phytophthora* mRNA as a tool to test the efficacy of novel wood treatments.

### ***Improving land reclamation following oil sands mining***

An industrial-scale pilot project using genomics tools to better understand tree-soil microbiome interactions is ongoing at oil sands reclamation sites in Fort McMurray. The results provide a picture of the above and below-ground genetic diversity observed in sites under reclamation, to understand how different reclamation strategies affect the dynamics of the whole biological system. The project will define how phytoremediation could be used in Alberta to return to an ecosystem similar to natural forests, which would improve the industrial and environmental competitive advantage of the Canadian oil sands operators.

### ***Ecosystem integrity in forest management***

A project was initiated in 2015-2016 to develop metagenomics tools that assess ecosystem integrity and the sustainability of forest management practices. In 2016-2017, the team sequenced a gene library of boreal forest soil invertebrates and selected 18 sites along New Brunswick watersheds for collecting aquatic microbial samples. Further analysis is ongoing to identify critical riparian hotspots for sustaining ecosystem integrity and inform forest management guidelines. A meta-barcoding technique was developed to analyze the aquatic microbial community of critical riparian habitats and assess them as indicators of biological responses to water-



borne nutrients. The tool could be used by regulators, certification bodies and forest industry to assess the sustainability of forest management practices.

### **Genomics knowledge and advice for the management of fisheries and oceans**

In 2016-2017, GRDI funded the final phase of six multi-year projects as well as two new research projects to:

- increase capacity for generating genome wide data of commercial sea scallop and invasive green crab populations to directly address management and conservation needs;
  - develop a genomics-based test for stock analysis to inform domestic and international Atlantic salmon fisheries;
  - develop new molecular marking tools for narwhal stock and population assessment for effective national and international allocation of the harvest;
  - identify adaptive mechanisms structuring and maintaining redfish genetic diversity in Atlantic Canada, while addressing knowledge gaps in redfish population structure;
  - quantify the genetic impacts of farmed escaped Atlantic salmon on wild salmon populations and the frequency of interbreeding in the wild;
  - produce a predictive "FIT-CHIP" tool to assess a variety of external stressors, pre-existing conditional states and important physiological impacts on salmon stocks; and
  - develop environmental DNA (eDNA) tools for detecting key aquatic invasive species as well as species at risk as a non-invasive monitoring technique to inform management.
- Examples of results and outcomes from DFO's GRDI-funded genomics research projects from 2016-2017 include the following:

### ***Impact of escaped farmed fish on wild Atlantic salmon populations***

It is estimated that up to two million farmed domesticated Atlantic salmon escape annually on a worldwide basis, often in areas where farmed caged salmon vastly outnumber wild populations. GRDI funding allowed DFO scientists to develop tools to examine the genetic interactions among escaped farmed salmon and wild populations in Newfoundland to better understand the impacts of aquaculture on wild populations. Results from this study directly support decisions related to DFO's Aquaculture Policy Framework, the implementation of DFO's Wild Atlantic Salmon Conservation Policy, and is informing decisions on whether to expand aquaculture in key areas, and allow farming of non-native aquaculture strains in Canadian waters. This will improve sustainable and low-impact aquaculture production and wild population conservation in Canada.

### ***Development of salmon "FIT-CHIPS" to rapidly determine health and condition of salmon***

Scientists from DFO have developed a series of "salmon FIT-CHIPS," a novel monitoring tool to predict salmon health. It identifies rapidly and inexpensively the presence of stressors (e.g. temperature, hypoxia), disease (viral, bacteria), and the state of preparedness for salinity shifts associated with migration. The application of these chips will: 1) optimize salmon hatchery culture and release strategies to improve salmon enhancement programs, 2) increase accuracy of marine survival estimates for harvest stock assessment by including information on health and impact of stressors, and 3) increase survival of salmon through the identification and mitigation of stressors. Results provide data to support science advice to managers in fisheries, aquaculture, enhancement, or environmental and university organizations. Outcomes of this research support DFO's Economically Prosperous Maritime Sector and Fisheries Plans and Priorities, and results are being made available to policy makers in the Aquaculture Management Division.

### ***Stock delineation of narwhals for conservation and traditional fisheries***

Narwhal is an Arctic whale considered of Special Concern by the Committee on the Status of Endangered Wildlife in Canada (COSEWIC). It is also an important cultural and subsistence resource harvested by Inuits in Canada, providing needed revenue of \$5M annually for northern communities. Under the Convention on the International Trade of Endangered Species (CITES), scientific evidence to support findings of non-detrimental impacts on the at-risk species is required to obtain permission for international trade. GRDI funding allowed DFO scientists to develop narwhal specific genetic markers and determine the differences among narwhal stocks, survey new and existing (archived) narwhal samples, and integrate this new genetic data with existing data. Results for this research allow managers to assess and update narwhal hunt boundaries and contribute directly to the ongoing development of Integrated Fisheries Management plans. Improved health and sustainable harvest of narwhal populations will directly impact the health and economic prosperity of Nunavut communities that depend on them, in a challenging and changing environment.

### ***Assessing scale of dispersal and connectivity of the invasive green crab***

The European green crab is a high impact aquatic invasive species and predator with large commercial and ecosystem consequences. It is inflicting serious damage on both the Atlantic and Pacific coasts. Green crabs compete with native crabs and lobster for food and shelter and can harbour pathogens to native decapods, reduce invertebrate and fish diversity, can destroy shellfish beds (quahog, oyster, clam and scallop), thereby threatening shellfish aquaculture, and damage eelgrass beds, essential habitats for many species. In GRDI funded projects, DFO scientists developed genomic markers and identified two different lineages of green crab, their invasion pathways and lineage-specific environmental tolerances, as well as the role of hybridization in the expansion of invasive populations. This information was used to determine likelihood of range expansion, and update risk assessment for temperate and northern

(Arctic) locations in Canada. The research contributes to understanding climate-associated adaptations, risk management strategies for invasive species, and legislation, regulation and compliance measures to prevent unwanted invasive species introductions and limit impacts post-invasion.

### ***Integrating adaptive and population structure genetic information in redfish fisheries***

The term redfish refers to a collective group of different *Sebastes* species that are a major commercial groundfish, with landings worth over \$40 million in 2015. The various redfish species and populations are difficult to distinguish, and those that are listed as threatened or endangered under COSEWIC are threatened by their inclusion in a single non-differentiated fishery. Two GRDI-funded projects at DFO have used current and archived redfish samples to genetically distinguish among different species and populations, examined how the populations have changed over time, identified adaptive mechanisms influencing genetic diversity and local adaptations, and spatially delineated some species and populations. This knowledge has led to the development of separately managed redfish fisheries where not previously possible, including species- and population-specific Total Allowable Catch and allocation rules, as well as the designation of one population as 'threatened' under COSEWIC with separate precautionary-approach conservation management strategies implemented. The research also facilitated a partnership with redfish harvesters, to establish the first industry-led monitoring program for redfish species.

### ***Improved mixed-stock analysis for domestic and international Atlantic salmon fisheries***

Regional stock identification for Atlantic salmon includes populations at various stages of risk of extinction, as well as populations originating from domestic and international waters. This project combined existing and new genomics resources to create an informative group of genetic markers to enable rapid and cost-effective genetic analysis. Results have clarified fine-scale and evolutionary population structure as well as individual fish sex and stock identification. This work directly informs Canadian policy regarding domestic (e.g. First

Nations fisheries) and international fisheries agreements (i.e. International Council for the Exploration of the Sea/ North Atlantic Salmon Conservation Organization), decisions related to the implementation of DFO's Wild Atlantic Salmon Conservation Policy, and the protection of genetic and geographic diversity needed for conservation of mixed stock fisheries. The tools developed will also be used for species and stock identification by DFO's Conservation and Protection for making decisions regarding potential violations in salmon subsistence and recreational fisheries.

### **Genomics-based tools and technologies for responsible environmental decision-making**

In 2016-2017, ECCC began a new research cycle (2016-19) in the development of genomics tools and approaches to support pollution prevention, regulatory compliance and enforcement, wildlife management, and risk assessment of potentially toxic substances.

The four priority research areas are described below.

#### ***Ecotoxicology***

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 toxicological effects of chemicals in both wildlife and aquatic life. For instance, genomics tools and approaches are in development 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 on biodiversity and ecosystem functions. Research focused on assessing the effects of exposure to chemicals of concern (including individual chemicals and complex mixtures) in avian, mammalian and aquatic species. A better understanding the molecular mode of action of chemicals significantly enhances the accuracy of models that contribute to improved risk assessment.

#### ***Environmental monitoring***

Activities also focused on understanding and monitoring aquatic and land-based ecosystems. For example, research focused on extending an established method for recovering biodiversity information from bulk envi-

ronmental samples. In the Great Lakes, DNA barcoding is being applied to monitor algal community compositions for harmful blooms, while changes to microbial diversity are being evaluated for their ability to provide early warnings of adverse changes to aquatic ecosystem health. The application of this work will increase our understanding of cumulative environmental impacts and related risks associated with multiple stressors interacting over time.

#### ***Wildlife conservation***

Genomic techniques were developed to better understand wildlife species and how they are responding to changes in their habitats due to disturbances, including climate change and natural resource development. For example, scientists are using genomics to study the impacts of cumulative stress associated with large scale environmental changes (e.g. climate change and pollution) in wildlife populations such as arctic nesting eiders. Tools are also being developed to delineate the geographical distributions of endangered, elusive, or invasive species using analyses of material found in environmental matrices. These efforts will support the management of wildlife species and increase our understanding of how populations adapt to changes in their environment.

#### ***Compliance and enforcement***

Scientists are developing various innovative methods and tools to support the enforcement of regulations to protect the environment and wildlife from pollution, wildlife trafficking and other threats, and to support regulatory monitoring programs. For example, genomic markers are under development to inform the harvest management of murre colonies in the North Atlantic.

### **Using genomics for food safety, animal health and plant protection**

#### ***Characterizing food-borne pathogens through the creation of genomics databases***

Scientists from CFIA have created a database of food-borne pathogens and new tools to enhance the capacity to detect the presence of microbial

hazards in food. More than 3000 pathogens that include strains of *Salmonella*, *Listeria*, *Escherichia coli*, *Shigella*, *Staphylococcus* and infectious bacteria related to food-borne illnesses have been fully sequenced and added to the database. Metagenomic sequence data from beef, pork and produce samples have been mined to inform the development of improved methods for pathogen detection. Automated bioinformatic processes for rapid sequence analysis have been developed to ensure data reliability.

### **Strengthening animal health diagnostic tools**

This project aims to enhance the CFIA's capability in the acquisition, management, analysis and utilization of genomic data. New wet bench methodologies and bioinformatics pipelines for the acquisition, assembly and annotation of the genomic sequences of known high priority, unknown or unexpected pathogens and differentiation of disease vectors from closely related species are being established. To date, this project has sequenced approximately 300 isolates of diagnostic, surveillance, archived and research samples representing 12 diverse viral families and 21 viral species. The CFIA created the reference genomic database of *Mycobacterium bovis* strains isolated between 1985 and 2016 from Canadian livestock and wildlife, and harmonised epidemiological investigations of bovine tuberculosis outbreaks with the USDA. Through the development of new, user-friendly methods for rapid detection and typing of high priority pathogens and vectors, this project is working to enhance CFIA's capability to prepare for and respond to high priority, new, emerging, and re-emerging animal health threats.

### **Detection and identification of invasive plants, plant pests, and plants with novel traits**

The CFIA is developing DNA barcoding and next generation sequencing to enhance its plant health regulatory capacity in the areas of detection and identification of invasive plants, regulated plant pests and pathogens, and plants with novel traits. Genomic regions from different organisms were sequenced and assembled for the development of markers to be used for identification and detection. Preliminary analyses of field samples have identified a putative new member of the rare genus

*Idaeovirus* that may be the causal agent of an uncharacterized disease in Ribes. Whole genome analysis of bacteria provided evidence to reclassify *Clavibacter michiganensis* subspecies at the species level.

Comparative genomics analyses led to the identification of pathogenicity islands in soft rot bacterial isolates from potatoes. Genetic markers were selected and validated to sequence a number of nematode genera, including *Pratylenchus*, *Meloidogyne*, *Xiphinema*, and *Ditylenchus*. Plant with Novel Trait (PNT) mapping and junction analyses were conducted for transgenic soybean, potato and corn samples. Asian gypsy moth and Asian long-horned beetle mitochondrial and nuclear regions were sequenced to rapidly and accurately identify species, population origins and genes associated with specific traits.

### **Development of genomics and bioinformatics tools**

The overarching goal of this project is to harmonize genomics activities across CFIA's three business lines, focusing on bacterial genome analysis. A web-based Genomics Portal has been developed to enable access to CFIA's databases of bacterial genomes. This portal includes a bioinformatics pipeline for genome assembly, a marker selection feature, tools for PCR primer verification, and tools for the detection of genes that confer antimicrobial resistance. Methods to analyze Single-Nucleotide Variants (SNVs) have also been incorporated into the portal. Another important activity undertaken by this project was an evaluation of bioinformatics processes and procedures to ensure that activities met quality assurance requirements for the Agency. The use of bioinformatics tools for diagnostic purposes is a new area for the CFIA, and it is important that strategies and procedures for data analysis, data management and data curation meet quality requirements. The CFIA leads an international working group on the development of quality assurance guidelines, which were published in the consensus standards Journal of Association of Official Analytical Chemists (AOAC) International. Documents describing how the CFIA is currently implementing these guidelines are under development.

## Annex 4 – Research Tools and Processes Produced by the GRDI

### Research tools

- Galaxy cluster in the cloud deployment tool (AAFC);
- Galaxy tools for IRODS data grid integration (AAFC);
- RAM: R for Amplicon-Sequencing-Based Microbial Ecology, version 1.2.1.7 (AAFC);
- Deposited 454 pyrosequencing demultiplexed data of 97 samples to Sequence Read Archive (AAFC);
- High-density marker profiling for ancestral genomes of *Avena* species and hexaploid oat (AAFC);
- Genes associated with the 2DL QTL locus for *Fusarium* head blight resistance (AAFC);
- Transcriptomic evidence for the control of soybean root isoflavonoid content by regulation of overlapping phenylpropanoid pathways (AAFC);
- Database and bioinformatics pipeline to identify sequences for the detection and identification of unknown plants with novel traits using next generation sequencing technology (CFIA);
- High-throughput method using barcoded adapters for whole genome sequencing of influenza A virus isolates from swab specimens (CFIA);
- Standardized method using next generation sequencing technology to generate barcode libraries of Avian Paramyxovirus-1 from isolates (CFIA);
- Standard procedures for whole genome sequencing of *Mycobacterium bovis* (CFIA);
- Bioinformatics pipeline for the analysis of fungi and oomycete from spore and insect traps (CFIA);
- Bioinformatics pipelines for the analysis of food-borne pathogen isolates (CFIA);
- Bioinformatics pipeline for the analysis of crop seed amplicon for the detection/identification of contaminated seeds (CFIA);
- Next generation sequencing procedure to detect regulated and quarantined pests in the potato post entry quarantine program (CFIA);
- Biportal that houses a number of tools for processing whole genome sequencing data, including GeneSipp, PCR verifier, AMR detector, and other tools (CFIA);
- R program (genepopedit) published as a simple and flexible tool for manipulating multilocus molecular data in R, broad genetic applications (DFO);
- Parallel\_Newhybrids: R package developed and published for efficient parallel identification of Atlantic salmon hybrids and hybrid classes (DFO);
- Validation of Viral Disease Development Biomarker panel for incorporation into salmon FIT-CHIPs to assess health status to inform management of salmon stocks (DFO);
- Smoltification Biomarker panel developed with TaqMan assay efficiencies species amplifications, and preliminary validations completed for incorporation into salmon FIT-CHIPs to assess migration-readiness (DFO);
- Thermal stress Biomarker panel with TaqMan assay efficiencies and species amplifications, and preliminary validations for incorporation into salmon FIT-CHIPs to assess stress history and preparedness (DFO);
- Hypoxia stress Biomarker panel with TaqMan assay efficiencies and species amplifications determined for incorporation into salmon FIT-CHIPs to assess stress history and preparedness (DFO);
- Biomarkers associated with imminent Mortality identified and TaqMan assays developed and efficiency tested and applied across multiple tracking and holding studies to be incorporation into salmon FIT-CHIPs (DFO);
- eDNA sampling protocol developed for aquatic invasive species biosurveillance to be used in shellfish transfers in British Columbia (DFO);



- Next generation sequencing (NGS) to detect microbial species within an artificial microbial blend (ECCC);
- Custom designed 4 X 44K microarrays for *S. tropicalis* (Agilent Technologies, California, USA) to perform high quality gene expression analysis (ECCC);
- Growth chambers for cyanobacteria and algal cultures (ECCC);
- ToxChip PCR array for a Pacific coastal seabird species (ECCC);
- A novel screening technique, which uses whole liver slice cultures to screen for chemical effects in wild and domestic species (ECCC);
- endpoint PCR and qPCR assays for detecting human, dog, ruminant, cow, and seagull fecal contamination in water (ECCC);
- qPCR array assay based on newly published human gut microbiome information to more comprehensively detect and characterize human fecal contamination in water samples (ECCC);
- eDNA sequencing and data analysis pipeline as an additional tool to get more source tracking information out of water samples (ECCC);
- Development and implementation of captive feeding studies in an avian model (ECCC);
- Mini-rotating annular reactors for controlled exposure and growth of microbial communities (ECCC);
- Glass-Agar Sandwich Reactive Oxygen Species assay (ECCC);
- Complete sequence of common murre genome (ECCC);
- Screening method for regulators to detect and identify microRNA changes in tissue exposed to fungal toxins and anthropogenic chemicals (HC);
- Data analysis tools and bioinformatics algorithms for regulators to screen nanomaterials with the potential to induce lung disease (HC);
- Animal models and assays for the evaluation of adverse reactions resulting from the exposure to the Respiratory Syncytial Virus for human health risk assessment (HC);
- Isolation methods for human mesenchymal stem cells (HC);
- Software to analyze genetic material (HC);
- Bioinformatics pipeline for applying next generation sequencing to simultaneously sequence large numbers of barcoded mutant genes for comparing mutagenic mechanisms of various agents among tissues and enabling improved evaluation of genotoxins (HC);
- Bioinformatics pipeline for applying next generation sequencing for analysis of complex and large genomic data for DNA changes in tissues exposed to toxins for human health risk assessment (HC);
- Refined biomarker to distinguish between genotoxic (DNA damaging) and non-genotoxic chemicals for human health risk assessment (HC);
- BMDEpress Data Viewer: toxicogenomics tool for human health risk assessment of chemicals, to be used as a prototype for future models at the US National Institute of Environmental Health Sciences (HC);
- High-throughput genotyping platform for wheat capable of simultaneously profiling SNP markers (NRC);
- Breeder friendly diagnostic markers for rust-resistance genes (NRC and AAFC);
- Two breeder-friendly Fusarium head blight-resistance molecular markers developed (NRC);
- Genes exhibiting extreme heat tolerance when highly expressed in wheat in growth chamber conditions (NRC);
- Identified markers for glaucousness, root proliferation, height, and seed size in wheat (NRC);
- Signalling factors involved in abiotic stress response in wheat for drought, heat, or cold tolerance (NRC);
- Gene expression atlas for wheat seed development (NRC);
- Gene targets for photosynthetic efficiency in wheat (NRC);
- Galaxy Bioinformatics platform for wheat sequence data analysis (NRC);

- A nested-association mapping (NAM) population of 4,700 RILs for dissecting genetic architecture of complex traits (NRC);
- Genomic tools for enhancing the frequency of meiotic recombination and CRISPR/Cas9-based gene editing in wheat (NRC);
- Integrated genomics approach for use in genetic mapping of economic traits in trees with complex genomes (NRCan);
- A novel SNP-based selection tool for use in resistance screening in western white pine breeding programs nationally and internationally (NRCan);
- Novel limber pine germplasm with major gene resistance for use in breeding program nationally and internationally (NRCan);
- Molecular approach to the identification of the geographic origins of gypsy moth samples intercepted at Canadian ports using SNP markers (NRCan);
- 12 validated molecular detection assays (qPCR) for Asian gypsy moth (NRCan);
- Molecular detection assays for the Canadian 50 most unwanted forest pathogens (NRCan);
- Asian gypsy moth and related species collection containing over 800 specimens (NRCan);
- Increased adoption of TreeTaggr, Twitter based application to report the presence of tree pests such as emerald ash borer (NRCan);
- Protocols for the extraction of nucleic acids from field and bulk samples (NRCan);
- New sets of primers for barcodes for forest Coleoptera (NRCan);
- Meta-barcoding tool to assess the terrestrial soil faunal community component of ecological integrity (NRCan);
- Meta-barcoding technique to assess aquatic microbial communities as indicators of biological response to water-borne nutrients from critical riparian habitats in an effective and cost-effective way (NRCan);
- SISTR: (<http://lfz.corefacility.ca/sistr-app>) a bioinformatics resource for multiple rapid *Salmonella* subtyping (PHAC);
- Panseq: (<http://lfz.corefacility.ca/panseq>) for the pan-genomic analyses of closed and draft genomic sequences (PHAC);
- SuperPhy: <http://lfz.corefacility.ca/superphy>: online predictive genomics platform provides near real-time analyses of thousands of genome sequences (PHAC);
- Phylotyper: <https://github.com/superphy/insilico-subtyping>: predicts biological subtypes from gene sequence data (PHAC);
- Ectyper: [https://github.com/phac-nml/ecoli\\_serotyping](https://github.com/phac-nml/ecoli_serotyping): predicts serotype from genomic sequence, and identifies known *Escherichia coli* virulence factors within whole-genome sequence data (PHAC);
- Feht: <https://github.com/chadlaing/feht>: A commandline program to automatically identify markers predictive of groups (PHAC);
- Development of protocols for the extraction of nucleic acids from *C. difficile* in 96 well format (PHAC);
- Application of targeted PCR and amplicon sequencing of SNVs of SE for identification of serotypes of *S. enterica* (PHAC);
- Application of the RNase-H dependent PCR (IDT Inc.) for detection of SNVs of *S. Heidelberg* strains using raw Illumina sequencing data or using unfinished genomes (PHAC);
- An online sequenced-based molecular antimicrobial resistance typing tool for tracking the global dissemination of *N. gonorrhoeae* strains (PHAC);
- A curated database of antimicrobial resistant gene sequences from Canada combined with publicly available alleles from around the globe (PHAC);
- A SNP-based pipeline for WGS analysis in the context of a hospital outbreak and antimicrobial resistance (PHAC);
- Illumina MiSeq next generation sequencing and the analysis of results using National Microbiology Laboratory IRIDA platform and BioNumerics software (PHAC);

- Salmonella Genosero typing Array (SGSA) for high throughput Salmonella typing (PHAC);
- HIV DR analysis (HyDRA) pipeline and web server (PHAC);
- Illumina MiSeq-based HIV DR typing protocol (PHAC);
- High resolution measles genotyping method for outbreak investigation (PHAC);
- The Salmonella In Silico Typing Server (SISTR): allows users to upload draft WGS assemblies and performs serovar prediction, cgMLST analysis, with meta-data driven interactive visualizations for phylogenetic and epidemiological analysis that allow the user to examine the phylogenetic, spatial, and temporal distribution of strains (PHAC);
- Methods for extraction of nucleic acids of priority pathogens from common clinical samples (PHAC); and
- Web application for rapid analysis of metagenomics sequence data for the identification of novel pathogens (PHAC).

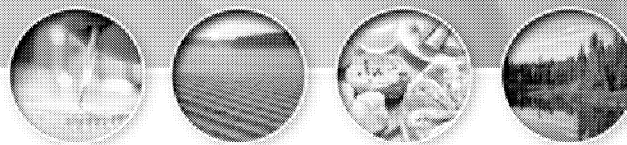
### Research processes

- High resolution mapping of the stem rust resistance gene SrCad (AAFC);
- Evaluation of RGAugury as an integrative bioinformatics tool for large scale genome-wide identification of resistance gene analogs (AAFC);
- Using Haplotag software for haplotype-based genotyping-by-sequencing analysis (AAFC);
- Protocols for generating WGS for Seneca Valley Virus from swabs (CFIA);
- Field experiment protocols for metabarcoding eDNA sampling, extraction, and bioinformatics to be used for field surveys for aquatic invasive species and species at risk management (DFO);
- 220K salmon SNP array as a genetic tool to inform domestic and international fisheries and conservation of Atlantic salmon (DFO);
- 49 SNP type assays to inform management of Atlantic salmon stocks (DFO);

- A 6K redfish SNP catalogue, to support research informing commercial stock assessment (DFO);
- Optimized protocol for Atlantic salmon genotyping on 96 SNP x 96 individual platform, for use in determining aquaculture introgression effects on wild populations, to inform management of aquaculture and conservation of wild stocks (DFO);
- A scallop panel of SNP-type assays for fisheries stock assessment (DFO);
- A green crab panel of SNP-type assays for aquatic invasive species assessment (DFO);
- Gill-tissue specific FIT CHIP for non-lethal measurement of salmon health indices to be used to inform salmon enhancement programs and fisheries management (DFO);
- Ion Torrent workflow for next generation sequencing of narwhal and beluga for population metagenomics investigations to inform marine mammal stock management (DFO);
- Narwhal mitogenome sequence analyzed and assembled for stock assessment information (DFO);
- Metabarcoding protocols developed for aquatic invasive species biosurveillance to be used in shellfish transfers in BC (DFO);
- RT-qPCR method for detecting norovirus GI and GII in waste water treatment plant samples (ECCC);
- NGS applications in microbial ecology studies applying microbial community end points, isolation of DNA from complex environmental samples, amplification of 16S cyanobacterial and 16S chloroplast (eukaryotic algae) RNA using specific designed primers and sequencing (ECCC);
- A novel and rapid process by which complex extracts are prepared (containing all organohalogen contaminants) from wild bird eggs (ECCC);
- A process/SOP for developing Avian ToxChip PCR arrays for any species of bird (ECCC);
- NGS applications in ecotoxicological studies applying microbial community end points, isolation of mRNA from complex environmental samples (ECCC);

- Protocol to multiplex more genetic samples in one single sequencing lane (ECCC);
- Animal model and assay protocols to analyze the immune response and adverse reactions resulting from the exposure to the respiratory syncytial virus for vaccine regulation (HC);
- Standardized method for assessing microbiome composition (HC);
- Transfection method for human mesenchymal stem cells (HC);
- Transcriptomics data from human mesenchymal stem cells derived from normal and leukemic patients (HC);
- SNP discovery approaches for wheat, including an automated DNA extraction and SNP analysis platform (NRC);
- Data analysis pipeline that integrates quantitative trait locus and expression quantitative trait locus mapping methods (NRC);
- Metabolomics methods for experimental analysis of wheat infected by fungi (NRC);
- Marker-assisted selection and rapid introgression methods to produce wheat germplasm with increased Fusarium head blight resistance (NRC);
- Mitochondrial DNA to identify novel gypsy moth ecotypes (NRCan);
- Updated Standard Operating Procedures (SOPs) for the maintenance of insect cell lines (NRCan);
- SOPs for the use of the Asian gypsy moth assays by end-users (NRCan);
- User Guide for the development and validation of real-time PCR assays (French and English versions) (NRCan);
- A new DNA extraction protocol for spore on silicone-coated rods (NRCan);
- Standard operating procedures (SOPs) for the collection of field insect samples (NRCan);
- SOP for curating and identifying insect samples (NRCan);
- SOP for processing and identifying insect samples with metagenomics and bioinformatic tools (NRCan);
- Optimized protocols for the extraction of nucleic acids from *C. difficile* in 96 well format suitable for WGS (PHAC);
- Improved analysis of whole genome sequencing data from *S. Heidelberg* (PHAC);
- Typing and tracking of *N. gonorrhoeae* via in silico antibiogram (PHAC);
- A knowledge translation pathway of synthesis, iterative tailoring, and application to provide comprehensive education, training and ongoing support for genomics to provincial public health labs and federal food safety partners that will introduce WGS into routine surveillance and outbreak response by the PulseNet Canada network (PHAC);
- Standard Operating Procedures for SGSA testing of Salmonella isolates (PHAC);
- The MiSeq-based HIV drug resistance testing platform (PHAC);
- A pipeline for the isolation, library construction, WGS generation, and SNP analysis for use during a hospital outbreak situation. The analysis pipeline includes specific analysis for SNPs within Tn4401, a transposon that carries the Klebsiella pneumoniae carbapenemase to track its movement between plasmids (PHAC);
- A novel pipeline for the rapid identification of plasmids from WGS data to rapidly identify the types of plasmids found in clinical isolates including those that harbour the KPC gene (PHAC);
- Protocol for generation of sequencing libraries for use in next generation sequencing of *Mycobacterium tuberculosis* (PHAC);
- A process for quantifying the strength of epidemiological relationships between bacterial isolates (PHAC);
- A set of methods (and method guidance) to optimize the extraction, preparation, and analysis of DNA from a newly emerged pathogen (PHAC); and
- A validated pipeline for pre-processing of WGS data, a process that allows users to take raw sequencing reads and perform assembly, gene prediction and annotation of WGS data in order to prepare it for downstream analyses (PHAC).

# APPENDIX B – GENOMICS R&D INITIATIVE



## Performance Measurement Framework Overview

A horizontal Performance Measurement Strategy was developed for Phase VI of the GRDI. This document covers fiscal years 2014-2015 to 2018-2019 and formalizes the roles and responsibilities of the eight departments and agencies involved in the initiative to support effective monitoring and evaluation activities.

The logic model presented in Figure 1 reflects the overall objectives for the GRDI:

*Through the GRDI, eight federal science departments and agencies collaborate in the field of high-impact genomics research to address biological issues that are important to Canadians, focusing on the innovative and regulatory role of federal government research and operational mandates in important areas such as safe guarding health, food safety, sound management of natural resources, a sustainable and competitive agriculture sector, and environmental protection.*

A number of activities are conducted to reach this objective, focused on: R&D activities; coordination of research, reporting and management activities; collaboration among stakeholders to access world-class research infrastructure and networks; and 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 for interdepartmental collaborations, scientific information and publications, research tools and products, and a highly skilled workforce. As immediate outcomes, these outputs will provide: structured collaboration mechanisms among participating departments and agencies; enhanced scientific leadership to support governmental mandates and priorities; knowledge, tools and advice for policy and regulatory decisions, as well as for the development of innovative tools and processes.

Intermediate outcomes consist in positioning federal science departments and agencies as genomics research leaders; use of research results by government policy makers and regulators for better informed evidence-based regulatory, policy, and resource management decisions; and use of research results by stakeholders to support innovation in Canada. Ultimately, the GRDI would be one of the factors contributing solutions to issues that are important to Canadians, and to the Government of Canada Outcomes: Healthy Canadians; Strong economic growth; An innovative and knowledge-based economy; and A clean and healthy environment.

### Important program elements

**Interdepartmental Governance:** While good management is an important aspect of any government program, it is particularly important for the GRDI because of the number of departments and agencies involved and the diversity of their respective mandates. It is thus important that practices put in place support effective departmental and interdepartmental coordination and provide a well-structured framework to clarify expectations and foster strategic approaches. It is critical that departmental and shared priorities be well defined so that the projects are selected to ensure government-wide priorities for genomics research information are addressed. Phase V of the GRDI demonstrated the viability of a truly interdepartmental approach and the ability of GRDI participating departments/agencies to work together, foster synergies, and add value to existing departmental resources. Phase VI builds on this successful model.



**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; reporting and management activities; building a highly qualified work force to ensure enhanced scientific leadership in support of government mandates and priorities; collaboration to access world-class research infrastructure and expertise, and dissemination and transfer of research results are all critical to ensuring progress towards outcomes.

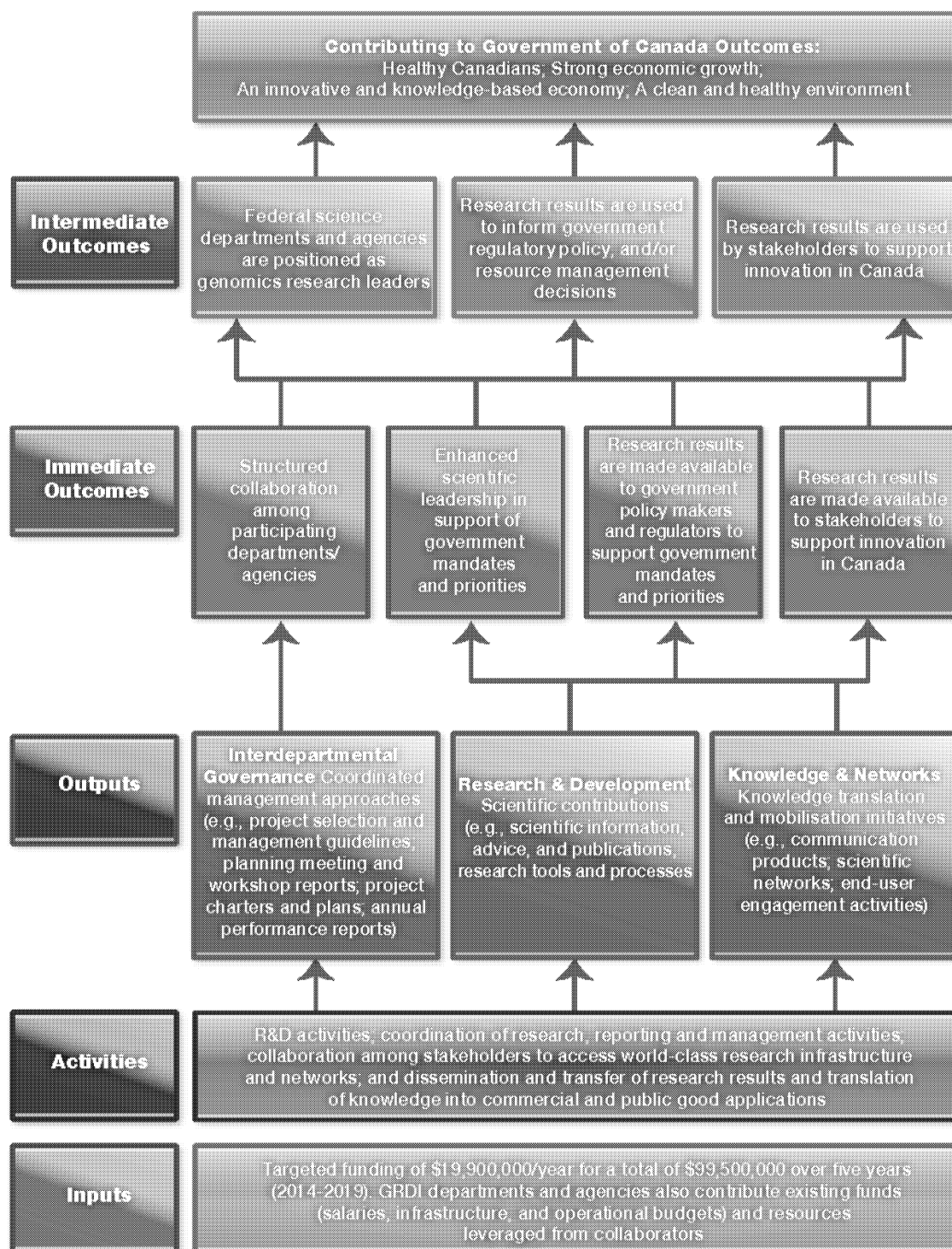
**Knowledge and Networks:** To maximize the value of the GRDI and move that value to users for commercial and public good applications as the initiative matures, knowledge translation and mobilization activities are required. These include the development of scientific networks, communications products, end-user engagement activities, science policy integration, science advice, transfer of protocols, field trials, outreach activities, etc. They ensure that research remains relevant to solve specific problems by maximizing opportunities to understand the needs of targeted end-users and active dissemination of GRDI results to them.

Table 1 outlines the performance indicators, sources and responsibility for the outcomes outlined in the logic model (Figure 1) 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 contribution of the GRDI to the Government of Canada Outcomes, as attribution becomes challenging. Rather, it will focus on the achievement of immediate and intermediate outcomes, and assess whether it is reasonable to expect that the achievement of these outcomes would contribute to the Government of Canada 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 agencies, and are not included as indicators of performance.

### **Figure 1: Logic model for the interdepartmental Genomics R&D Initiative Phase VI**

Through the GRDI, eight federal science departments and agencies collaborate in the field of high-impact genomics research to address biological issues that are important to Canadians, focusing on the innovative and regulatory role of federal government research 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.



**Table 1: Program Performance Measurement Strategy Framework**

**Project Information** developed by all participating departments/agencies towards the start of every phase (Descriptive, within departments/agencies)

- Project titles and summary descriptions (key objectives and impact areas)

**Financial Information** reported annually by all participating departments/agencies (descriptive)

- Internal \$ leveraged from A-base resources
- Other funding by collaborators (OGDs; universities; international organizations; private sector; etc.)
- In-kind contributions by collaborators

**End-users** determined by all participating departments/agencies at project planning stage (descriptive)

- List of stakeholders and end-users available for each research project (including contact information)

| OUTPUTS                                                                      |                                                                                                            |                                                                                                                                                                              |                |                     |                                    |                                          |
|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------------------|------------------------------------|------------------------------------------|
| Area                                                                         | Indicator                                                                                                  | Methodology/Source                                                                                                                                                           | Frequency      | Target <sup>1</sup> | Date to achieve target             | Responsibility                           |
| <b>Interdepartmental Governance</b><br><br>Coordinated management approaches | % of processes, templates and guidelines for interdepartmental shared priority projects approved by ADM CC | Processes (e.g., for collective decisions on priorities and projects) and documents (e.g., Project Charter template and annexes) approved by ADM CC. Source: meeting minutes | Once per phase | 100%                | March 2016                         | NRC secretariat and departments/agencies |
|                                                                              | % of departments/agencies sharing information on management approaches for mandated research projects      | Departmental processes in place and shared in GRDI Best Practices Document                                                                                                   | Once per phase | 100%                | September 2014                     | Departments/agencies                     |
|                                                                              | % of publicly available GRDI-level annual performance reports completed                                    | GRDI Annual Performance Report approved by ADM CC and published online                                                                                                       | Annual         | 100%                | September of following fiscal year | NRC secretariat                          |
|                                                                              | % of project performance reports completed for internal management                                         | Project performance reports produced according to department/agency requirements                                                                                             | Annual         | 100%                | September of following fiscal year | Departments/agencies                     |

| OUTPUTS                                                                                 |                                                                    |                                                                                                                                                                              |           |                                                                          |                        |                      |
|-----------------------------------------------------------------------------------------|--------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------|------------------------|----------------------|
| Area                                                                                    | Indicator                                                          | Methodology/Source                                                                                                                                                           | Frequency | Target <sup>1</sup>                                                      | Date to achieve target | Responsibility       |
| <b>Research and Development</b><br><br>Scientific contributions                         | # of key scientific contributions by type demonstrating leadership | Annual reporting in project reports (e.g., publications in refereed journals, publications in refereed conference proceedings, book chapters, invited presentations, etc.)   | Annual    | Within the range recorded for Phase V (1472, avg. 490/yr.) <sup>1</sup>  | By end of phase        | Departments/agencies |
|                                                                                         | # of other scientific contributions by type                        | Annual reporting in project reports (e.g., technical reports, poster presentations, deposits in genomics related databases or libraries, etc.)                               | Annual    | Within the range recorded for Phase V (1445, avg. 482/yr.) <sup>1</sup>  | By end of phase        | Departments/agencies |
|                                                                                         | # of research tools produced<br># of research processes produced   | Reporting of tools and processes produced in project reports                                                                                                                 | Annual    | Within the range recorded for Phase V (283, avg. 94/yr.) <sup>1</sup>    | By end of phase        | Departments/agencies |
| <b>Knowledge and Networks</b><br><br>Knowledge translation and mobilisation initiatives | # of contributions to scientific networks by type                  | Annual reporting in project reports (e.g., participation in meetings related to regulations or policy, participation in national or international research committees, etc.) | Annual    | Within the range recorded for Phase V (252, avg. 84/yr.) <sup>1</sup>    | By end of phase        | Departments/agencies |
|                                                                                         | # of research collaborations by organization type                  | Annual reporting in project reports (e.g., universities (Canadian and international), other research organizations, private sector, etc.)                                    | Annual    | Within the range recorded for Phase V (1,101, avg. 367/yr.) <sup>1</sup> | By end of phase        | Departments/agencies |
|                                                                                         | # of communications products by type                               | Annual reporting in project reports (e.g., media interviews, press releases, newspaper and magazine articles, brochures, web pages, etc.)                                    | Annual    | Within the range recorded for Phase V (241, avg. 80/yr.) <sup>1</sup>    | By end of phase        | Departments/agencies |
|                                                                                         | # of projects that included end-user engagement activities         | Annual reporting in project reports                                                                                                                                          | Annual    | 100%                                                                     | By end of phase        | Departments/agencies |



| IMMEDIATE OUTCOMES                                                                                                                  |                                                                                             |                                                                                                                                                                          |                |                                                                          |                        |                                          |
|-------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|--------------------------------------------------------------------------|------------------------|------------------------------------------|
| Area                                                                                                                                | Indicator                                                                                   | Methodology/Source                                                                                                                                                       | Frequency      | Target <sup>1</sup>                                                      | Date to achieve target | Responsibility                           |
| <b>Structured collaboration among participating departments/agencies</b>                                                            | % of GRDI shared priority projects managed using interdepartmental governance structures    | Meetings of project management teams and ADM CC, decisions recorded in meeting minutes                                                                                   | Once per phase | 100%                                                                     | By end of phase        | NRC Secretariat and Departments/agencies |
|                                                                                                                                     | % of resources allocated to interdepartmental collaborations                                | Funding allocations approved by ADMCC and transferred by NRC to participating departments/agencies according to formal Project Charters                                  | Annual         | 20%                                                                      | By end of phase        | NRC Secretariat                          |
|                                                                                                                                     | # of departments involved in shared priority projects                                       | Shared priority project planning meetings, Project Charters                                                                                                              | Once per phase | At least three per project                                               | By end of phase        | Departments/agencies                     |
| <b>Enhanced scientific leadership in support of government mandates and priorities</b>                                              | # of research and technical personnel                                                       | Annual reporting in project reports (e.g., research scientists and professionals, post-doctoral fellows, students, etc.)                                                 | Annual         | Within the range recorded for Phase V (2,410, avg. 803/yr.) <sup>1</sup> | By end of phase        | Departments/agencies                     |
| <b>Research results are made available to government policy makers and regulators to support government mandates and priorities</b> | % of projects leading outreach activities for disseminating results to identified end-users | Annual reporting in project reports (e.g., end-user consultations, workshops, transfer of methods and protocols, science advice, etc.)                                   | Annual         | 100%                                                                     | By end of phase        | Departments/agencies                     |
| <b>Research results are made available to stakeholders to support innovation in Canada</b>                                          | # of transfer activities by type                                                            | Annual reporting in project reports (e.g., collaborative agreements, workshops, material transfer agreements, standard operating procedures, disclosures, patents, etc.) | Annual         | Within the range recorded for Phase V (398, avg. 133/yr.) <sup>1</sup>   | By end of phase        | Departments/agencies                     |



| INTERMEDIATE OUTCOMES                                                                                          |                                                                                                                                                                             |                    |               |                                                            |                        |                |
|----------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|---------------|------------------------------------------------------------|------------------------|----------------|
| Area                                                                                                           | Indicator                                                                                                                                                                   | Methodology/Source | Frequency     | Target <sup>1</sup>                                        | Date to achieve target | Responsibility |
| <b>Federal science departments and agencies are positioned as genomics research leaders</b>                    | Scientific production and impact in genomics                                                                                                                                | Evaluation         | Every 5 years | On par or better than other genomics researchers in Canada | By end of phase        | Evaluators     |
| <b>Research results are used to inform government regulatory, policy, and/or resource management decisions</b> | Case analysis of examples where risk assessment, regulatory, policy, and resource management decisions have been informed by GRDI research (federal, provincial, municipal) | Evaluation         | Every 5 years | n/a (qualitative/descriptive)                              | By end of phase        | Evaluators     |
| <b>Research results are used by stakeholders to support innovation in Canada</b>                               | Case analysis of examples where innovative tools and processes have been adopted in Canada based upon GRDI research (# of people interviewed who have used GRDI research)   | Evaluation         | Every 5 years | n/a (qualitative/descriptive)                              | By end of phase        | Evaluators     |

<sup>1</sup> Quantitative targets have been established based on GRDI Phase V Annual Performance Reports between 2011 and 2014.

## ANNEX I

### SUPPLEMENTAL INFORMATION

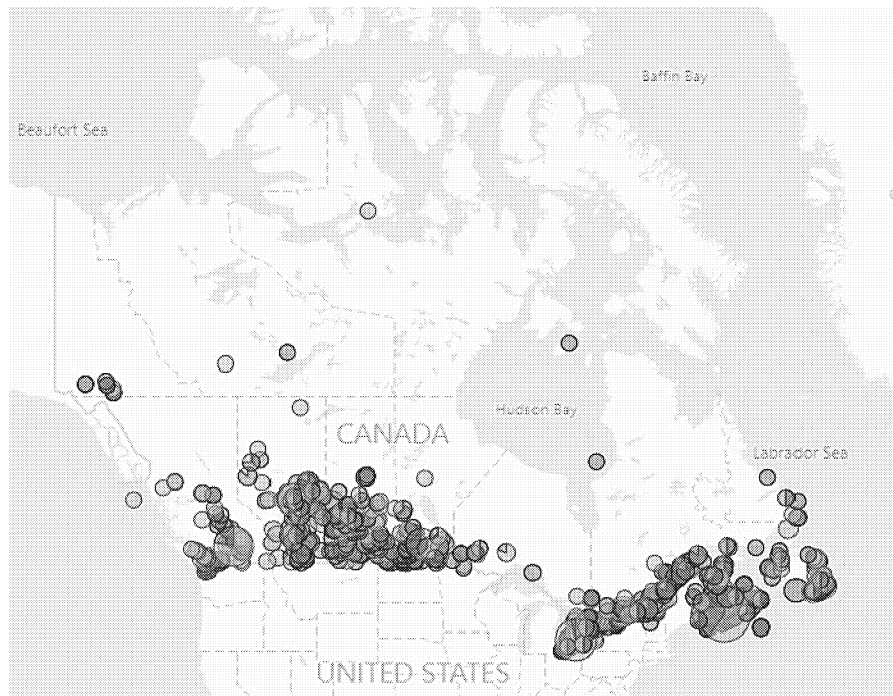


Figure 1. Distribution of 2,612 Highly Pathogenic Avian Influenza cases in wild birds and wild mammals in Canada between November 2, 2021 and March 2, 2023. Map was produced on March 14, 2023 using ECCC's internal Surveillance Reporting Tool that compiles data collected through Canada's Interagency Wild Bird Surveillance Program.

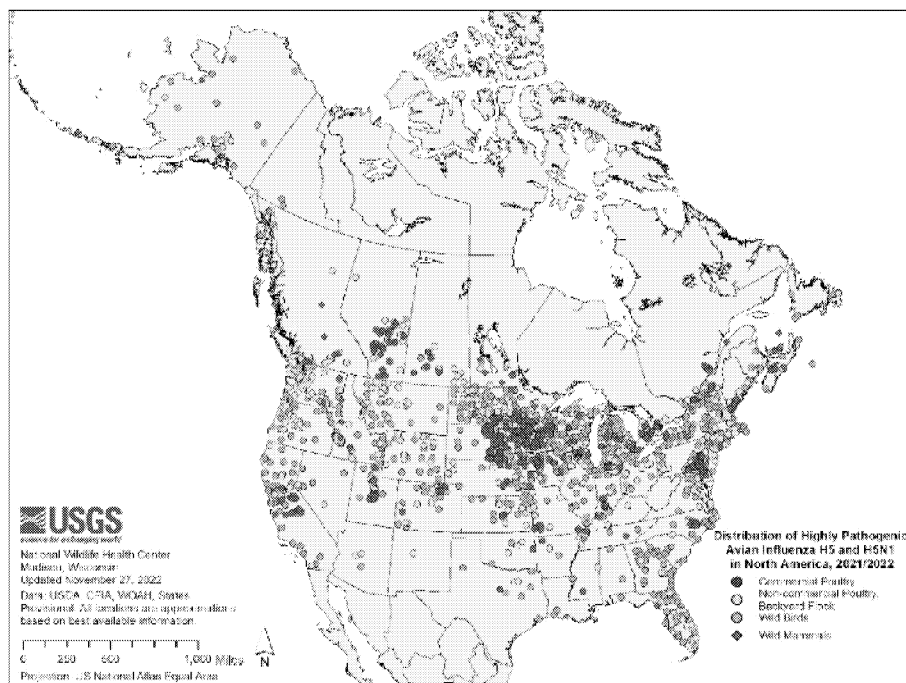


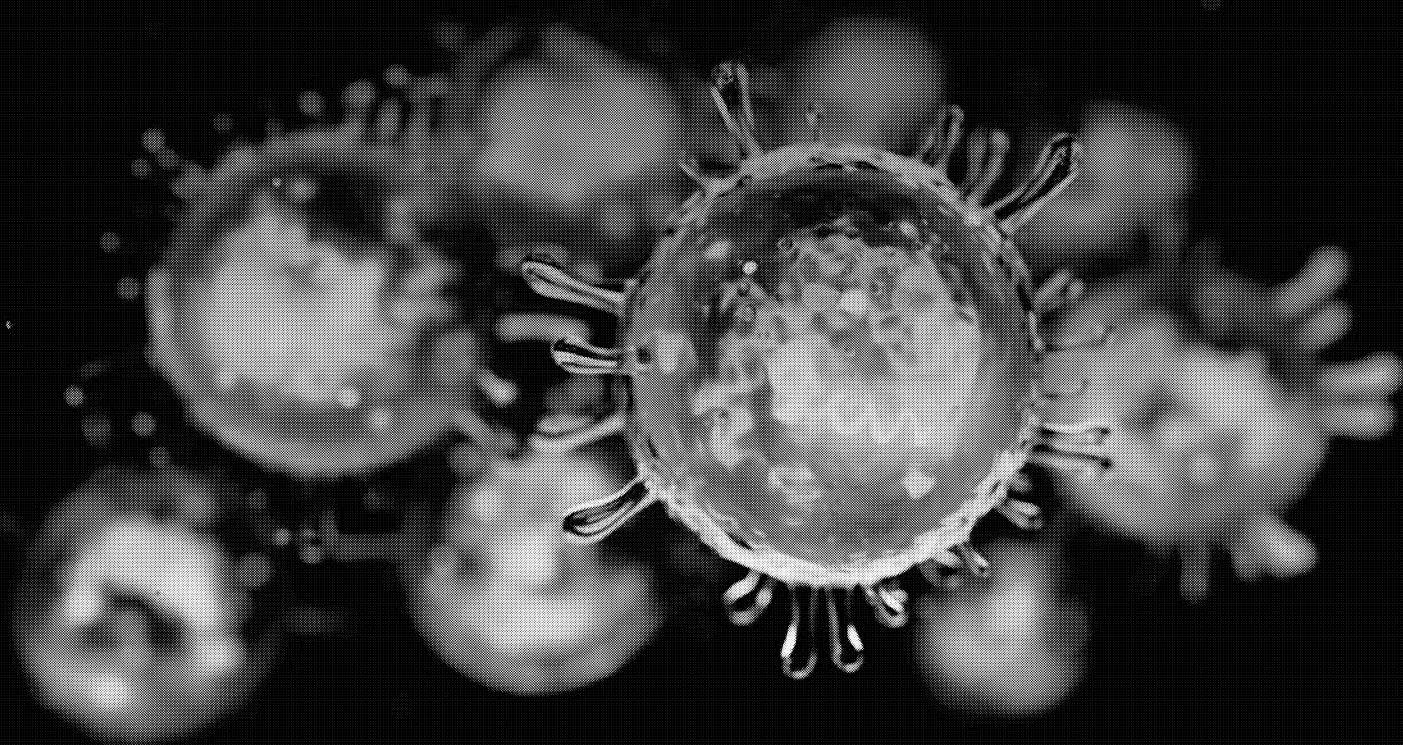
Figure 2. Distribution of Highly Pathogenic Avian Influenza cases in wild birds, domestic poultry, and wild mammals in North America during 2021/2022. Map last updated November 27, 2022 by the USGS National Wildlife Health Center.

# Managing Avian Flu: **A Science Roadmap and Action Plan**

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A Report from the Chief Science  
Advisor of Canada

February 2025



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Advisor of Canada (2025)

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# MANAGING AVIAN FLU: A SCIENCE ROADMAP AND ACTION PLAN

## EXECUTIVE SUMMARY

### Context

Large-scale outbreaks of highly pathogenic avian influenza are currently spreading across several countries, affecting many animal species beyond birds. The disease, commonly known as avian or bird flu, is caused by the H5N1 virus, which has spread widely among wild birds around the globe since 2020-21, resulting in unprecedented mortality in wild birds and domestic poultry. The current virus strain, clade 2.3.4.4b, differs from the one circulating prior to 2020. It is increasingly spreading beyond wild birds to a wide variety of land and marine mammals, including more recently to dairy cattle in the US. In addition to its devastating effect on the welfare of birds and other animals, there are increasing socioeconomic concerns stemming from the impact of H5N1 on the agrifood sector with consequences on food security and pricing. The detection of the H5N1 virus in hundreds of bird species and over 200 mammals highlights its threat to biodiversity and species at risk.

The new H5N1 virus clade has also demonstrated the ability to spread to humans through contact with infected animals, making it an occupational hazard for farm workers, veterinarians and those handling wild species. The disease presentation in humans includes mild to severe respiratory symptoms and pink eye. So far, there is no evidence of human to human transmission, but the current circulating H5N1 strain has the potential to evolve or reassort (including with other influenza viruses) which could result in a virus capable of widespread infection and severe illness in people with little forewarning.

### What is Needed

All influenza viruses that affect people and other mammals were initially derived from avian influenza viruses, necessitating a One Health approach with integrated, unifying actions to balance and optimize the health of people, animals and the environment. Among other, scientific data is urgently needed about where and how the H5N1 virus is spreading (transmission) and on animal and environmental reservoirs of the virus. Basic knowledge of virus biology is essential, including how the virus evolves and how it interacts with different hosts to cause infections that range from mild to fatal, depending on the species (pathogenicity). Host characteristics influencing susceptibility to infection and immunity to the virus need to be clarified and target organs must be identified. Methods should be elaborated for effective environmental monitoring and detection in many species and contexts (monitoring and diagnostics) as well as preventative infection control approaches. Last, but not least, effective vaccines and treatments that can be deployed at-scale must be developed to prevent and control outbreaks in animals and humans.

### Science Roadmap and Action Plan

It is with this in mind that an integrated science roadmap and action plan (the Roadmap) is being proposed. Key principles underpin the Roadmap recommendations and deliverables. They include evidence informed decisions, open and secure science, equity and trust, harm reduction and respectful community engagement.

Given the progression of H5N1 within and across species, it is suggested that priority efforts focus on advancing H5N1 fundamental knowledge, data and medical countermeasures. Similar approaches can be ultimately extended to other avian flu viruses, such as highly pathogenic H7.

## SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

### CROSS-CUTTING OBJECTIVES

- Rapid avian flu virus detection for timely response and risk assessment
- Continued protection of agrifood, wildlife and eco-systems
- Prevention, treatment and management of avian flu infection and illness in animals and people

| Pathway Goals                                                                                       | Recommended Priority Scientific Actions                                                                                                                                                                                                                                                                      |
|-----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Pathway #1</i><br><b>Monitor Avian Flu Virus Spread and Understand the Virus and its Threats</b> | <ol style="list-style-type: none"> <li>1. Data and situational awareness</li> <li>2. Risk assessment</li> <li>3. Pathogenicity and virus biology</li> <li>4. Modes of transmission</li> </ol>                                                                                                                |
| <i>Pathway #2</i><br><b>Mitigate Avian Flu Impact on the Environment, Animals and Humans</b>        | <ol style="list-style-type: none"> <li>5. Strengthen virus detection and monitoring</li> <li>6. Limit animal spread</li> <li>7. Reduce spillover and infection in people</li> </ol>                                                                                                                          |
| <i>Pathway #3</i><br><b>Enhance Avian Flu Pandemic Prevention, Readiness and Response</b>           | <ol style="list-style-type: none"> <li>8. Deploy effective medical countermeasures for people and animals</li> <li>9. Adopt prevention and preparedness strategies</li> <li>10. Protect vulnerable populations and promote occupational health and safety</li> <li>11. Minimize impact on society</li> </ol> |
| <i>Pathway #4</i><br><b>Strengthen Supportive Platforms and Systems</b>                             | <ol style="list-style-type: none"> <li>12. Effective monitoring systems, laboratory and testing capacity</li> <li>13. Integrated one health partnerships, networks and governance models leveraging current capabilities</li> <li>14. Open and secure science and data platforms</li> </ol>                  |

## Conclusion

The ongoing spread of H5N1 to a large number of wild, farmed and companion animals must be urgently addressed and requires focused and coordinated research, data collection and tools development. H5N1 is considered to be among the most pathogenic of the avian flu viruses with associated high mortality rates in birds and mammals, including humans. Even though the risk of illness from H5N1 infection for the general population is currently characterized as low with little to no evidence of transmission between people, the increased spread provides a potential for the virus to evolve or reassort into one that is far more efficient at infecting people and causing a new pandemic. It is therefore essential to monitor and limit virus spread and to prepare effective medical countermeasures to prevent and manage disease in animals and humans alike.

*The Science Roadmap and Action Plan for Avian Flu Management serves as a guide for collaborative avian flu scientific action to optimize the interconnected health and well-being of humans, animals and the environment. It addresses the four essential elements that underpin effective emergency preparedness and response, namely data; fundamental knowledge of virus-host interactions; medical countermeasures tools and products; and, methods and platforms, including effective communication. Advancing proposed priorities will require collaboration, coordination and data sharing among many federal government departments, as well as with sub-national governments and academic and industry partners. Addressing the evidence gaps and developing effective medical countermeasures is instrumental to enhancing our prevention efforts and our state of readiness to protect economic security and well being.*



# SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

## I. CURRENT SITUATION AND CONTEXT

There is currently a large scale, global, *panzootic* (affecting many different animals) outbreak of highly pathogenic avian influenza caused by the H5N1 virus, commonly known as avian or bird flu<sup>1</sup>. Panzootic H5N1 has spread widely among wild birds around the globe since 2020-21 with unprecedented numbers of deaths in wild birds and domestic poultry. Panzootic H5N1 virus clade 2.3.4.4b is different from previous circulating avian flu prior to 2020. It is increasingly spreading beyond wild birds to a wide variety of land and marine mammals<sup>1</sup>, including more recently to dairy cattle in the U.S.<sup>2</sup>. In addition to the devastating impact of avian flu on the welfare of birds and other animals, there are serious concerns regarding potential repercussions on the agrifood sector and food pricing as well as negative environmental effects, including on biodiversity and species at risk.

Currently, the risk of H5N1 infection for the general population is characterized as low with little to no evidence of transmission between people<sup>3</sup>. Direct exposure to H5N1 infected animals, as well as contaminated environments, pose the greatest risk for human H5N1 infection. Precautions to minimize or avoid exposure and spread are recommended.

Avian influenza is not new<sup>4,5</sup>. Prior to the relatively recent emergence of H5N1, large scale poultry outbreaks of virulent H7 subtype avian flu, known early on as "fowl plague", were documented from the turn of the 19th century<sup>4,5</sup>. H7 continues to circulate. In 2024, Australia experienced multiple avian influenza poultry outbreaks, specifically involving H7N3, H7N9, and H7N8 subtypes<sup>6</sup>. H7 has also been associated with human infections, for example, resulting in over 600 deaths between 2013 to 2017 in the People's Republic of China; cases stopped after a poultry vaccination program was introduced<sup>4</sup>. There is the potential for the current circulating H5N1 strain of avian flu to evolve or reassort (including with H7 or another influenza virus) into a virus capable of widespread infection and severe illness in people, with little forewarning.

## II. WHY A FEDERAL SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU?

Avian flu outbreak surveillance, preparedness and response requires coordination and harmonization across a large number of Canadian federal departments and agencies. Key organizations include the Canadian Food Inspection Agency with the lead role in responding to animal influenza outbreaks. Partners include Environment and Climate Change Canada who is responsible for conservation and protection of migratory birds, Parks Canada responds to detections in wildlife in national parks, Fisheries and Oceans helps with sample collection and testing of wild marine mammals, and Agriculture and Agrifood Canada provides support to industry for the impacts of outbreak response.

The Public Health Agency of Canada is responsible for addressing human pandemic influenza preparedness and response, while Health Canada ensures regulatory preparedness and plays a role in assessing food safety. Indigenous Services Canada supports preparedness and response efforts in First Nations on reserve and for Inuit. Public Safety operates the Government Operations Centre for emergency events of national significance. Innovation, Science and Economic Development Canada (ISED) supports innovation through science and technology, notably through *Canada's Biomanufacturing and Life Sciences Strategy*<sup>7</sup>. Lastly, Health Emergency Readiness Canada is a recently created special operating agency within ISED, supported by Health Canada and the Public Health Agency of Canada. It is focused on ensuring that Canada can respond to health emergencies by supporting the development and production of medical countermeasures (MCMs), including vaccines, therapeutics, and diagnostic tools. Annex 1 provides an overview of federal organizations implicated in avian flu outbreaks, adapted from the *North American Plan For Animal and Pandemic Influenza*.



A key lesson from the recent COVID-19 pandemic is the importance of science prioritization, science advice coordination and a whole-of-government approach to ensure availability of evidence for decision making and emergency management. Given the unusual scale and impact of avian flu in birds and an increasing concern about the rising number of species affected globally, in May 2024, the Chief Science Advisor (CSA) convened Canadian federal organizations involved in emergency preparedness and management activities related to the current animal outbreak of avian flu. The meeting was arranged in consultation with the Canadian Food Inspection Agency and the Public Health Agency of Canada to focus on science needs and knowledge gaps for mitigating the spread and impact of avian flu. All participants agreed on the need for a coordinated scientific research approach to avian flu in Canada to fill knowledge gaps and support science-informed policies and public communication.

The *Science Roadmap and Action Plan for Avian Flu Management* will support evidence-informed, concerted action for early detection and containment of avian flu in Canada. This proposed approach supports the objective of Canada's Federal Policy for Emergency Management to "*promote an integrated and resilient whole-of-government approach to emergency management planning, which includes better prevention/mitigation of, preparedness for, response to, and recovery from emergencies*". The scientific updates and deliberations from the May 2024 meeting noted above, recent scientific literature up to December 2024, and expert input inform this report. The roadmap relates to flu of avian origin, including highly pathogenic avian flu viruses (H5 and H7), as well as other emergent strains. Given the present state of H5N1 spread, priority action should be on H5N1.

### III. WHAT WE KNOW ABOUT THE CURRENT H5N1 OUTBREAK

During 2020, H5N1 clade 2.3.4.4b viruses evolved in Asia and Europe. In late 2021, these viruses crossed to Canada and the United States, spreading through migratory wild birds, and subsequently spread to South America in October 2022<sup>8</sup>. The saliva, nasal secretions, feathers litter, and feces of infected birds, as well as contaminated surfaces and water, are sources of infection for other birds and animals who can, in turn, spread it further<sup>9,10</sup>. Human influenza viruses are predominately transmitted through the respiratory route, whereas avian influenza viruses are spread between birds primarily through direct contact<sup>11,12</sup>. Influenza is a well-studied virus which has developed devastating strains causing global pandemics in the past, such as the 1918-20 avian influenza virus H1N1 also known as the Spanish Flu, which killed more than 50 million people worldwide, including nearly 50,000 Canadians<sup>13</sup>.

### Avian Flu Affects Many Wild and Domestic Birds and Mammals

The United Nations recently reported that avian flu has led to the death of over 300 million birds worldwide affecting 108 countries and five continents. Avian flu is a significant threat to biodiversity<sup>14</sup>, for wild bird populations (decimating colonies of endangered species, reaching critical areas) and mammals with mass mortality events<sup>15</sup>.

Since 2022, mass die-offs have occurred in a broad range of infected wild bird species as well as poultry on farms which undergo strict protocols to stamp out all infection to keep the food supply as safe as possible. The USDA APHIS has reported H5N1 virus in more than 200 mammals, including domestic cats, dogs, wild and farmed foxes, farmed mink and alpacas, as well as marine animals, such as seals<sup>16</sup>. While some ducks and other birds act as reservoirs of infection, the H5N1 virus is lethal in many birds and scavenging mammals that have ingested contaminated carcasses. The current outbreak of avian flu has resulted in the deaths of over 11 million birds in Canada alone, either from infection or through culling to stop the spread<sup>17</sup>. Cats have also had a high death rate (50%) after consuming raw milk from H5N1 infected dairy cows in the US<sup>18</sup>.

In October 2024, an H5N1 virus infection was confirmed in a pig in a backyard farm in the US for the first time<sup>19</sup>. Pigs are a particular concern as they are susceptible to influenza viruses spread from other pigs, humans and birds. Reassortment or avian flu viral gene swapping in pigs likely led to the 2009 influenza A (H1N1) pandemic. By the end of 2024, H5N1 was detected in poultry in almost all US states and in dairy cattle across more than 14 states. To date, there have been no dairy cattle or swine cases of H5N1 reported in Canada. With the fall bird migration, in November 2024, there were rising active avian flu infected premises of bird flocks in Canada, the majority in British Columbia, and western Canada<sup>17</sup>.

### Food Safety

Research studies show that pasteurization inactivates H5N1 virus<sup>20</sup>. All retail milk sampling and testing for avian flu in Canada to-date have been negative<sup>21</sup>. Raw milk is never safe to consume given the risk of many foodborne illnesses and it is against the law to buy and sell raw milk in Canada<sup>22</sup>. A recent US Department of Agriculture study showed that avian flu virus is inactivated using recommended cooking procedures (above 63C) in ground beef<sup>23</sup>. Evidence also demonstrates that standard pasteurization methods inactivate influenza viruses in milk<sup>24</sup>. There is no evidence to suggest that the consumption of pasteurized milk or fully cooked poultry, beef, game meat, organs or eggs can transmit influenza virus to humans.

## Human Cases are Slowly Rising

Globally, from 2003 to September 2024, 904 cases of human infection with H5N1 virus were reported from 24 countries. Of these 904 cases, 464 were fatal (case fatality rate of 51%)<sup>25</sup> which could be an overestimate given mild or asymptomatic cases often go unreported.

There were about 65 sporadic human avian flu cases reported in the US during the 2024 outbreak<sup>26</sup> and 76 cases worldwide, mostly farm workers<sup>14</sup>. Note that before 2024, only one human H5N1 case had been reported in the US<sup>27</sup>. At the time this report was written, almost all of the US human cases reported originated from close contact with infected poultry or cattle<sup>26</sup>. There was one case of life-threatening H5N1 illness in Louisiana related to exposure from backyard birds (a D1.1 genotype also detected in wild birds and poultry in the United States)<sup>28</sup>. The majority of the recent US cases had clinically mild illness, most with conjunctivitis and a third with respiratory illness; early detection and antiviral treatment may have played a role<sup>27</sup>. Two confirmed H5N1 cases had no identified route of exposure in 2024. One was an adult Missouri resident with a history of severe underlying clinical illness<sup>29</sup> and the second was a young child from California with a confirmed H5N1 clade 2.3.4.4b infection consistent with genotype B3.13 viruses detected in the US in humans, dairy cattle and poultry<sup>30</sup>. A recent analysis of exposed dairy farm workers in two US states reported that 7% had serologic evidence of infection with H5N1<sup>31</sup> indicating it is likely people have been infected without being aware. While human avian flu cases are slowly rising, there is no evidence to-date of sustained human-to-human transmission<sup>3</sup>.

Canada had its first human case of avian influenza in mid-November 2024 reported in British Columbia (BC), with a severe clinical presentation. The 13-year-old girl who was previously healthy with a history of mild asthma and an elevated body mass index was hospitalized in critical condition with acute respiratory distress<sup>32</sup>. The source of exposure remains unknown despite extensive investigation<sup>33</sup>. The viral genome sequence uploaded to GISAID<sup>34</sup> confirmed H5N1 clade 2.3.4.4.b D1.1 which is related to the same strain circulating in wild birds and poultry in BC<sup>35</sup>. Two rare mutations<sup>32</sup> were identified that could signify a concerning shift to a potential preference for  $\alpha 2,6$  sialic acid receptors found in mammals, versus the  $\alpha 2,3$  sialic acid receptors predominantly in birds<sup>36</sup>. In this case, as in the other human cases, there was no evidence of human-to-human transmission after extensive testing of possible contacts<sup>32</sup>.

The World Health Organization considers avian flu H5Nx viruses of the Orthomyxoviridae family, including H5N1, to be priority pathogens capable of causing a pandemic. Avian flu viruses are classified as either high (H5 and H7) or low pathogenicity (LPAI) to poultry and are important to monitor. H5N1 could rapidly mutate and evolve to a strain that is more easily spread between people. Seasonal human influenza viruses (e.g. H1, H2 and H3) that circulate every year could mix or reassort with H5N1 and lead to a serious form of human flu; with little prior population immunity such a flu strain could have devastating consequences, including high death rates and increased hospitalizations.

## IV. WHAT WE KNOW ABOUT THE H5N1 VIRUS

### Virus Biology

There are two distinct types of influenza viruses that cause annual seasonal influenza outbreaks in humans – A and B<sup>37,38</sup>. H5N1 avian flu is a highly pathogenic influenza A virus. Influenza A viruses are further classified into subtypes based on 2 surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA); there are 16 HA and 9 NA subtypes circulating in birds<sup>39</sup>. Subtypes are named by combining the H and N numbers – e.g., A(H1N1), A(H3N2), and so on<sup>40</sup>. Several influenza A subtypes have previously caused human epidemics – H1, H2, H3 and N1 and N2<sup>41</sup>. The first known human infections of H5N1 were identified in 1997 (18 cases with 6 fatalities in Hong Kong)<sup>42</sup>. The two surface glycoproteins – HA and NA – play balanced, complimentary roles in the life cycle of the flu virus. HA and NA bind to host cell receptors containing sialic acid residues. HA initiates the entry of the virus into the host cell and NA helps new virus bud from infected host cells, after it has replicated<sup>43</sup>.

Characteristics of both the H5N1 virus and the host animal influence avian flu infection dynamics. The current H5N1 clade 2.3.4.4b circulating globally has resulted in high death rates in wild birds and poultry as the virus preferentially binds to abundant  $\alpha 2,3$ -linked sialic acid receptors in the respiratory and intestinal tracts of waterfowl and poultry<sup>44</sup>. With mutations in the HA and polymerase subunits that improve the ability to enter the host cells and to replicate, the current circulating H5N1 virus has a wide host range with cross species infection in wildlife and domestic animals<sup>37</sup>. There is evidence of  $\alpha 2,3$  receptors in the mammary glands of dairy cattle which could explain the infection and replication in mammary glands of cattle and the unprecedented outbreak in dairy cattle in the US<sup>45</sup>, which is thought to primarily transmit cow-to-cow through using the same milking devices.

One of the main factors limiting transmission to humans is receptor binding. The HA of human flu viruses have a strong preference for  $\alpha 2,6$  receptors found on human cells, while avian flu virus HA prefer  $\alpha 2,3$  receptors found on avian epithelia<sup>39</sup>. However, avian preferred  $\alpha 2,3$  receptors can be found in the human lower respiratory tract and in the human eye, whereas human  $\alpha 2,6$  receptors are more plentiful in the human upper respiratory tract<sup>46</sup>. At least one study has shown that human gut tissues express SA receptors with avian flu preferred  $\alpha 2,3$  linkages<sup>47</sup>.

H5N1 is considered to be among the most pathogenic of the avian flu viruses with associated high mortality rates in birds and mammals, including humans<sup>37</sup>. The H5N1 virus could adapt to infect people more easily and to spread among human populations through mutations, such as in the polymerase enzyme needed to replicate the virus or in the HA portion so it could attach more easily to human cells<sup>48</sup>. Evolving mutations in HA and NA can also lead to “antigenic drift and shift” rendering vaccines and anti-virals less effective<sup>49</sup>. Of concern is a recent study using lab-based structural analysis and binding assays which showed that a single mutation could switch bovine H5 HA to be receptive to human-type receptors<sup>50</sup>. Cats infected by H5N1 have showed infection in multiple organs and widespread co-expression of sialic acid  $\alpha 2,6$  and  $\alpha 2,3$  receptors, suggesting cats could also serve as mixing vessels<sup>51</sup>, similar to what has been observed in swine<sup>52</sup>.

### Animal Infection

As noted earlier in the text, most of the currently circulating H5N1 viruses described since 2020 belong to clade 2.3.4.4b<sup>5</sup>. Since 2022, H5N1 has been detected in more than 200 mammals, including dairy cattle in the US<sup>16,26</sup>. H5N1 is impacting a greater and ever-increasing number of mammal species than seen with previous circulating strains of H5N1 prior to 2020 and has proved capable of leading to massive deaths (including of more than 20,000 South American sea lions), raising concern for species at risk<sup>53</sup>. The current panzootic H5N1 clade 2.3.4.4b has expanded to new geographic regions and continents, including to North and South America, and recently found in multiple avian species and two seal species the Antarctic Region<sup>54</sup> as well as seals near Resolute Bay, Nunavut<sup>55</sup>.

It is likely that close contact with and eating infected birds is the most common source of infection for mammals, with H5N1 infection disproportionately affecting scavenging and carnivorous animals<sup>53</sup>. Avian reservoirs, such as aquatic bird species, maintain H5N1 virus and transmit to other birds, poultry, swine, fur animals and other mammals<sup>56</sup>. Stressors related to ecosystem changes, and intensified farming practices may be contributing to the vulnerability of a wider array of animals to avian flu. Symptoms of H5N1 infection in mammals reportedly include runny nose, high fever, respiratory distress, hemorrhage, and neurological symptoms<sup>37</sup>. H5N1 infection can lead to both neurologic and/or respiratory effects in mammals, as seen for example in tigers, mink, sea lions, among others, suggesting an ability to invade neural tissue (neurotropism) in mammals, similar to birds<sup>53</sup>. Mammal-to-mammal transmission of H5N1 may have occurred, for example in American sea lions, tigers and farmed minks, and warrants further investigation<sup>53</sup>. A ferret study showed that a recent mammal H5N1 avian flu strain and an H5N1 virus strain from an infected Texas dairy worker had low, but increased ability to transmit by air compared to older H5N1 strains<sup>57</sup>.

Importantly, prevention against an avian flu pandemic includes reducing spillover of infection within and between animals and people which requires characterization of the virus and ongoing close monitoring of wildlife as well as commercial farms<sup>58</sup>. Furthermore, mutations in the current circulating H5N1 virus are aligned with an increased risk of human infection<sup>56</sup> emphasizing the importance of biosecurity measures to contain H5N1 viral spread and the need to assess ongoing genetic changes in the virus<sup>58</sup>.

## Human Infection

Even though the current H5N1 outbreak is a panzootic event primarily affecting animals, sporadic human cases have been slowly increasing since 2021<sup>26</sup>. Contact with sick poultry is a major source of human infection. In the recent H5N1 outbreak in the US, close contact with infected dairy cattle has been linked to more than half of the approximately 60 sporadic human cases. The 2024 human cases show no evidence to-date of sustained human-to-human transmission of H5N1<sup>3</sup>, yet limited human-to-human spread cannot be entirely ruled out for cases where no source of exposure was identified.

As described above, the distribution of receptors in the human upper and lower respiratory tract may help explain why humans are not readily infected by H5N1, as the lungs are not as accessible to airborne virus; when avian flu strains do infect the human lung, acute respiratory distress and a severe and rapidly progressive pneumonia may result with high case fatality rates<sup>41</sup>. The  $\alpha 2,3$ -linked sialic acid receptors, present in the lower respiratory tract of humans<sup>39,41,46</sup> are also present on the conjunctiva of the eye<sup>59</sup>, likely explaining the recent human H5N1 cases with only ocular involvement. The lack of  $\alpha 2,3$ -linked sialic acid receptors in the upper respiratory tract and tissues surrounding the eye explains why these infections don't spread beyond the eye, despite the tear ducts being contiguous with the respiratory tract.

A response to a pathogen can vary widely and is influenced by variable characteristics of the virus and the host (i.e. animal or person infected). The virus biology and pathogenicity as well as the site of infection, route and scale of exposure, virulence, and transmissibility influence the degree of illness<sup>39</sup>. Host characteristics include degree of previous exposure, and demographic factors, such as age, underlying illness, and obesity<sup>60</sup>. Understanding the immune response and susceptibility to flu infection and severity of illness is complex. The first influenza virus infection or "immune imprinting", influences subsequent infections and vaccinations as well as "immune memory"<sup>61</sup>. H1N1 and H5N1 viruses share the same neuraminidase subtype, N1. There is evidence that H1N1 neuraminidase antibodies cross-react with H5N1 viruses<sup>62</sup>. A recent serum study showed high titers of NA-inhibiting antibodies to clade 2.3.4.4b in 97%

of serum samples collected in 2020 while low titers were found before 2009 H1N1 exposure, suggesting that there may be some existing protective immunity for people previously exposed to, or vaccinated for H1N1, such as from the 2009 H1N1 outbreak<sup>63, 42</sup>. Earlier data have shown that children and young adults may be more susceptible than other age groups to severe illness from an H5N1 infection<sup>64</sup>, which could be related to a lack of previous exposure to N1. Ongoing epidemiological regional assessments can provide insight into risk assessment and response as the H5N1 clade 2.3.4.4b virus evolves<sup>65</sup>.

## Medical Countermeasures for People

Influenza viruses, including H5N1, continually change, and are "predictably unpredictable". H5N1 virus mutations over time can affect the severity of illness, how easily the virus spreads within and between animals and humans and the effectiveness of medical countermeasures used to diagnose and treat and infection – that is, vaccines, therapeutics and tests. Our ability to fight H5N1 influenza is currently limited.

## Vaccines

The constantly evolving nature of influenza viruses requires frequent reformulation of influenza vaccines<sup>49, 66</sup>. As of February 2024, there were three H5N1 clade 2.3.4.4b candidate vaccine viruses (CVV) listed by the World Health Organization<sup>67</sup>. Canada has agreements with several national and international vaccine manufacturers and under these agreements, the pandemic influenza vaccine production process would be initiated in response to a pandemic influenza declaration by the World Health Organization<sup>68</sup>. However, time would be needed to tailor the vaccine to a specific virulent pandemic strain and production technology capacity would be required to scale-up manufacturing with logistical capabilities in place to distribute them. Some countries, such as the US, have stockpiled prepandemic CVV<sup>69</sup>, as they may offer partial protection. Different vaccine platforms merit investigation as well as expanded manufacturing capacity along with talent and supportive skills. There is a limited ability for making avian flu egg-based vaccines without impeding seasonal influenza vaccine production and few of these facilities reside in Canada. It is worth noting that there is a global egg shortage<sup>70</sup>. Other platforms, including cell-based vaccines, recombinant and mRNA vaccines hold promise for avian influenza vaccines<sup>42</sup>.

Health Canada has authorized three pandemic influenza vaccines that can be updated to counter new strains: Arepanrix and Foclivia (developed using H5N1) and Panenza (developed using H1N1). As of December 2024, one vaccine targeting the updated H5N1 strain was under review<sup>71</sup>.

## Antivirals

There have been four classes of antivirals approved for pandemic or seasonal flu. These include adamantanes (amantadine, rimantadine), nucleoside analogues (favipiravir), neuraminidase inhibitors (oseltamivir, zanamivir, peramivir, laninamivir), and cap-dependent endonuclease (CEN) inhibitors (baloxavir marboxil – BXM)<sup>38,56</sup>. Adamantanes are not recommended as a monotherapy for avian flu due to resistance<sup>56,72</sup>. At least one case of H5N1 drug resistance to oseltamivir known as Tamiflu has been reported; drug resistance in H5N1 isolates from neuraminidase treated patients should be monitored<sup>73</sup>. There are also small molecule inhibitors which do not target the neuraminidase or polymerase protein approved in some countries and studies would be required to determine effectiveness for avian flu. Monoclonal antibodies (mAbs) are another treatment possibility and an area of preclinical development<sup>56</sup>. New flu antivirals are also in development<sup>74</sup>.

Antivirals have been approved in Canada for the treatment of seasonal flu, while there are no antivirals approved by Health Canada specifically targeting the treatment or prophylaxis of avian H5 influenza. Off-label use of these drugs for avian H5 influenza is regulated at the provincial and territorial levels. Scientific research on available and upcoming antivirals is important for preparedness, and, as above, there remain uncertainties about the efficacy of existing therapeutics to treat H5N1 illness<sup>42</sup>. To illustrate, changes in N1 subtype viruses could reduce oseltamivir (Tamiflu) susceptibility, raising concern for the emergence of antiviral-resistant variants and the possibility of similar resistance developing for other antiviral drugs.

## Tests

Rapid detection of avian flu is essential for overall situational awareness to inform response, as well as for the timely and appropriate treatment. Antivirals are important treatments for individuals infected or exposed to H5N1, but timely and accurate testing is essential so antivirals can be started as soon as possible; delay reduces effectiveness. A recent review of detection techniques for H5N1 described serological, immunological, molecular biology, genetic and biosensor technology with varying associated sensitivity and specificity<sup>75</sup>. While there are excellent laboratory-based tests that can distinguish H5N1, including assays like ELISA and RT-PCR, rapid tests that can be used on site (in homes, on farms, in the field, etc.) are lacking.

Health Canada has received no applications for rapid tests related to avian flu, and the currently licensed influenza tests cannot distinguish between infection with seasonal influenza or novel influenza A.

## Medical Countermeasures for Animals

There is no treatment for H5N1 virus in animals and sick cows typically recover within 2 weeks<sup>76</sup>. The mass culling of infected poultry and biosecurity measures are the two main control strategies to prevent and reduce spread of H5N1 in animals<sup>77</sup>, each with economic burden and mental health impact.

While the World Organization for Animal Health has recommended vaccination as part of an avian flu control measure strategy, vaccination of animals remains controversial<sup>78</sup>. In addition to fear of international trade restriction, concerns include that animal vaccination against avian flu could hide subclinical infections or lead to more virulent avian flu virus strains through recombination and genetic assortment with circulating field strains<sup>78</sup>. However, some countries vaccinate poultry flocks against avian flu, including China, Hong Kong, Indonesia, Mexico, Vietnam and France<sup>79</sup>. A recent systematic review demonstrated vaccine efficacy in poultry against avian flu mortality ranging from 78% to 97%<sup>77</sup>. Like the US, Canada does not currently vaccinate commercial livestock or poultry against avian flu and is currently exploring the use of vaccination as an additional tool. For example, Canada has a Highly Pathogenic Avian Influenza Vaccination Task Force examining the development and implementation of vaccination for avian flu in Canada and there are two H5N1 vaccine candidates for use in dairy cows in field trials underway in the US<sup>80,81</sup>.



## V. A ONE HEALTH APPROACH

The evolution of avian flu and the related degree of harm it can cause to animal species and humans is influenced by interactions within and between animals, humans and ecosystems. A long view to limit the impact of avian flu on animal, human and environmental health requires taking a One Health approach supporting the Quadripartite One Health Joint Plan of Action (2022-2026)<sup>82</sup>. One Health is described as “An integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent”.

Lessons from the COVID-19 global pandemic illustrate the complexity of actions required to promote and protect human health during a global pandemic. Layering on animal and environmental health adds even more complexity, considering spillover of infection at the margins, harm to animals, ecosystems, biodiversity and species at risk, as well as environmental stressors. Key areas requiring research and action are at the intersecting margins of human, animal, and environmental health; examples are described in Table 1.

**Table 1: One Health Approach and Avian Influenza**

| Human/Environment Margin                                               | Human/Animal Margin                                                       | Animal/Environment Margin                                                    |
|------------------------------------------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Human activity creating environmental stressors                        | Avian flu virus transmission within and between wild and domestic animals | Environmental stressors influencing animal avian flu virus genomic evolution |
| Wildlife health and welfare                                            | Animal to human and human to animal transmission                          | Avian flu infection impacts on ecosystems, biodiversity, and species at risk |
| Environmental contamination as reservoirs of human avian flu infection | Medical countermeasures for people and animals                            | Avian flu infection impacts on ecosystems, biodiversity, and species at risk |
| Wastewater sampling                                                    | Resilient health systems                                                  |                                                                              |

This composite landscape requires multidisciplinary and multisectoral approaches with integrated systems, as well as effective governance models for timely information sharing, and adaptive, collaborative actions. An effective One Health approach demands early and strong multisectoral coordination and collaboration between public health and animal sectors, with clear lines of responsibility<sup>27</sup>.

## VI. ENHANCING READINESS THROUGH SCIENCE AND RESEARCH

Scientific evidence is required to make effective decisions for limiting spread and preventing or treating illness and efficiently mitigating economic impact. An integrated One Health approach requires aligning research activities to address gaps in rapid detection; continuing to protect agrifood, ecosystems and wildlife; and preventing, treating and managing avian flu in animals and people.

At present, many knowledge gaps need to be addressed to enhance prevention and response to avian flu outbreaks. For example, knowledge of the modes by which the H5N1 virus is transmitted within and across species is incomplete. Similarly, potential animal and environmental reservoirs of infection remain uncertain. Much also needs to be elucidated with respect to basic virus biology and pathogenicity, meaning how infection leads to disease of varying severity in different species.

Additionally, host characteristics that modulate susceptibility to infection and disease severity including immunity conferred by prior infection or vaccination to other avian flu viruses needs to be better understood. On the other hand, controlling infection and managing outbreaks requires the development of medical and non-medical interventions including rapid tests, effective vaccines and therapies as well as evidence-informed protective behaviours and infection control measures.

Table 2 below provides an overview of the key knowledge needs as well as science and data gaps within each one that need to be prioritized to enhance preparedness and response to avian flu outbreaks and epidemics. Given the current context, focus should be on H5N1. Ultimately a similar approach can be adopted to manage other avian flu viruses and strains over time.



**Table 2: Key Knowledge Needs and Priority Gaps\***

*H5N1 is the current priority, eventually considering H7, as well as other emergent subtypes and strains*

| Key Knowledge Need                          | Priority Gap                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Transmission pathways                    | <ul style="list-style-type: none"> <li>Predominant mode(s) and relative contribution of transmission between and across animal species e.g., close contact with an infected host, contaminated environments, scavenged meat, airborne, surface contact, bodily fluids, waterborne, reservoirs, etc. and which animal species require more focussed surveillance</li> <li>Virus half-life on surfaces, biologic samples, air, etc., the importance of which depending on the mode of transmission being addressed</li> </ul> |
| 2. Virus Biology and Pathogenicity          | <ul style="list-style-type: none"> <li>Evolving H5N1 biology and genomics, selection pressures</li> <li>Viability and pathogenicity of potential reassortants (e.g. mixing of seasonal flu with avian flu strains to develop a new human strain)</li> <li>Host-pathogen interactions that can determine susceptibility and pathogenicity beyond sequence-based analysis</li> <li>How the virus causes disease - infective dose, permissive factors, viral evolution</li> </ul>                                              |
| 3. Virus Biology and Pathogenicity          | <ul style="list-style-type: none"> <li>Accurate and rapidly accessible PCR/molecular tests for both diagnosis and surveillance</li> <li>Affordable, highly sensitive, point of care rapid tests that are deployable in the community</li> <li>Field and laboratory monitoring for situational awareness data collection</li> </ul>                                                                                                                                                                                          |
| 4. Host Characterization                    | <ul style="list-style-type: none"> <li>Extent of infection and magnitude of impact on wild animals, including animals hunted for food, e.g., through host susceptibility testing</li> <li>Animal host characteristics that increase susceptibility to avian flu infection</li> <li>Host susceptibility testing</li> <li>How the virus enters the host, receptor locations in animals and humans and tissue distribution</li> <li>Clinical presentation and prognosis</li> </ul>                                             |
| 5. Immunity and Immunology                  | <ul style="list-style-type: none"> <li>Pre-existing immunity from previous exposure to other influenza viruses including the 2009 H1N1 outbreak and seasonal influenza, particularly the N-1 subtype</li> <li>Understanding immune response and immunopathology to evolving and reassortment strains</li> <li>Tests to measure H5N1 antibodies</li> </ul>                                                                                                                                                                   |
| 6. Infection Prevention and Control         | <ul style="list-style-type: none"> <li>Preventive and innovative interventions and biosecurity measures where animals are kept and transported to reduce virus exposure, e.g. ventilation, filtration, sterilization, personal protective equipment.</li> <li>Methods of humane depopulation</li> <li>Vaccination strategies</li> </ul>                                                                                                                                                                                     |
| 7. Tools and Medical Countermeasures        | <ul style="list-style-type: none"> <li>Focused research and development for effective, targeted animal and human vaccines</li> <li>Therapeutics, antivirals, diagnostics and vaccines for animals and humans</li> <li>Integrated systems and platforms for expanded surveillance to support early detection</li> <li>Manufacturing at scale for cross-cutting access to medical countermeasures.</li> </ul>                                                                                                                 |
| 8. Socio-behavioural and Risk Communication | <ul style="list-style-type: none"> <li>Effective protective behaviour and biosecurity practices in physical environments.</li> <li>Effectively targeted risk communication and approaches to reduce infection and protect livelihoods</li> </ul>                                                                                                                                                                                                                                                                            |

## VII. SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

The *Science Roadmap and Action Plan for Avian Flu Management* (the Roadmap) is meant to serve as a guide for an integrated and multidisciplinary approach to avian flu research and development in Canada. A One Health approach is recommended. The Roadmap and its priority actions should be regularly reviewed as the situation evolves, especially in the event of sustained H5N1 human-to-human transmission.

The Roadmap consists of three cross-cutting, horizontal objectives, five principles, and four pathway goals with related priority scientific actions. It calls for cross-sectoral collaboration and coordination, including at national and international levels.

### CROSS-CUTTING OBJECTIVES

1. Rapid avian flu virus detection for timely response and effective risk assessment
2. Protection of agrifood safety, eco-systems, and wildlife health
3. Prevention, treatment and management of H5N1 infection and illness in animals and people

### PRINCIPLES

1. Evidence-informed decision-making
2. Open and secure science, research and data
3. Trust, excellence and equity
4. Societal harm reduction
5. Respectful engagement and collaboration with at-risk communities

### PATHWAY GOALS

The Roadmap follows three pathway goals to help achieve the target outcomes, each with associated priority scientific actions, currently at various stages of development:

1. Monitoring avian flu virus spread and understand the virus and its threats
2. Mitigating avian flu impact on the environment, animals and humans
3. Enhancing avian flu pandemic prevention, readiness and response.

To be successful, the *Science Roadmap and Action Plan for Avian Flu Management* must be accompanied by actions in the fourth pathway, "Strengthen supportive platforms and systems" with stable funding mechanisms that enable integrated approaches and collaborations.

**Table 3: At a Glance - Science Roadmap and Action Plan for Avian Flu Management**

| <b>Science Roadmap and Action Plan for Avian Flu Management</b>                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                          |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p align="center"><b>Cross-Cutting Objectives</b></p> <ul style="list-style-type: none"> <li>• Rapid avian flu virus detection for timely response and risk assessment</li> <li>• Continued protection of agrifood, wildlife and eco-systems</li> <li>• Prevention, treatment and management of avian flu infection and illness in animals and people</li> </ul> |                                                                                                                                                                                                                                          |
| <b>Pathway Goals</b>                                                                                                                                                                                                                                                                                                                                             | <b>Recommended Priority Scientific Actions</b>                                                                                                                                                                                           |
| <i>Pathway #1</i><br><b>Monitor Avian Flu Virus Spread and Understand the Virus and its Threats</b>                                                                                                                                                                                                                                                              | 1. Data and situational awareness<br>2. Risk assessment<br>3. Pathogenicity and virus biology<br>4. Modes of transmission                                                                                                                |
| <i>Pathway #2</i><br><b>Mitigate Avian Flu Impact on the Environment, Animals and Humans</b>                                                                                                                                                                                                                                                                     | 5. Strengthen virus detection and monitoring<br>6. Limit animal spread<br>7. Reduce spillover and infection in people                                                                                                                    |
| <i>Pathway #3</i><br><b>Enhance Avian Flu Pandemic Prevention, Readiness and Response</b>                                                                                                                                                                                                                                                                        | 8. Deploy effective medical countermeasures for people and animals<br>9. Adopt prevention and preparedness strategies<br>10. Protect vulnerable populations and promote occupational health and safety<br>11. Minimize impact on society |
| <i>Pathway #4</i><br><b>Strengthen Supportive Platforms and Systems</b>                                                                                                                                                                                                                                                                                          | 12. Effective monitoring systems, laboratory and testing capacity.<br>13. Integrated one health partnerships, networks and governance models, leveraging current capabilities<br>14. Open and secure science and data platforms          |



# Recommended Avian Flu Priority Scientific Actions and Sub-Actions by Pathway:

## PATHWAY #1 MONITOR AVIAN FLU VIRUS SPREAD AND UNDERSTAND THE VIRUS AND ITS THREATS

### 1. Data and Situational Awareness

- 1.1. Monitor changes in avian flu viruses in birds and non-human mammals to detect mutations that may affect disease severity across species, including through enhanced observational and experimental data gathering.
- 1.2. Enhance data capture of animals currently affected in Canada, especially of priority migratory birds, susceptible animals and species at risk, including live animal sampling and serological data.
- 1.3. Improve the range of diagnostic tests for avian flu and subtypes for a broad range of situations, environments and species. This includes point of care rapid tests for animals and humans.
- 1.4. Determine the effectiveness of different sampling methodologies in various species and environments, such as blood sampling for serology or fecal fluid, tissue and carcass sampling, among other.
- 1.5. Enhance laboratory and testing capacity including for wastewater testing and sequencing.

### 2. Risk Assessment

- 2.1. Proactively ensure that epidemiological, clinical, demographic and genomic data are available publicly in real time and over the long-term to promote trust and support research and evidence informed decisions.
- 2.2. Test the use of space-based and artificial intelligence technologies to augment early warning systems.
- 2.3. Conduct research on avian flu viral strains to estimate both the emergence and impact risks, applying the Influenza Risk Assessment Tool (IRAT) and the Tool for Influenza Pandemic Risk Assessment (TIPRA) to investigate viral properties, human population attributes, and epidemiology in animal hosts<sup>83,84,85</sup>.
- 2.4. Conduct data analysis and scenario modelling on likelihood of widespread avian flu outbreaks in animals and humans and effectiveness of prevention/mitigation measures, while communicating risk assessments publicly and directly to professional and high-risk communities.

### 3. Pathogenicity and Virus Biology

- 3.1. Elucidate avian flu virus biology and host-pathogen interactions, including viral evolution, factors affecting infectivity, reproduction, biologic fitness and the relationship of viral load to disease presentation.
  - 3.1.1. Advance *in vitro* and *in vivo* experimental disease and transmission models.
  - 3.1.2. Apply computational biology and genomic epidemiology to understand how genetic variants influence disease.
- 3.2. Identify key host characteristics and virus interactions that determine species susceptibility to the evolving virus. This includes assessing the affinity of host cell receptors.
- 3.3. Increase understanding of the biological characteristics and disease presentation of avian flu viruses in humans and other species, particularly for H5N1 clade 2.3.4.4b and the impact of infection on organs and biological systems.

### 4. Modes of Transmission

- 4.1. Investigate avian flu transmission pathways within and across species. This includes domestic and wild birds, mammals (including marine mammals), domestic and wild ruminants, swine, companion animals, and humans (particularly between wild birds and animals on farms).
- 4.2. Study the ability of the avian flu virus to survive and transmit on surfaces, in water, through air, and in biologic fluids and systems, including human saliva, and gastrointestinal fluids.
- 4.3. Maintain food safety.
  - 4.3.1. Study potential risks and impacts of avian flu on hunting and traditional foods, working with Indigenous partners.
  - 4.3.2. Study possible infectivity of some agrifood products, such as raw milk cheeses.
  - 4.3.3. Assess potential avian flu risks from feeding animal products and byproducts such as food waste to other animals, including pets (e.g. raw pet food, fish food).
  - 4.3.4. Evaluate the effectiveness of food grade cleaning agents on the inactivation of avian influenza virus and virus survival on food contact surfaces.

## PATHWAY #2 MITIGATE AVIAN FLU IMPACT ON THE ENVIRONMENT, ANIMALS AND HUMANS

### 5. Strengthen Virus Detection and Monitoring

- 5.1. Expand wastewater surveillance as an early warning signal for increased avian flu infection in vulnerable environments and communities across Canada, including remote and rural locations.
- 5.2. Develop targeted surveillance of potential bridging species, adjusting to include other species as new evidence emerges (live, harvested, sick and dead animals).
  - 5.2.1. Identify and characterize host range of key wild birds and other animals that are potential bridging species that may act as vectors of infection, including animals hunted for food.
  - 5.2.2. Carry out whole genome sequencing of as many virus isolates as possible to investigate localized clusters of infection and where particular wild bird species may play an important role in disease circulation.
- 5.3. Monitor long-term trends in avian flu dynamics.
  - 5.3.1. Increase coordinated approaches and necessary data linkages to determine spread, changes in virus distribution and markers of viral evolution linking data to case information, genomic and transmission studies.
  - 5.3.2. Support phylogenetic studies to assess viral evolution in host species.
  - 5.3.3. Evaluate past exposure of wildlife to H5N1 and other influenza viruses through serological testing and enhance understanding of pre-existing immunity.
  - 5.3.4. Design/advise on effective and scalable surveillance methods to optimize the detection and characterization of avian influenza viruses in wild birds across seasons and in all North American flyways.
  - 5.3.5. Enhance research opportunities and sampling for avian influenza as they arise for dead or harvested animals, including marine mammals<sup>66</sup>.
  - 5.3.6. Enhance wild bird and mammal surveillance to determine potential avian flu exposure in wildlife species in national parks, national marine conservation areas and national historic sites in Canada.

### 6. Limit Animal Spread

- 6.1. Evaluate the factors that contribute to environmental contamination, persistence, and avian flu virus transmissibility. This includes viral transmission within and between birds and wild and domesticated animals, as well as ongoing spread within infected animal populations and beyond (e.g. bird to cow and subsequent cow to cow, etc.)

- 6.1.1. Develop experimental *in vitro* and *in vivo* models for known and potential hosts.
- 6.1.2. Investigate water as a potential reservoir that could sustain the virus.
- 6.1.3. Examine effects of human activity, such as deforestation and other environmental stressors on increased susceptibility of wildlife to avian flu.
- 6.2. Evaluate methods for animal carcass monitoring and disposal to effectively contain spread.
- 6.3. Design, evaluate and promote innovative tools and approaches for biosecurity and infection prevention and control, considering the differing context of farms, and human activities therein.
- 6.4. Develop tests/assays to facilitate the differentiation of infected and vaccinated animals.

### 7. Reduce Spillover and Infection in People

- 7.1. Minimize infectious disease transmission at the animal-human interface on and between farms, including monitoring poultry and cattle, as well as swine which are potential "mixing vessels" capable of generating pandemic influenza strains.
  - 7.1.1. Assess effectiveness of PPE and decontamination practices in different contexts, as evidence on the predominant modes of avian flu transmission evolves.
  - 7.1.2. Develop evidence-based recommendations to enhance protective behaviour, such as wearing appropriate PPE and isolating when infected, among others.
  - 7.1.3. Develop and communicate avian flu infection prevention and control, as well as farmed animal biosecurity best practices in a targeted and context sensitive manner.
- 7.2. Enhance understanding of human infection and illness associated with avian flu viruses, such as clinical presentation, susceptibility and pathophysiology. This includes virologic, immunologic, genomic and epidemiologic characteristics.
  - 7.2.1. Analyze the potential of immunity acquired from previous influenza virus exposure (e.g. 2009 H1N1) to protect against avian flu-induced human disease.
  - 7.2.2. Conduct antibody (serology) testing in human populations potentially exposed to animals infected with avian flu. This includes exposure to infected wild, domestic and farmed animals such as migratory birds infected with avian flu, especially geese and ducks (waterfowl hunters, indigenous hunters, researchers), and individuals at higher risk, such as veterinarians and farm workers, especially individuals working in cattle milking parlours.

- 7.3. Engage in open dialogue with higher risk populations to inform research, prevention and response needs. This includes producers, animal and wildlife workers; agricultural sector workers; fur industry; hunters and trappers; and, Indigenous communities relying on traditional foods, among other.
- 7.4. Conduct behavioural science studies to inform risk communication and medical and non-medical prevention approaches.

### **PATHWAY #3 ENHANCE AVIAN FLU PANDEMIC PREVENTION, READINESS AND RESPONSE**

#### **8. Deploy Effective Medical Countermeasures for People and Animals (tests, vaccines, and therapeutics).**

- 8.1. Urgently develop an H5N1 medical countermeasures research and development action plan, considering the latest scientific evidence on the effectiveness of available therapeutics and vaccines against the current clade, and the lack of rapid diagnostic tests.
- 8.1.1. Align medical countermeasure research and development across diagnostics, therapeutics and vaccines for H5N1, consistent with the goals of the 100 Days Mission<sup>87</sup>.
- 8.1.2. Support research into the development of universal flu therapeutics and vaccines for animals and people.
- 8.2. Use innovative platforms and technologies, such as artificial intelligence, to accelerate medical countermeasure development, e.g. mapping virus evolution, increased infectivity or pathology and ability to evade acquired immunity.
- 8.3. Develop functional serology assays for humans and animals that can be used rapidly to detect exposure to novel subtypes of avian flu viruses that may not yet be well characterized.
- 8.4. Develop prototype candidate vaccine viruses (CVV) using various technologies that can be scaled up by manufacturers to produce an effective H5N1 flu vaccine.
- 8.5. Evaluate feasibility and effectiveness of animal vaccination along with criteria or guiding principles for vaccinating priority animal species.
- 8.6. Expand the knowledge of avian flu animal vaccine development in Canada and how the immune system responds to vaccines in poultry, cattle, swine, goats, and susceptible companion animals, such as dogs and cats.

#### **9. Adopt Prevention and Preparedness Strategies**

- 9.1. Map and assess current avian flu emergency response capabilities in Canada.
- 9.2. Link avian flu stockpile requirements to mission critical research needs, including for avian flu diagnostics, vaccines and therapeutics, leveraging Canada's Biomanufacturing and Life Sciences Strategy (BLSS).
- 9.3. Develop, validate, and stockpile reagents for conducting high priority influenza research.
- 9.4. Identify and address regulatory and procedural barriers to a rapid and early avian flu response.
  - 9.4.1. Streamline regulatory, clinical trial, and research ethics review processes within and between jurisdictions as part of pandemic preparedness to protect animal and public health across the life course.
  - 9.4.2. Ensure emergency data sharing and material transfer agreement protocols are in place.

#### **10. Protect Vulnerable Populations and Promote Occupational Health and Safety**

- 10.1. Set-up monitoring studies in at-risk environments, including for occupational exposure, ideally through longitudinal cohort studies. This will shed light on exposure routes, and how to limit human spread.
- 10.2. Prioritize vaccination for at-risk individuals, updating guidance as the evidence evolves, including on vaccine effectiveness against specific viral clades.
- 10.3. Enhance safe and secure work practices, including infection prevention and control strategies based on prevalent modes of transmission.
- 10.4. Develop evidence-based measures to protect the health of at-risk individuals and limit ongoing transmission. This includes for such activities as removal of infected animal carcasses.
- 10.5. Proactively establish implementation science mechanisms to integrate research and care as the situation evolves; this will ensure that acute and chronic health impacts resulting from avian flu infection are readily captured, studied and effectively treated.
- 10.6. Develop and implement evidence-based approaches to address mental health issues in individuals involved with culling animals, including vets, farmers and their families, among others.

## 11. Minimize Impact on Society

- 11.1. Conduct and leverage behavioural science studies for effective communication to individuals and communities at-risk so they are empowered to make evidence-informed choices about avian flu protective behaviour and response, including related to food, health and economic options.
- 11.2. Promote science literacy and proactively mitigate and address threats posed by misinformation, highlighting scientific action that reduces the health and economic impact of vaccine preventable diseases between and during pandemics.
- 11.3. Build health system resilience in the event of a rapid rise in human avian flu cases. This includes awareness, human resources and infrastructure for testing, vaccination, and treatment.
- 11.4. Determine and address socioeconomic impacts over the short and longer term.
- 11.4.1. Study the impact of policy levers such as taxation measures or compensation programs, among others, on availability of testing data for scenario planning, risk assessment and decision making, considering socio-economic factors.
- 11.4.2. As part of the scientific approach, identify and meaningfully engage (including in different languages) with communities vulnerable to H5N1 impact, taking steps to understand local perspectives and avoid worsening existing inequities.

## PATHWAY #4 ENHANCE SUPPORTIVE PLATFORMS AND SYSTEMS

- 12. **Enhance effective monitoring systems, laboratory and testing capacity** for surge capacity readiness and avian flu surveillance networks. This includes assessment of the current capacity for avian flu research in containment environments in Canada and ways to streamline related processes during a pandemic response, while upholding research security.
- 13. **Establish integrated one health partnerships, networks and governance models, leveraging current capabilities.** This includes bringing together academic as well as private and public sectors, in-line with the recommendations of the Chief Science Advisor of Canada report on *Strengthening the Use of Science for Emergency Management in Canada*<sup>88</sup> and the *Report of the Expert Panel for the Review of the Federal Approach to Pandemic Science Advice and Research Coordination*<sup>89</sup>.
  - 13.1. Develop a Canadian pandemic readiness science and research framework as part of a broader pandemic preparedness planning strategy, modelled after this avian flu framework.
  - 13.2. Foster avian flu collaborative models, networks and partnerships with other countries, such as the US given the shared North American Plan for Animal and Pandemic Influenza<sup>90</sup>, and with international funders and regulatory bodies.
- 14. **Uphold open and secure science and data platforms.** This includes open data and sample sharing practices within collaborative networks and systems, while maintaining research ethics, safety and research security.
  - 14.1. Ensure that genome sequences with complete metadata on sequencing and assembly are rapidly shared and stored on public databases to support phylogenetic analysis and other avian flu research.
  - 14.2. As a top priority, ensure data and sample sharing agreements and protocols are proactively in place with security cleared researchers and organizations to facilitate research and development of medical countermeasures, support biobanks and robust biobanking networks, as appropriate.
  - 14.3. Develop dynamic modelling platforms and ensure the availability of timely data to inform policy, considering health and food security, as well as socioeconomic needs.

## VIII. HOW TO USE THE ROADMAP

This Roadmap is meant to serve as a guide for collaborative avian flu scientific action to optimize the interconnected health and well-being of humans, animals and the environment. It addresses the four essential elements that underpin effective emergency preparedness and response goals, namely data; fundamental knowledge of virus-host interactions; medical countermeasures tools and products; and methods and platforms, including effective ways to communicate.

Given the large and growing number of birds and mammals affected by H5N1, and the steady rise of human H5N1 cases globally, there is a sense of urgency to address the many persisting knowledge gaps. Specific current and future efforts can be "mapped" by partners against the framework to amplify research synergies, address persistent gaps, and streamline collective efforts. Partners include Canadian federal departments and agencies, provincial, territorial and international governments, along with academic, not for profit (e.g. Canadian Wildlife Health Cooperative) and private sectors including farming.

## IX. CONCLUSION

The flu virus is notoriously difficult to predict given its ability to mutate, but the unprecedented panzootic spread of H5N1 is heightening the need for preparedness and response<sup>91,92</sup>.

Implementing the *Science Roadmap and Action Plan for Avian Flu Management* will improve avian flu virus detection for timely response and risk assessment, protect the agrifood sector, and improve the prevention, treatment and management of avian flu infection and illness in animals and people in Canada.

As an evolving virus with a relatively new circulating H5N1 clade, a broader basis of fundamental knowledge of the virus biology and how it interacts with hosts is essential for effective avian flu prevention and management. There is a pressing need to improve the understanding of predominant transmission pathways, including through bridging species capable of contributing to widespread outbreaks in animals and people. Early containment mitigates impact. We must also make targeted efforts to study the extent and role of prior avian flu immunity in humans and animals to understand how severe an outbreak could be.

Protocols and methods for data and sample sharing need to be in place now. Front-end development of functional serology assays to detect exposure to viruses that are not well characterized should be an immediate priority. With the large-scale outbreak in the US and on some poultry farms in Canada, farm biosecurity measures in Canada must be enhanced to keep avian flu away from animals, property and people. Health system resilience and readiness including health care worker training and awareness, and support for priority populations who are most likely to be exposed to avian flu virus, would help mitigate the potential health and social impact of avian flu. Regulatory and procedural barriers to a rapid and early avian flu response need to be identified and quickly addressed.

For an effective response, research efforts that are part of an overall avian flu medical countermeasures strategy are required to accelerate the development, use and accessibility of avian flu tests, vaccines, and therapeutics. Testing capability is urgently needed that can rapidly differentiate between seasonal flu, COVID-19 and highly pathogenic flu strains and subtypes. Avian flu rapid tests at home and in the field for animals and people are essential for early detection, situational awareness and timely treatment. Evolving research to develop and deploy well matched avian flu candidate vaccine viruses (CVV) is also key. Avian flu stockpile requirements need to inform mission critical research, including for avian flu diagnostics, vaccines and therapeutics, leveraging *Canada's Biomanufacturing and Life Sciences Strategy* (BLSS).

Implementing the Roadmap will enhance integration across sectors, reduce fragmentation and minimize gaps, effectively operationalizing a One Health approach. Advancing the 14 recommended priority scientific actions and sub-actions will require collaboration, coordination and data sharing among many partners. This includes within and between Canadian federal departments and agencies, such as the Canadian Food Inspection Agency, the Public Health Agency of Canada, Health Canada, Environment and Climate Change Canada, Health Emergency Readiness Canada, Parks Canada, Department of Fisheries and Oceans, Indigenous Services Canada, among others listed in Annex 1. In this regard, it is commendable that the Public Health Agency of Canada and the Canadian Food Inspection Agency have proactively mobilized and sought input from external scientific experts taking a One Health approach to avian flu from the outset. Importantly, partners also extend to provincial, territorial and international levels of government and institutions, producers in the agrifood sector, academic centres and experts as well as other non-governmental and private partners.



## X. ACKNOWLEDGEMENTS

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## XI. ANNEX I: FEDERAL ORGANIZATIONS IN CANADA IMPLICATED IN THE AVIAN FLU RESPONSE<sup>93</sup>

- **Fisheries and Oceans Canada (DFO):** Provides scientific expertise and advice on marine mammals to other agencies, permitting around possession and hunting of marine mammals, facilitating sample collection and testing of wild marine mammals, promoting the reporting of marine mammal mortality events, coordinating responses to marine mammals in distress.
- **Parks Canada Agency (PC):** responds to detections in wildlife in national parks, national marine conservation areas and reserves, supporting ECCC and provincial and territorial responses. Provides information to the public visiting parks, including information on human-wildlife interactions.
- **Agriculture and Agri-Food Canada (AAFC):** Connecting to the agriculture sector, national and local industry, as well as FPT governments, provides programs, services and support to industry for the impacts of the outbreak response. Promotes and supporting biosecurity best practices within the agricultural sector.
- **The Public Health Agency of Canada (PHAC):** monitors the international and domestic influenza situation and has developed The Canadian Pandemic Influenza Plan for the Health Sector in collaboration with provincial/territorial representatives. PHAC is the primary federal agency addressing pandemic influenza preparedness and response, supported by PS and Health Canada. PHAC also engages and coordinates efforts among domestic and international health partners. The IHR National Focal Point for Canada is in the Centre for Emergency Preparedness and Response within PHAC.
- **Health Canada (HC):** is responsible for ensuring regulatory preparedness, including accelerated approval of a pandemic influenza vaccine; and spearheading federal workplace health initiatives. Health Canada also provides risk assessment to support food safety investigations and minimize public health risks from the consumption of contaminated foods.
- **Indigenous Services Canada (ISC):** is responsible for supporting preparedness and response efforts in First Nations on reserve and Inuit communities.
- **Health Emergency Readiness Canada (HERC):** is a recently created special operating agency within Innovation, Science, and Economic Development (ISED), supported by Health Canada and the Public Health Agency of Canada. It is focused on ensuring that Canada can respond to health emergencies by supporting the development and production of medical countermeasures (MCMs), including vaccines, therapeutics, and diagnostic tools. The Agency helps grow the Canadian life sciences and biomanufacturing ecosystem and strengthens international partnerships.
- **The Canadian Food Inspection Agency (CFIA)** is mandated to take the lead role in responding to animal health emergencies and has developed many detailed plans and procedures in collaboration with the Public Health Agency of Canada (PHAC), WHO and others. The CFIA is the primary agency responsible for prevention, preparation and response to an animal influenza outbreak, supported by PS. The CFIA has collaborative agreements with federal and provincial government partners that outline roles and responsibilities prior to and during an animal influenza outbreak.
- **Environment and Climate Change Canada (ECCC):** The identification of risks associated with outbreaks in wildlife and the overall health of wildlife is the collective responsibility of both federal and provincial/territorial departments, ministries, and agencies as well as through academic partnerships (particularly the [Canadian Wildlife Health Cooperative](#)). ECCC is the lead federal organization responsible for the conservation and protection of migratory birds and animals listed under the Species at Risk Act (SARA).

- **National Research Council Canada (NRC):** The NRC is responsible for undertaking, assisting or promoting scientific and industrial research in fields of importance to Canada. This includes providing vital scientific and technological services to the research and industrial communities, establishing, operating and maintaining a national science library, and publishing and selling or otherwise distributing such scientific and technical information.
- **Canadian Institutes of Health Research (CIHR):** As the federal funding agency responsible for investing in health research, and situated within the Health Portfolio, CIHR plays a central role in supporting a coordinated and prioritized research response to pandemic threats. Through the Centre for Research on Pandemic Preparedness and Health Emergencies (CRPPHE) and its scientific institutes, CIHR works to ensure that Canada has an emergency-ready health research system.
- **Public Safety Canada (PS):** is the federal department that coordinates the overall federal government's domestic response efforts and provides support to government and key national players in responding to events of national significance. Within PS, the Government Operations Centre (GOC) operates around the clock as a mechanism to communicate and coordinate with federal, provincial and territorial emergency operations centers.
- **The Department of Foreign Affairs and International Trade (DFAIT):** is responsible for the coordination of Canada's international response, including international efforts to contain the spread of a pandemic virus; communicating with foreign governments and international organizations; and managing foreign offers of assistance. DFAIT is also responsible for providing travel advice and responding to the consular needs of Canadians in distress.
- **Innovation, Science and Economic Development (ISED):** works in partnership with the members of the Innovation, Science and Economic Development Portfolio to leverage resources and exploit synergies in several specific areas, including innovation through science and technology. ISED leads Canada's Biomanufacturing and Life Science Strategy which aims to improve Canada's long-term pandemic resilience and promote growth in the domestic life-sciences sector.

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WLSD records identified as related to file A-2025-00030 under the *Access to Information Act* (the Act) for the following request:

**"All studies in the possession/custody/control of "Environment and Climate Change Canada", authored by anyone, anywhere:**

- 1) that scientifically prove/provide evidence of the existence of the alleged "avian influenza virus" (showing that the alleged particles exist, invade and replicate in "host" cells and cause the illness/symptoms that they are alleged to cause), or;**
- 2) (if no records exist for #1) that at least describe the purification of particles that are alleged to be "avian influenza virus" directly from bodily fluid/tissue/excrement of so-called "hosts", with purification confirmed via EM imaging, or;**
- 3) wherein the purported "genome" of any alleged "avian influenza virus" was found intact in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or;**

- Seyer, Y., Guillemette, M. 2023. Situation of the Northern Gannet colony of Bonaventure Island (QC) following the outbreak of highly pathogenic avian influenza (HPAI) virus in the spring of 2022 in eastern Canada. [CWS Unpublished contract report that would be in their holdings]
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**4) that scientifically demonstrate contagion of the illness / symptoms that are allegedly caused by purported "avian influenza viruses", or;**

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- McPhail, G. M., S. M. Collins, T. V. Burt, N. G. Careen, P. B. Doiron, S. Avery-Gomm, T. Barychka, M. D. English, J. A. Giacinti, M. E. B. Jones, J. F. Provencher, C. Soos, C. R. E. Ward, S. Duffy, S. I. Wilhelm, J. Wight, I. Rahman, K. E. Hargan, A. S. Lang, and W. A. Montevecchi. 2024. Geographic, ecological, and temporal patterns of seabird mortality during the 2022 HPAI H5N1 outbreak on the island of Newfoundland. *Canadian Journal of Fisheries and Aquatic Science*, Just-IN [10.1139/cjz-2024-0012](https://doi.org/10.1139/cjz-2024-0012)
- Avery-Gomm, S., T. Barychka, M. English, R. Ronconi, S. I. Wilhelm, J.-F. Rail, T. Cormier, M. Beaumont, C. Bowser, T. V. Burt, S. Collins, S. Duffy, J. A. Giacinti, S. Gilliland, J.-F. Giroux, C. Gjerdrum, M. Guillemette, K. E. Hargan, M. Jones, A. Kennedy, L. Kusalik, S. Lair, A. S. Lang, R. A. Lavoie, C. Lepage, G. McPhail, W. A. Montevecchi, G. J. Parsons, J. F. Provencher, I. Rahman, G. J. Robertson, Y. Seyer, C. Soos, C. R. E. Ward, R. Wells, and J. Wight. 2024. Wild bird mass mortalities in eastern Canada associated with the Highly Pathogenic Avian Influenza A(H5N1) virus, 2022. *Ecosphere*, 15(9), e4980. [10.1002/ecs2.4980](https://doi.org/10.1002/ecs2.4980)
- Lane, J. V., Jeglinski, J. W. E., Avery-Gomm, S., Ballstaedt, E., Banyard, A. C.,

Barychka, T., Brown, I. H., Brugger, B., Burt, T. V., Careen, N., Castenschiold, J. H. F., Christensen-Dalsgaard, S., Clifford, S., Collins, S. M., Cunningham, E., Danielsen, J., Daunt, F., D'entremont, K. J. N., Doiron, P., Duffy, S., English, M. D., Falchieri, M., Giacinti, J., Gjerset, B., Granstad, S., Grémillet, D., Guillemette, M., Hallgrímsson, G. T., Hamer, K. C., Hammer, S., Harrison, K., Hart, J. D., Hatsell, C., Humpidge, R., James, J., Jenkinson, A., Jessopp, M., Jones, M. E. B., Lair, S., Lewis, T., Malinowska, A. A., McCluskie, A., McPhail, G., Moe, B., Montevecchi, W. A., Morgan, G., Nichol, C., Nisbet, C., Olsen, B., Provencher, J., Provost, P., Purdie, A., Rail, J.-F., Robertson, G., Seyer, Y., Sheddan, M., Soos, C., Stephens, N., Strøm, H., Svansson, V., Tierney, T. D., Tyler, G., Wade, T., Wanless, S., Ward, C. R. E., Wilhelm, S. I., Wischniewski, S., Wright, L. J., Zonfrillo, B., Matthiopoulos, J., Votier, S. C., 2023. High Pathogenicity Avian Influenza (H5N1) in Northern Gannets (*Morus Bassanus*): Global Spread, Clinical Signs and Demographic Consequences. *Ibis*. 166(2), 633-650. <https://doi.org/10.1111/ibi.13275>

**5) wherein any test that purportedly relates to the alleged "avian influenza virus" was validated (logically, this would require the alleged virus to first be proven to exist).**

**• Urgency & Danger to Animal Life and Well-being**

**This is an urgent issue: farmers are being harassed to "dispose of" their animals and take other disruptive measures under the premise of a never-shown-to-exist virus.**

**• Publicly Available Records**

**If any records match the above description of requested records and are currently available to "the public" elsewhere, please assist me by providing enough information about each record so that I may identify and access each one with certainty (i.e. title, author(s), date, journal, location). Please provide URLs and/or DOIs where possible.**



WLSO records identified as related to fileA-2025-00030 under the *Access to Information Act* (the Act) for the following request:

**3) wherein the purported "genome" of any alleged "avian influenza virus" was found intact in the bodily fluid/tissue/excrement of a "host" (as opposed to fabricated in silico aka a mere made-up computer model), or;**

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Wright, L. J., Zonfrillo, B., Matthiopoulos, J., Votier, S. C., 2023. High Pathogenicity Avian Influenza (H5N1) in Northern Gannets (*Morus Bassanus*): Global Spread, Clinical Signs and Demographic Consequences. *Ibis*. 166(2), 633-650.  
<https://doi.org/10.1111/ibi.13275>



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

**A-2025-00030****Christine, an unincorporated woman** <cmssyc@gmail.com>

Mon, Nov 3, 2025 at 8:25 PM

To: "Carle,Yves (ECCC)" &lt;Yves.Carle@ec.gc.ca&gt;, Susan.Drysdale@ec.gc.ca

November 3, 2025

To:  
Susan Drysdale, acting as "Director, Access to Information and Privacy"

Thank you for your response letter dated October 21, 2025, the "complete response package" and list of publications.

On pages 000001 - 000053 of the "complete response package", you have provided the "Genomics R & D Initiative Annual Performance Report 2016-2017", published by "Government of Canada". An annual performance report is obviously not a study showing the existence of a virus, a "genome", purified particles, contagion or validation of tests and is therefore irrelevant to my order.

On pages 000054 - 000080 of the package, you have provided a 2025 "Science Roadmap and Action Plan" on "Managing Avian Flu" from "the Chief Science Advisor of Canada" (pgs xxx and here). An action plan is also not a study; it too is irrelevant to what I actually ordered.

On the final 2 pages of the package (000081, 000082) are excerpts from my order along with citations of supposedly responsive/relevant studies. These are the same studies that are cited in the Word document and thus are the only studies cited by ECCC. No studies have been provided.

For the first 2 parts of my order, for studies that scientifically prove or provide evidence of the existence of the alleged virus or that at least describe the essential foundational step: purification of particles suspected of being a virus directly from bodily fluid or tissue, no studies are cited (because none exist, anywhere on Earth). This is an indirect "no records" official legal confession.

Under the 3rd part of my order, for studies wherein the purported "genome" of any alleged "avian influenza virus" was found intact in bodily fluid or tissue, 2 unhelpful records are cited.

The first (alleged) study is described as: "CWS Unpublished contract report that would be in their holdings". Apparently this alleged report is not held by ECCC and I cannot find any trace of it online. How did you verify that Seyer and Guillemette actually found the purported "genome" intact in bodily fluid or tissue? And why did you cite this study if it is not held by ECCC?

In the 2nd study cited in the "genome" section, the authors took swabs from carcasses of wild birds and added "appropriate transport medium" - meaning that they likely contaminated the swabs with cow serum and toxic chemicals - and then stored the swabs between -20 and -80°C (which could also affect the contents). Later, the likely-contaminated swabs were tested with tests that don't test for a virus. The authors then imaginarily "isolated" the imaginary viruses from samples that tested "positive" on the tests that don't test for a virus by adding the samples to embryonated chicken eggs. As usual in virology, mixing complex substances together and blaming observed effects on an imagined virus = "isolation". Because virology isn't a science.

"Full genome segments" (more accurately known as "sequences smaller than the imaginary genome and of unknown origin") detected in clinical specimens or "isolates" (egg/swab mixtures), not in purified samples of suspected viruses, were then assembled into fake/fraudulent and meaningless "genomes". This is obviously not the same thing as finding an alleged "genome" intact and thus this study is irrelevant to my order.

Under the 4th part of my order, which is for studies that scientifically demonstrate contagion of the (non-specific) so-called "bird flu" illness / symptoms, 5 studies are cited. The first is the same not-held, not-available study that was already discussed under the "genome" section above.

Regarding the 4 remaining, supposedly-scientific studies showing contagion: none of these studies are experimental in design, while the scientific method requires falsifiable hypotheses to be tested via valid rigorous controlled experiments. Thus, none of these studies are scientific. None of them contain scientific evidence that the presence of sick birds makes healthy birds sick, or that the imagined virus has been transmitted.

Instead, invalid, indirect tests relating to the imaginary health threat were implemented in wildly unscientific settings, combined with wild leaps of illogic, and misinterpreted by study authors and/or whoever came up with the list of studies to falsely (re)affirm that "bird flu" is the reason birds have died and is a contagious illness.

For the 5th part of my order, which is for studies wherein any test that purportedly relates to the alleged "avian influenza virus" was validated, of course ZERO studies are cited, because none exist, anywhere.

What is passed off as "avian influenza" is not even a distinct illness and the entire "bird flu" narrative is a sick and deadly criminal hoax.

Christine, agent  
(not surety or trustee)  
for Massey, Christine Anne and all derivatives  
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[Quoted text hidden]



Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

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**A-2025-00030**

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**Drysdale,Susan (elle | she, her) (ECCC)** <Susan.Drysdale@ec.gc.ca>

Fri, Nov 7, 2025 at 12:37 PM

To: "Christine, an unincorporated woman" &lt;cmssyc@gmail.com&gt;, "Carle,Yves (ECCC)" &lt;Yves.Carle@ec.gc.ca&gt;

Hello Christine,

In response to the comments below, the package you received was per the scope of the request. If you are seeking additional information, a new request will need to be made which articulates what information will meet your needs.

Regards,

*Susan Drysdale*

Directrice /Director

Accès à l'information et de la protection des renseignements personnels /Access to Information and Privacy

Environnement et Changement climatique Canada / Gouvernement du Canada

Environment and Climate Change Canada / Government of Canada

**343-998-7299**[Susan.Drysdale@ec.gc.ca](mailto:Susan.Drysdale@ec.gc.ca)

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**From:** Christine, an unincorporated woman <cmssyc@gmail.com>**Sent:** Monday, November 3, 2025 8:26 PM**To:** Carle,Yves (ECCC) <[Yves.Carle@ec.gc.ca](mailto:Yves.Carle@ec.gc.ca)>; Drysdale,Susan (elle | she, her) (ECCC) <[Susan.Drysdale@ec.gc.ca](mailto:Susan.Drysdale@ec.gc.ca)>**Subject:** Re: A-2025-00030

You don't often get email from [cmssyc@gmail.com](mailto:cmssyc@gmail.com). [Learn why this is important](#)

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Christine, an unincorporated woman &lt;cmssyc@gmail.com&gt;

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**A-2025-00030**

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**Christine, an unincorporated woman** <cmssyc@gmail.com>

Fri, Nov 7, 2025 at 1:04 PM

To: "Drysedale, Susan (elle | she, her) (ECCC)" &lt;Susan.Drysedale@ec.gc.ca&gt;

Cc: "Carle, Yves (ECCC)" &lt;Yves.Carle@ec.gc.ca&gt;, charmaine.williams@pc.ola.org, amandeep.sodhi@parl.gc.ca

Susan,

I am not seeking "additional information", rather I have pointed out that the response is misleading and that the referenced studies are **not** within the scope of the order.

An honest and accurate response would have been "no such records exist".

Environment and Climate Change Canada agents are complicit in a horrific and deadly fraud.

No one has *any* valid scientific evidence of *any* alleged virus, ever. Virology has always been illogical, unscientific and idiotic. I say this based on the virological literature itself and on literally hundreds of similar FOI confessions and failures from 40 different countries, all of which are readily available on my website. Furthermore, the illness passed off as "bird flu" isn't even a distinct illness and has never been shown to be contagious (which is why ECCC couldn't provide or cite any scientific studies showing contagion).

Hundreds of FOI confessions from 40 countries:

<https://www.fluoridefreepeel.ca/fois-reveal-that-health-science-institutions-around-the-world-have-no-record-of-sars-cov-2-isolation-purification/>

<https://www.fluoridefreepeel.ca/fois-reveal-that-health-science-institutions-have-no-record-of-any-virus-having-been-isolated-purified-virology-isnt-a-science/>

<https://www.fluoridefreepeel.ca/freedom-of-information-responses-re-contagion/>

<https://www.fluoridefreepeel.ca/do-virologists-perform-valid-control-experiments-is-virology-a-science/>

Yet everyone in "government" and media is turning a blind eye to the idiocy of the pseudoscience and the blatant fraud that is being committed with deadly results.

Christine

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