

# Annual Progress Report

## CIHR Canadian Immunization Research Network (CIRN)

### June 1, 2018 to May 31, 2019

Submitted: July 22, 2019

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## 1.0 Executive Summary

This annual progress report highlights our progress from June 1, 2018 through to May 31, 2019. In some cases, where applicable, information from 2017-18 is included for clarity.

Led by Dr. Julie Bettinger, the **Canadian National Vaccine Safety Network (CANVAS)** initiated its tenth annual influenza vaccine safety surveillance campaign, with more than 47,000 participants providing safety data. Adults and parents of children vaccinated with the seasonal influenza vaccine participated in web-based active surveillance of vaccine safety by completing an online survey for health events occurring in the first 7 days after vaccination; participants who received the influenza vaccine in the previous year and participated in the study served as unvaccinated controls. They received an online survey 7-14 days before the start of the immunization campaign. CANVAS submitted weekly safety reports to the Public Health Agency of Canada from October to December 2018, with safety information on the following seven influenza vaccines captured: Flumist, Fluviral, Vaxigrip, Agriflu, Fluzone, Influvac and Fluad. No unexpected side effects were observed in adults or children following the 2018 influenza vaccine campaign, although in both 2017 and 2018, higher rates of events were reported following seasonal influenza vaccination than in the pre-vaccination period. This signal was associated with several seasonal influenza vaccine products.

In addition to monitoring seasonal influenza vaccine safety, CANVAS continues to monitor vaccine safety for other and new vaccines (such as meningococcal B vaccine), and provides a platform for vaccine acceptability studies.

The **Special Immunization Clinics (SIC) Network** was established across Canada in 2013 by infectious disease specialists and allergists to provide expert advice to patients who had experienced adverse events following immunization (AEFI), and those who have medical conditions that may affect their immunizations. There are 11 Special Immunization Clinics across Canada, and the network's focus is to improve the management of patients with potential contraindications to vaccination, as well as those with AEFI who require additional doses of the implicated vaccine(s). The network also provides in-depth investigation, diagnosis, and management of patients presenting with AEFI of special public health interest, with the clinics being optimal as a platform for observational research. Results to date indicate that the risk of a recurrence of the adverse event is low in most patients and that such recurrences are generally milder than the first event. Patients with AEFI continue to be referred to the clinics, and an analysis of outcomes of patients evaluated for AEFIs from 2013-2018 is currently planned. Other ongoing studies conducted by the SIC network include "*Vaccinating children after chemotherapy for acute lymphoblastic leukemia (ALL)*" (manuscripts for this study are in preparation) and "*Immunization practices in children with primary immune deficiencies (PID)*," of which the data cleaning and analysis plan are being finalized. In May 2018, the network's study proposal for "*Optimizing Varicella Immunization in Children with Solid Organ Transplant to Prevent Disease and Improve Long-Term Health*" was awarded funding. This study will look at evaluating the implementation of a new guideline for live varicella vaccination in solid organ transplant recipients. Protocol development is currently underway, with a planned start date for fall 2019.

The **Provincial Collaborative Network (PCN)** brings together leading researchers from multiple provincial governments, public health agencies, and research institutes to conduct a wide range of public health-relevant research and evaluation. PCN studies characteristically do not involve collecting information directly from people or clinical studies, but rather bring together a range of existing types of large-scale data to answer important questions efficiently and effectively. These studies increase the evidence base to inform immunization strategies and programs in Canada and beyond. This past May, two new PCN studies were funded: "*Effectiveness of influenza vaccination during pregnancy on laboratory-confirmed seasonal influenza among infants under 6 months of age*", and "*The benefits of pneumococcal immunization programs for preventing invasive pneumococcal disease (IPD), acute otitis media (AOM), community-acquired pneumonia (CAP) in British Columbia and Ontario.*" The infant flu study will evaluate the effectiveness of maternal seasonal influenza vaccination during pregnancy on laboratory-confirmed influenza outcomes among infants aged <6 months, while the pneumococcal immunization programs study aims to strengthen policy-relevant evidence on prevention of pneumococcal disease in order to optimize decision-making. Investigators on the pneumococcal project are also part of a separate study looking at the benefit of pneumococcal vaccination for seniors, which will offer the opportunity to leverage resources and find synergies to elevate each project. Project initiation activities such as data access requests and contract drafting for both studies are underway. PCN goals for 2019-2020 include continuing to seek opportunities for partnerships, such as ICES, the Vector Institute, Alberta Health, PopDataBC, and the newly launched Centre for Vaccine Preventable Diseases at the University of Toronto. The network also hopes to access multi-provincial data through the new CIHR-funded Strategy for Patient-Oriented Research (SPOR) Canadian data platform, and plans to explore how it can mobilize the knowledge generated by PCN studies to maximize their impact on health outcomes. Though the projects within the network are diverse, they share similar challenges in terms of access to data at one end of the research lifecycle, and in translating research for policy at the other end.

The **Clinical Trials Network (CTN)** aims to increase clinical trial capacity in Canada, answering public health questions about immunization and vaccines by conducting randomized controlled clinical trials. Several CTN study activities are ongoing, with enrollment continuing for "*A randomized controlled trial to compare a 1-dose vs 2-dose priming schedule of 13-valent pneumococcal conjugate vaccine (PCV13) in Canadian infants*", led by Dr. Manish Sadarangani, with an expected study completion date of March 2020. Additionally, enrollment in "*A randomized controlled trial to compare protection in adolescents between different meningococcal immunization schedules used in Canada*" is also ongoing as administrative delays postponed the study start date, with recruitment planned into the 2019 school year. Data for "*Impact of repeated vaccination against influenza on influenza antibody titres and laboratory-confirmed illness*" led by Dr. Brenda Coleman was completed in June 2018, with study outcomes demonstrating that repeated annual influenza vaccination does not impact vaccine effectiveness in adults. Manuscript preparation is underway with a planned submission for September 2019. The network continues to do important research within Indigenous communities; work on "*Studies in support of a new vaccine to prevent invasive Haemophilus influenzae type a (Hia) disease in Canadian Indigenous communities*" is ongoing at several of the study sites (detailed update on CTN studies answering important questions related to Indigenous health can be found in section 5.0), while the work being done out of the Vaccine Evaluation Centre in BC and the University of Saskatchewan by Drs. Manish Sadarangani and Ben Tan respectively has been completed. In May 2019, CIRN funded "*Burden Ethnographic Modeling Evaluation Qaujilisaaqtuq (BEMEQ) RSV*", a multi-network study that will take place in Inuit communities in Nunavut (more information on this study can be found in section 5.0).

The **Serious Outcomes Surveillance Network (SOS)** continues to demonstrate the importance of vaccines as a key part of an overall strategy for healthy aging, and leads the field in the study of the impact of frailty and how frailty is used to measure the effectiveness of vaccines. SOS data have demonstrated that 15% of people 65 years of age and older admitted to the hospitals with influenza don't get back to their usual baseline of activity, and may never get that function back. For the 2018-19 influenza season, surveillance of influenza vaccine effectiveness was funded through an external contract with Public Works Canada via the Public Health Agency of Canada, which will continue into the 2020-21 influenza season (with the potential for further extension). Two additional sites were added to the network this season to expand geographic coverage, and research will continue to focus on hospitalized influenza burden of disease, and interim/end of season vaccine effectiveness (with a continued focus on outcomes relevant to older adults including frailty/function). Enrollment for "*Sentinel surveillance for pneumococcal disease among Canadian adults*" ended in December 2017, with an active surveillance period of February 2016 – March 2018. Data has been cleaned and analysis is currently ongoing to assess the cost of hospitalized pneumococcal CAP in Canada, and the impact of CAP on functional outcomes in older adults. The network's collaboration with the Global Influenza Hospital Surveillance Network (GIHSN) will be maintained as the SOS Network continues to contribute Canadian data in an effort to calculate global vaccine effectiveness estimates. Yousef Bolus, a Research in Medicine student with Dalhousie University, is currently working on the analysis for "*Resource Utilization and cost of community acquired pneumonia requiring hospitalization in Canada*", which is looking at estimating the cost in Canada of an adult hospitalized due to CAP, and identifying key factors that influence the cost of a CAP case requiring hospitalization including patient and disease characteristics, treatment received, and outcome.

The **Social Sciences and Humanities Network (SSHN)** is a multidisciplinary network of social scientists and humanities researchers across Canada to examine the ethical, legal, and social implications of vaccine programs. SSHN projects focus on vaccine acceptance and vaccine hesitancy with the goal of generating evidence and approaches that will enable vaccination programs, healthcare providers, and policy decision-makers to address vaccine hesitancy and achieve greater vaccination acceptance. "*Addressing Vaccine Hesitancy: Pan-Canadian validation of an effective strategy*" and "*Developing and evaluating public health messages to address vaccine hesitancy*" (led by Drs. Arnaud Gagneur and Michelle Driedger, respectively) are currently in the analysis phase with manuscript preparation underway. "*Identifying effective communication materials to enhance vaccine acceptance*" (Dr. Eve Dubé) will be wrapping up in late fall, with a content analysis of existing Canadian vaccination materials targeting childhood vaccines having already been completed. Phase 1 of "*Determinants of HPV vaccine uptake in school-based programs in Canada*" has been completed, which included an environmental scan to gain an overview of the HPV vaccination program. Phase 2 of the study is currently underway, which involves conducting individual/group interviews in person or via telephone with decision-makers and public health experts at local or regional levels, immunization managers and school principals at local levels and schools nurses, teachers and parents and students (if 12 years or older). Additionally, project teams will undertake community engagement research to develop partnerships with Inuit communities in Nunavut and Nunavik to expand the project into these communities. "*Unpacking Vaccine Hesitancy among Perinatal Healthcare Providers: Influences on Beliefs and Practices*" is a 3 phase qualitative study which aims to understand the knowledge, attitudes, beliefs and behaviors (KABB) of maternity care providers around immunization in pregnant women. Interviews have been conducted in British Columbia, Manitoba, Ontario, Québec, and are ongoing in Alberta and Nova Scotia. The network will also be participating in the newly funded CTN RSV project, which is a multi-disciplinary study that will have SSHN researchers exploring KABB and structural/contextual barriers related to childhood vaccination

and RSV prevention in Inuit communities in Nunavik and Nunavut. Protocol development is underway. Additionally, another newly funded study will make use of the SSHN expertise and team members: *“A multifaceted evaluation of provincial maternal Tdap immunization programs”* will strive to inform the implementation of Tdap programs by evaluating demand-side and access side components.

CIRN's **Reference Laboratory Network (RLN)** continues to focus on studies of population immunity to vaccine-preventable diseases, as well as support laboratory testing for studies led by other networks (notably providing influenza testing for several on-going or completed studies for members of CIRN and the SOS Network surveillance studies). The network will also begin providing support to the newly funded SIC network study, *“Optimizing varicella immunization in children with solid organ transplants to prevent disease and improve long-term health”* by performing the varicella serology as well as the varicella-zoster virus (VZV) genotyping. The network will soon begin work on the study *“Is Ontario prepared for the return of Measles?”* which will evaluate whether population immunity in Ontario is sufficient to avoid large outbreaks, and to predict when waning immunity may become a risk to measles control. Previous RLN study activities are ongoing, as are the network's efforts to expand the ability to perform sero-epidemiology studies to include new methods, data sources, and disease targets. The network is also focused on promoting inclusion into the RLN of investigators from other CIRN networks who are using laboratory methods, and has planned an international workshop funded through CIRN, CIHR, and CAIRE on sero-epidemiology as part of the upcoming CIRN Annual General Meeting in November.

The **Modeling and Economics Research Network (ModERN)** continues to work toward its goal of building modeling capacity in an effort to help inform immunization policy decisions in Canada. In February 2019, data collection was completed for the CIRN 1 project *“Measuring social and sexual contact patterns in Canada to improve the control and prevention of infectious diseases”* with more than 5,000 participants in Canada (analyses are currently underway). The development and calibration of the model for *“Effectiveness of interventions to control pertussis using agent-based modeling”* has been completed; main experiment testing vaccine interventions have been coded into the model with an expected study completion date of March 2020. Several presentations and publications relating to the two aforementioned studies are currently being prepared. A new network study being led by Dr. Shannon MacDonald of the University of Alberta was funded this past May 2019. *“Using dynamic transmission and economic modelling to inform RSV immunization policy”* will develop a Canadian RSV transmission model with an economic component to model disease outcomes and disease and intervention costs with the ultimate goal of providing NACI with a model to test the cost-effectiveness of future RSV vaccines licensed in Canada. Additionally, the CTN-driven project *“Burden Ethnographic Modeling Evaluation Qaujilisaqtuq (BEMEQ) RSV”* will utilize expertise from within ModERN by using modeling and simulations to evaluate the potential impact of RSV preventive interventions on the disease burden in infants in Nunavut and the cost effectiveness of these strategies. Protocol development for this study is currently underway.

CIRN's **Network Management Office (NMO)** continues to be based out of Dalhousie University in Halifax. The NMO has successfully built capacity with the implementation of designated network project managers, which has streamlined data collection related to reporting (both network wide and study-specific) as well as the process for drafting inter-

institutional agreements and initiating network funding. The CIRN Management Committee (MC) continues to meet on a monthly basis by teleconference to report on study activities as well as other CIRN-related issues. The network did not hold an annual general meeting in 2018, and instead capitalized on the December 2018 Canadian Immunization Conference (CIC) in Ottawa as an opportunity to hold a face-to-face meeting of the MC, and will continue to alternate between holding an AGM (upcoming November 2019) and scheduling side meetings off the larger CIC conference. This past fall, the NMO undertook a labour intensive stakeholder engagement process which served to inform the 2018-19 call for project proposals (outlined in detail in section 5.0). Seven new projects were funded for year three of the CIRN grant, many of which are interdisciplinary and will rely on expertise spanning networks.

## 2.0 Progress on Relevant Research Areas

The following table identifies ongoing and completed projects from 2017-18, as well as newly funded projects from 2018-19 (project titles for newly funded studies are bolded for clarity). Additional information includes the networks they fall under, the specific objectives the project addresses, secondary relevant research areas and also includes the additional areas the project address. Finally a summary column of the status of what stage the project is currently in and whether external funding or in-kind support was obtained is also included.

The network was mandated to allocate \$2,000,000 in funding for projects addressing vaccine coverage; to date, \$1,629,435 has been allocated to this research area. Additionally, CIRN was required to support three new investigators within the first three years of the grant, which has been accomplished with the network’s support of Drs. Shelly Bolotin (PHO), Manish Sadarangani (BC Children’s Hospital), Ann Burchell (St. Michael’s Hospital), and Deshayne Fell (CHEO).

Research Area	Project Title	CIRN Network	Specific Objectives the Project Addresses	Other (Secondary) Relevant Research Areas Project Addresses	Additional Areas the Project Addresses	Status	External Funding or in-kind support
C: Rapid evaluation of candidate vaccines for safety and immunogenicity in persons of all ages	<b>Project A: A randomized controlled trial to compare a 1-dose vs 2-dose priming schedule of 13-valent pneumococcal conjugate vaccine (PCV13) in Canadian infants</b>	CTN	A – i, ii, iii, v B	E	G	In progress, ongoing enrollment	Yes (BC Immunization Committee, QC Immunization Committee)
	<b>Project B: A randomized controlled trial to compare protection in adolescents between different meningococcal</b>	CTN	A – i, ii, iii, v B	E	G	In progress, ongoing enrollment into 2019 school year	Yes (AB Health)

	immunization schedules used in Canada						
	Project C: Is MF59-adjuvanted influenza vaccine (IV) a preferred priming vaccine for naive infants 6 - <24 months of age? A randomized controlled observer blind trial	CTN	A – i B		G	In progress, ongoing enrollment	Yes (Seqirus)
	<b>Project V: Optimizing varicella immunization in children with solid organ transplants to prevent disease and improve long term health</b>	SIC	A – I, iii, v	E	G, J, K	Start up	
D: Population based methods to evaluate vaccine effectiveness and safety following release for general use (including adverse events following immunization)	Project D: Impact of repeated vaccination against influenza on influenza antibody titres and laboratory-confirmed illness	CTN	A – i		G, K	Completed, ongoing	Yes (in-kind)
	Project E: Canadian National Vaccine Safety (CANVAS) Network: Influenza Vaccine Surveillance	CANVAS	A – i, iv, v B		G, I, J	Completed, ongoing (yearly study)	
	Project F: Immunizing patients with prior adverse events following immunization and potential contraindications to immunization	SIC	A – i, iv B	C, E	G	In progress, ongoing	
	Project G: Intraseason waning of influenza vaccine effectiveness	PCN	A – i, iv		G	In progress, analysis in progress	
	Project H: Engage-HPV: Human papillomavirus prevention for gay, bisexual and other men who have sex with men (MSM) in Vancouver, Toronto, and Montreal	PCN, SSHN, ModERN	A – ii, iii, iv	E, F	G, J	In progress, specimens shipped and analysis plan being finalized	



	Project I: Sero-epidemiology network – Population immunity to mumps in Canada	RLN	A – i, ii	F	G, I	In progress, ongoing	Yes (Bio-Rad, NML, PHO)
	<b>Project R: Effectiveness of influenza vaccination during pregnancy on laboratory-confirmed seasonal influenza among infants under 6 months of age</b>	PCN	A – ii, v		G	Start up	
	<b>Project S: The benefits of pneumococcal immunization programs for preventing invasive pneumococcal disease (IPD), acute otitis media (AOM), community acquired pneumonia (CAP) in British Columbia and Ontario</b>	PCN	A – I, ii, iii, iv, v	F	G	Start up	Yes (PHO, UBC)
	<b>Project T: Is Ontario prepared for the return of measles?</b>	RLN	A - ii		G	Start up	Yes (PHO, CIHR)
E: Research on interventions that can help to improve vaccine acceptance and uptake including consideration of priority research projects to inform	Project J: Impact on infants' vaccine coverage of an educational intervention using motivational interviewing techniques delivered in maternity wards in Canada	SSHN	A – iii			In progress, data collection ongoing	
	Project K: Identifying effective communication materials to enhance vaccine acceptance	SIC, SSHN	A – iii, iv, v		J	In progress, ongoing, content analysis completed	

current and future policy	Project L: Unpacking Vaccine Hesitancy among Perinatal Healthcare Providers: Influences on Beliefs and Practices	SSHN	A – iii, iv, v		G, J	In progress, interviews ongoing	
	Project M: Determinants of HPV vaccine uptake in school-based programs in Canada	SSHN	A – iii, iii, v		G, J	In progress, ongoing, environmental scan and survey completed	
	Project N: Studies in support of a new vaccine to prevent invasive <i>Haemophilus influenzae</i> type a (Hia) disease in Canadian Indigenous communities	SOS, CTN, SSHN, ModERN	A – iv		H, J	In progress, ongoing	Yes (in-kind OGS)
	<b>Project U: A multifaceted evaluation of maternal Tdap immunization programs</b>	SSHN	A – ii, iii B		G, J	Start up	
F: Vaccine modeling and economic analysis work	Project O: Effectiveness of interventions to control pertussis using agent-based modeling	ModERN	A – i, iv B		G, J	In progress, ongoing, development and calibration of model completed	
	<b>Project P: Burden Ethnographic Modeling Evaluation Qaujilisaqtuq (BEMEQ) RSV</b>	CTN, SSHN, ModeERN	A – ii, iii, iv, v	E, F	G, H, J	Start up	Yes (CFI)
	<b>Project Q: Using dynamic transmission and economic modelling to inform RSV immunization Policy</b>	ModERN	A: ii, iv, v B		G	Start up	Yes, (University of Alberta)

**Legend** (Includes metrics on how many projects address the particular objective/area):

Specific Objectives the project addresses:

- A. Support a formal organizational infrastructure to facilitate collaborative research amongst vaccine and immunization researchers, clinicians, public health professionals, and policy makers to:
  - i. Develop methodologies to test vaccines safety, short- and long-term effectiveness and protection, and adverse reactions (n=11)
  - ii. Evaluate current immunization programs for coverage and effectiveness (n=11)
  - iii. Improve immunization coverage rates in Canada (n=11)
  - iv. Train the next generation of vaccine and immunization researchers (n=11)
  - v. Improve knowledge exchange mechanisms between the stakeholders (n=11)
- B. Support a rapid response research capacity (n=8)

Other Relevant Research Areas project addresses

- C. Rapid evaluation of candidate vaccines for safety and immunogenicity in persons of all ages (n=1)
- D. Population based methods to evaluate vaccine effectiveness and safety following release for general use (including adverse events following immunization) (n=0)
- E. Research on interventions that can help to improve vaccine acceptance and uptake including consideration of priority research projects to inform current and future policy (n=6)
- F. Vaccine modeling and economic analysis work (n=4)

Additional areas the project addresses

- G. Sex and gender considerations in methodologies (n=19)
- H. Research on Indigenous populations (n=2)
- I. Official Languages Minority Communities (n=2)
- J. Ethical, legal and social implications (ELSI) such as recruitment of study subjects from vulnerable populations or information sharing with public health organizations (n=10)
- K. Importance of leveraging a wide range of existing immunization clinical trials and utilizing a variety of methodologies inclusive of other clinical trials (n=2)

Project list:

- Project A: A randomized controlled trial to compare a 1-dose vs 2-dose priming schedule of 13-valent pneumococcal conjugate vaccine (PCV13) in Canadian infants
- Project B: A randomized controlled trial to compare protection in adolescents between different meningococcal immunization schedules used in Canada
- Project C: Is MF59-adjuvanted influenza vaccine (IV) a preferred priming vaccine for naive infants 6 - <24 months of age? A randomized controlled observer blind trial
- Project D: Impact of repeated vaccination against influenza on influenza antibody titres and laboratory-confirmed illness
- Project E: Canadian National Vaccine Safety (CANVAS) Network: Influenza Vaccine Surveillance
- Project F: Immunizing patients with prior adverse events following immunization and potential contraindications to immunization
- Project G: Intraseason waning of influenza vaccine effectiveness

- Project H: Engage-HPV: Human papillomavirus prevention for gay, bisexual and other men who have sex with men (MSM) in Vancouver, Toronto, and Montreal
- Project I: Sero-epidemiology network – Population immunity to mumps in Canada
- Project J: Impact on infants' vaccine coverage of an educational intervention using motivational interviewing techniques delivered in maternity wards in Canada
- Project K: Identifying effective communication materials to enhance vaccine acceptance
- Project L: Unpacking Vaccine Hesitancy among Perinatal Healthcare Providers: Influences on Beliefs and Practices
- Project M: Enhancing HPV vaccine uptake in school-based programs in Canada
- Project N: Studies in support of a new vaccine to prevent invasive *Haemophilus influenzae* type a (Hia) disease in Canadian Indigenous communities
- Project O: Effectiveness of interventions to control pertussis using agent-based modeling
- Project P: **Burden Ethnographic Modeling Evaluation Qaujilisaqtuq (BEMEQ) RSV**
- Project Q: Using dynamic transmission and economic modelling to inform RSV immunization policy
- Project R: Effectiveness of influenza vaccination during pregnancy on laboratory-confirmed seasonal influenza among infants under 6 months of age
- Project S: The benefits of pneumococcal immunization programs for preventing invasive pneumococcal disease (IPD), acute otitis media (AOM), community-acquired pneumonia (CAP) in British Columbia and Ontario
- Project T: Is Ontario prepared for the return of measles?
- Project U: A multifaceted evaluation of provincial maternal Tdap immunization programs
- Project V: Optimizing varicella immunization in children with solid organ transplants to prevent disease and improve long-term health

Further comments regarding additional areas the projects address:

Prior to the call for proposals for year three projects, CIRN stakeholders identified specific priorities to be considered when evaluating submitted proposals (see Appendix 2.1). The following projects address the priority areas identified during the stakeholder engagement process last fall:

Project	Stakeholder Priority(ies) Addressed
Burden Ethnographic Modeling Evaluation Qaujilisaqtuq (BEMEQ) RSV (Project P)	Indigenous populations, Northern communities, Respiratory Syncytial Virus (RSV) burden and planning for RSV vaccines
Using dynamic transmission and economic modelling to inform RSV immunization policy (Project Q)	New vaccine readiness: RSV- Economic modeling studies
Effectiveness of influenza vaccination during pregnancy on laboratory-confirmed seasonal influenza among infants under 6 months of age (Project R)	Maternal immunization

The benefits of pneumococcal immunization programs for preventing invasive pneumococcal disease (IPD), acute otitis media (AOM), community-acquired pneumonia (CAP) in British Columbia and Ontario (Project S)	Pneumococcus/pneumococcal vaccine - looking beyond IPD Evaluating burden of non-IPD in Canada (CAP and AOM)
Is Ontario prepared for the return of measles? (Project T)	Measles: Linking sero-epidemiology and modeling – evaluation of timing of the first dose Measles: Linking sero-epidemiology and modeling – evaluation of optimal timing of second dose related to vaccine coverage
A multifaceted evaluation of provincial maternal Tdap immunization programs (Project U)	Evaluation of maternal Tdap programs: Acceptability factors of maternal Tdap Evaluation of maternal Tdap programs: Uptake and understanding the effectiveness of the maternal Tdap program
Optimizing varicella immunization in children with solid organ transplants to prevent disease and improve long-term health (Project V)	Leverages SIC Network resources and builds on previous SIC studies

**Comment on Minister’s mandate letter regarding increasing vaccination rates:**

As reported in the 2017-18 report, while 11 CIRN projects currently focus on both evaluating current immunization programs for coverage and effectiveness (five ongoing from 2017-18 and six newly funded projects) and improving immunization coverage rates in Canada (seven ongoing studies from 2017-18 and four newly funded projects), none of the 2017-18 projects are at a stage in which this data could be provided, and all new studies addressing these priorities are currently in the start-up/initiation phases. Due to the fact that many CIRN projects are multi-year, this impact will likely be assessed and demonstrated in year four or five of the grant.

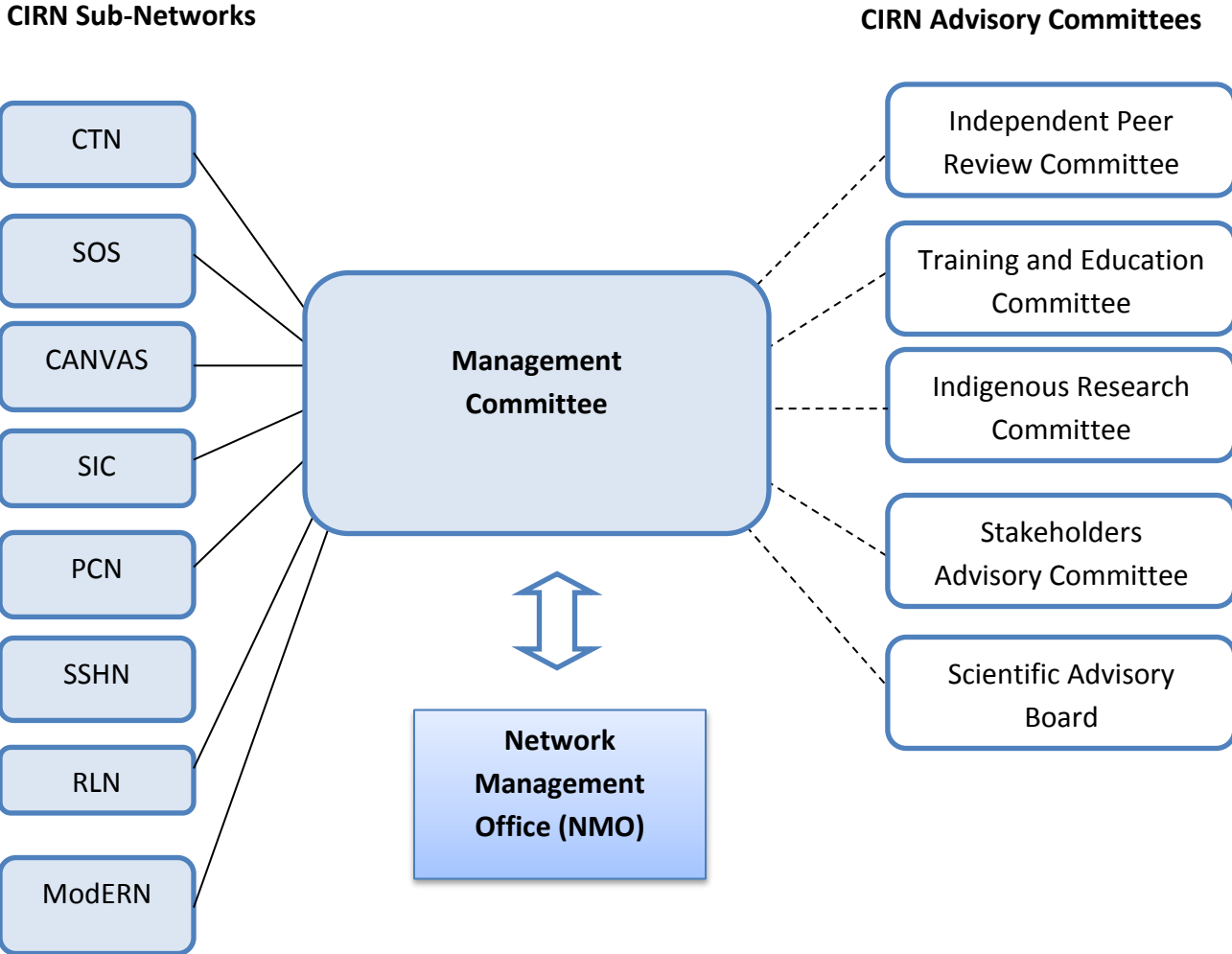
**3.0 Leadership & Governance**

The following summarizes CIRN’s governance, which is unchanged from the renewal application and the 2017-18 report to CIHR:

- CIRN **Management Committee (MC)** is tasked with operational, financial, and strategic decision making for the network. The MC comprises the Nominated Principal Applicant (NPA) who acts as Chair, Principal Applicants (PA) who lead sub-networks, the chairs of the CIRN Committees, members-at-large, and one non-voting representative from both PHAC and CIHR (**Appendix 3.1**). The committee meets monthly; if there are no items on the agenda or if quorum cannot be reached the meetings are cancelled and agenda items are added to the following month or discussed via email as required.

- CIRN **Indigenous Research Committee (IRC)** membership is still being confirmed; securing appropriate members to serve on this committee has proven challenging due to the complicated nature regarding conducting research in these communities. However, important connections and collaborations are being made currently by CIRN network investigators within the SSHN and CTN networks; it is our goal that an established membership will be finalized and committee activities underway by late fall 2019. . This committee will be tasked with implementing a strategy to ensure the participation and support of Indigenous communities where the research occurs.
- The **Stakeholder Advisory Committee (SAC)** was revitalized beginning late summer of 2018 as the CIRN NMO rolled out an engagement strategy that informed the call for year three project proposals. Comprised of provincial and territorial public health practitioners, policy- and decision-makers, the SAC will continue to be tasked with providing input into research priorities for the upcoming years.
- The **Scientific Advisory Board (SAB)** will consist of senior global scientific experts, and will be tasked with reviewing CIRN projects for highest scientific and public health merit. Securing membership for the committee is an immediate priority for the network in anticipation of a possible renewal.
- The **Independent Peer Review Committee (IPRC)** meets as required for review of project proposals. The committee is intended to be formed annually with four reviewing members and one chair. In late 2018 the committee was formed, and a face-to-face meeting to review submitted proposals took place in April 2019. The review process mirrored that of CIHR (see section 5.0 for more detail).
- The **Training and Education Committee (TEC)** was formed in late 2017 and meets on a monthly basis. The committee is tasked with conducting full reviews of all trainee candidates for CIRN funding and also oversees the CIRN education program (section 6.0 for a complete update).
- The **Network Management Office (NMO)** (based out of Dalhousie University in Halifax) continues to provide program management for CIRN, including administration, financial oversight, communication and KT, facilitation of peer reviews, and training and mentoring. The NMO acts as an information hub for CIRN and develops strategies to support this vision and operational requirements.

CIRN Organizational Chart June 2017



## 4.0 Scientific Productivity & Excellence

All funded projects from the grant renewal are currently in progress with ongoing study activities (see section 2.0 project table), with the exception of the CTN study “*Impact of repeated vaccination against influenza on influenza antibody titres and laboratory-confirmed illness*”. Study outcomes show that repeated annual influenza vaccination does not impact vaccine effectiveness in adults. An abstract was presented at ECCMID in Amsterdam in April 2019, with a manuscript currently being drafted for a late September submission.

An additional seven projects were funded through CIRN in May 2019 for a total of \$1,294,787 which address the priorities laid out in the original RFP, as well as additional priorities identified by CIRN stakeholders. The next call for proposals will include both years four and five of the grant, with \$2,587,213 allocated for new studies. The following table is a representation of network productivity since 2017.

Number of LOIs submitted to CIRN	74
Number of full proposals invited by CIRN	43
Number of full proposals submitted to CIRN	37
Number of full proposals approved by CIRN	22
Number and list of CIRN supported projects by stage (e.g., pilot, full protocol);	22 (Appendix 1.1)
Number and percent (%) of full trials/projects that leveraged additional funding from non-CIRN sources (e.g., CIHR, NIH);	10/22 or 45% of projects secured additional funding from non-CIRN sources
Number of networking conferences/meetings organized by the Network	5
Number and list of peer reviewed publications resulting from CIRN projects (specify whether each were supported fully or partially by CIRN)	26 (Appendix 4.1)
Number and list of other knowledge products developed (e.g., reports, books, invited presentations);	73 (Appendix 4.2)
Number of organizations CIRN members provide a service to within Canada and internationally	



**Please indicate the number of each of the following items produced by CIRN since June 2017**  
 Note: This section is aligned with the CIHR electronic final report format. **Please include a list of publications in an appendix.**

	# Submitted	# Published
Journal Articles	26	26
Books/Book chapters	0	0
Reports/Technical reports	0	0

	# Invited	# Others
Presentations	73	6

## 5.0 Stakeholder Engagement

### Engagement of stakeholders at all research stages in CIRN's activities and research process:

**Background (taken from the 2018 Report to CIHR):** *CIRN has a broad network of external stakeholders, including multiple public sector organizations (provincial & territorial public health; PHAC, CIHR and IDRC; universities and hospitals; regulatory bodies), private sector organizations (industry including manufacturers and contract research organizations), and other communities and networks (Indigenous communities; CAIRE; IMPACT).*

*CIRN is structured to ensure that research teams and formal governance infrastructures are integrated with an array of stakeholders. Many of CIRN's researchers, including the NPI and leads for the CTN, SOS, SIC, PCN, and the RLN, are also clinicians or public health officials working actively within their local health authority or hospital. Each sub-network includes research team members who are also clinicians or public health specialists, and CIRN's MC, Stakeholder Advisory Committee, and Indigenous Research Committee provide a link at the strategic planning level to policy makers at the provincial, territorial, and federal levels. CIRN has formal interactions with NACI and CIC which provides two way knowledge exchange related to public health research priorities and the relevance and potential of proposed studies to answer questions of public health importance.*

Beginning in late 2018, the CIRN NMO undertook an intensive stakeholder engagement process as part of the planning for the grant's year three funding call. Working closely with the CIRN Management Committee, the NMO developed a strategy for engagement that involved carefully considered communications beginning with a request to MC members and other investigators to provide names in their jurisdictions. Once contacted, these individuals were asked to identify other appropriate invitees. Following these initial communications with potential SAC participants, individuals were invited to participate on one of two scheduled engagement teleconference calls, which would create an opportunity for the Management Committee to hear feedback from participants. Prior to the calls, stakeholders were given a briefing document prepared by the CIRN NMO (Appendix 2.1) which provided relevant background information and existing research priorities, as well as a list of funded CIRN studies and the research areas they addressed. The goal was to prime participants with the information necessary to generate the most valuable and relevant feedback regarding issues of the greatest public health priorities. Both calls were successful in generating a number of priorities that were considered during the subsequent peer review process for submitted proposals, as well as the final decision making process by the CIRN Management Committee. Additional priorities identified by the Stakeholder Advisory Committee during the call can be found in Appendix 2.1, along with the list of participating stakeholders and their affiliation.

The NMO put out a call for interested researchers to prepare a Letter of Intent (LOI) in December 2018, receiving 35 total submissions from investigators across Canada. Using the criteria for research priorities as outlined in the call for LOIs, 17 of the 35 were invited to submit a five-page research proposal, detailed budget, and budget justification for their project. The NMO received a total of 15 five page proposals for review by the CIRN Independent Peer Review Committee (IPRC). Invitations were distributed to potential IPRC participants, and once formed, the committee included one chair and four reviewing members.

<b>CIRN 2019 Independent Peer Review Committee Members</b>	
Mark Loeb (Committee Chair)	Professor, Department of Pathology and Molecular Medicine
Frank DeStefano (reviewer)	Director, Immunization Safety Office, Centers for Disease Control and Prevention
Greg Hammond (reviewer)	Professor, Department of Medical Microbiology, University of Manitoba
Ian Gemmill (reviewer)	Consultant in Public Health Medicine, Queen's University
Saad Omer (reviewer)	Director, Yale Institute for Global Health

The review process undertaken by the committee was modeled after and mirrored the CIHR peer review process. Committee members were provided with relevant review materials including the submitted research proposals, and briefing documents outlining the steps for review and scoring mechanism. In April 2019, a face-to-face meeting was held in Toronto, where reviewers followed a detailed format for discussing the scientific merit and subsequently assigning a score to each proposal. The proceedings were recorded and a summary report was prepared for consideration by the CIRN Management Committee at a follow-up in person meeting, also held in Toronto at the end of April 2019.

After reviewing the comments and scores provided by the IPRC and discussing funding recommendations, the CIRN MC made its final project selections, deciding to fund seven of the 14 submitted proposals. Applicants were notified of their successful/unsuccessful applications in May; successful applicants were asked to address any issues or provide clarity on their proposals where applicable. The CIRN NMO is currently working with project leads to put in place the inter-institutional subsite agreements in order to initiate the funding process for year three projects.

The NMO is preparing to commence Stakeholder engagement once again in the upcoming weeks to prepare for the project intake for years four and five. Given the success of the most recent engagement process, the same strategy will be employed with the MC providing guidance and insight to improving upon the process as needed.

**CIRN's community engagement process with respect to establishing relationships with First Nations, Inuit, and northern communities:**

Indigenous engagement continues to be a challenging endeavor; however, the network has made great strides in regards to the initiation of research projects in First Nations and Indigenous communities, while building important foundations for continued engagement and consultation with First Nation community members. *"Studies in support of a*

*new vaccine to prevent invasive Haemophilus influenzae type a (Hia) disease in Canadian Indigenous communities*” is an extension of ongoing research which involved collaboration with Indigenous communities and organizations in NWO, including WNHAC, Sioux Lookout First Nations Health Authorities, Nishnawbe Aski Nation, Métis Nation of Ontario, Grassy Narrows First Nation, Fort William First Nation, and in Southern Ontario (Saugeen First Nation). The study, which aims to address research questions that have major importance for the prevention of serious infections in Indigenous communities, was built on solid collaboration with Indigenous communities and organizations that have been gradually developed over the last 9 years. The project represents part of a large program conducted by Marina Ulanova’s group at the Northern Ontario School of Medicine, which involves productive collaborations with the NML (R. Tsang), NRC (A. Cox), Public Health Ontario (F. Jamieson), International Circumpolar Surveillance Network (R. Tsang, M. Bruce, K. Rudolph), and Agent-Based Modelling Laboratory, York University (S. Moghadas). Over the past two years, development of further collaboration within CIRN (with regards to clinical trial design and involvement of IMPACT Centers) has been an important part of the work, spanning the expertise of the SOS, CTN, SSHN, and ModERN CIRN networks.

The study is currently ongoing; the NOSM branch plans on requesting an extension to continue looking at the prevalence of Hia among invasive and non-invasive H. influenzae isolates and of Hia carriage in Indigenous communities of Northern Ontario. The work being done by Kristin Burnett at Lakehead University is ongoing as well; planned activities for this summer include five one-on-one interviews with health care practitioners, and interviews with health care providers working at nursing stations/health centers on reserves to explore their perceptions and knowledge about vaccines generally and Hia specifically in order to better understand their work and relationships with First Nations (stemmed from conversations with community members participating in focus groups). Already completed were 11 focus groups with community members in road access communities and in Thunder Bay. In total there are 72 community members that have shared their knowledge/experiences. 10 one-on-one interviews with community members from remote First Nations were also completed.

*“A multifaceted evaluation of provincial maternal Tdap immunization programs, Burden Ethnographic Modeling Evaluation Qaujilisaqtuq (BEMEQ) RSV”* is a newly funded multi-faceted CTN study that spans several disciplines, including social sciences, modelling, and disease burden. Currently in the start-up phase, this project will explore knowledge, attitudes and beliefs, values and behaviors (KABB) and structural/contextual barriers related to RSV preventative interventions in Inuit communities, estimate the burden of RSV in LRTI-H in <12-month-olds from Inuit communities, and use modeling and simulations to evaluate the potential impact of RSV preventive interventions on the disease burden in infants in Nunavut and the cost effectiveness of these strategies. All three components of the study will incorporate principles of the Inuit Qaujimajatuqangit (IQ) Education Framework. Qaujilisaqtuq refers to “The Emergent Learner” as characterized by listening and observing. This qualitative component of the study will be based on Inuit knowledge, experience and culture, be community-based, and will use a participatory research framework. This approach emphasizes relationship building, empowerment, knowledge sharing, and working together to address health challenges and disparities in indigenous contexts. Inuit Advisory Committees in Nunavut and Nunavik will be created to facilitate this collaborative work.

With many important connections and collaborations being made currently by CIRN network investigators, it is our goal that an established membership for the Indigenous Research Working Group will be finalized and committee activities underway by late fall 2019.

**Number and type of partnered activities (e.g., workshops, conference booths, press releases):**

- CIRN Investigators published 26 peer reviewed publications since 2017 (see **Appendix 4.1**).
- CIRN produced 52 knowledge products since 2017 (see **Appendix 4.2**).

**Amount of CIRN-secured partner contributions (cash and in-kind cash equivalent) by partner type, location and contribution amount (if applicable):**

CIRN Stakeholder	Location	Contribution Amount (contracted and/or committed)
CAIRE	National – Vancouver Head Office	N/A
IMPACT	National – Vancouver Head Office	N/A
IDRC	Ottawa	\$3.6 million
Government of Canada/PHAC	Ottawa – Public Works Office	\$2.8 million
Province of British Columbia	Victoria, BC	\$100,000
Province of Alberta	Calgary, AB	\$100,000
Foundation de France	Paris, FR	\$160,000
Institute national de santé publique du Québec	Québec, PQ	\$100,000
GlaxoSmithKline	London, UK	\$1.07 million
GlaxoSmithKline	Mississauga, ON	\$260,000
Merck	Kenilworth, NJ, USA	\$2.4 million
Sanofi	Toronto, ON	\$267,000
Sequiris	Maidenhead, UK	\$210,000
Variation Biotechnologies	Cambridge, MA	\$3.7 million

## 6.0 Training

The CIRN Training and Education Committee (TEC) was formed in September 2017 to update the CIRN Trainee program and launch the 2018 CIRN Trainee Scholarship Competition. The committee meets via teleconference on a monthly basis, unless action items are determined appropriate to complete via email. All meetings are attended by an NMO staff member, who prepares agendas and minutes for all meetings (**Appendix 5.1**). A CIRN Trainee also sits on the TEC committee.

Members	Institutions
Dr. Karina Top, Chair	Dalhousie University, CIRN SIC Network Lead
Dr. Shelly Bolotin	Public Health Ontario, RLN Network Co-Investigator
Dr. Julie Bettinger	University of British Columbia, CIRN CANVAS Network Lead
Guillaume Béraud	Université Laval
Ann Burchell	St. Michael's Hospital
Natalie Giorgis	CIRN Network Management Office

### 2018-19 CIRN Trainee Scholarship Competition

The CIRN Management Committee (MC) allocated \$200,000 over a two-year period for scholarships for graduate students and postdoctoral fellows, and tasked the TEC with the responsibility of conducting an open, peer-reviewed competition. In June 2018, the TEC received 19 trainee applications for its inaugural intake, which included 1 Master's, 14 PhDs, and 4 Post-doctoral applicants. The scholarship review committee consisted of five reviewers (three from the TEC and two CIRN investigators), with the results of the review presented to the MC in July 2018. Applications were reviewed and ranked based on CIHR criteria, and a total of nine trainees were funded. Appendix 5.8 provides a summary of current trainees and their projects. Trainees who were successful in their original applications are currently being notified of the status of their second year renewal funding.

Before the competition was launched in 2018, the TEC developed materials to clearly define the process and competition:

- CIRN Trainee Scholarship Standard Operating Procedure (**Appendix 5.2**)
- CIRN Trainee eligibility requirements (**Appendix 5.3**)
- CIRN Trainee Scholarship application form (**Appendix 5.4**)

- CIRN Trainee Scholarship notification letter templates (**Appendix 5.5**)
- CIRN Trainee Scholarship review criteria (**Appendix 5.6**)
- CIRN Trainee project database (**Appendix 5.8**)

**Curriculum and Network Engagement**

As part of their funding requirement, mandatory participation in the CIRN Trainee Curriculum is expected. The program was launched in September 2018, consisting of trainee-focused seminars on core topics of vaccinology. Appendix 5.9 provides a detailed list of the 2018-19 trainee seminars. Additionally, the upcoming November 2019 CIRN network AGM will dedicate a portion of its meeting program to highlighting the work of trainees (both CIRN scholarship funded and other non-CIRN funded trainees) through poster sessions as well as opportunities to present oral abstracts. CIRN will continue to encourage the development of Canada's future vaccine researchers and place training and mentoring high on the list of network priorities and initiatives.

**Current CIRN Trainees**

Training Stage	Number of Trainees	Networks
Undergraduate	0	
Master's	3	PCN, SSHN, ModERN
PhD	3	CTN, SSHN, PCN
Postdoctoral fellows	3	PCN, ModERN



## 7.0 Appendices

- 1.1 – CIRN Project Management Project Progress Report
- 2.1 – CIRN Stakeholder Engagement
- 3.1 – CIRN Management Committee Membership and Meetings
- 4.1 – CIRN Peer Reviewed Publications
- 4.2 – CIRN Knowledge Products
- 5.1 – CIRN TEC Agendas
- 5.2 – CIRN Trainee Scholarship Standard Operating Procedure
- 5.3 – CIRN Trainee eligibility requirements
- 5.4 – CIRN Trainee Scholarship application form
- 5.5 – CIRN Trainee Scholarship notification letter templates
- 5.6 – CIRN Trainee Scholarship review criteria
- 5.7 – CIRN Trainee Scholarship website
- 5.8 – CIRN Trainee project database
- 5.9 – CIRN Trainee 2018 presentation schedule