
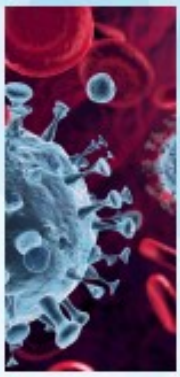










HEALTH CANADA

Compilation of Research Abstracts

2020-2021

Health Canada Santé Canada

Canada

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INTRODUCTION

This document encompasses in-house research including contracted social, physical and natural science activities toward generation of new knowledge conducted within Health Canada in 2020-2021. In this context, research is defined as:

"*the systematic investigative process of inquiry, including development, testing and analysis, carried out in pursuance of the departmental mandate, in order to discover, interpret or analyse facts, events or behaviours, to develop and revise theories, or to make practical applications with the help of such facts, laws or theories designed to develop or contribute to knowledge.*"[1]

Such research includes:

- methods development,
- adaptation of methods should they be publishable and thereby making a contribution to scientific knowledge,
- monitoring, surveillance and testing to inform risk assessments and risk management options, or to characterise a situation and establish trends,
- clinical research,
- epidemiological studies, and
- new methods for data analysis, including non-laboratory based methods such as algorithms and data mining.

The importance of research within Health Canada cannot be overstated: the various projects, collaborations, and expertise pursued by the Department demonstrate its commitment to protecting the health and safety of Canadians.

This document should be viewed as a reference tool, a summary of many of the research projects being undertaken in the Department. Developed to support Branch and Departmental programs and in particular research, risk assessment, management and policy communities, it has the potential to support broader collaboration and partnerships in addition to supporting the exchange and/or uptake of information to assist evidence-based decision making and policy objectives.

Attempts have been made to provide each project summary in non-technical language, and to include a short description of how the research relates to Health Canada's mandate. For ease of reference, the work has been grouped by theme.

[1] Definition developed by HECSB Research Governance Committee and approved by HECS Executive Committee, June 2013

Contents

LEGEND

AAPHI	Addressing Air Pollution Horizontal Initiative (formerly Clean Air Regulatory Agenda [CARA])
ADME	Absorption, distribution, metabolism, and excretion
AHTI	Air health trend indicator
AMAP	Arctic Monitoring and Assessment Programme
ANFCAP	Atmospheric nuclear forensics capability advancement project
AOP	Adverse outcome pathway
AQBAT	Air quality benefits assessment tool
AQHI	Air Quality Health Index
ARB	Angiotensin II receptor blockers
ARTSSN	Alberta real time surveillance system network
BCC	Burkholderia cepacia complex
BCCSU	British Columbia Centre on Substance Use
BLL	Blood lead level
CAMAPS	Canadian Atlantic Marine Air Pollution Study
CANDU	CANada deuterium uranium
CARA	Clean Air Regulatory Agenda
CC	Climate change
CCHS	Canadian Community Health Survey
CCIB	Climate Change and Innovation Bureau
CCRPB	Consumer and Clinical Radiation Protection Bureau
CDSS	Canadian Drugs and Substances Strategy
CEPA	Canadian Environmental Protection Act, 1999
CHMS	Canadian Health Measures Survey
CHPSD	Consumer and Hazardous Product Safety Directorate
CIHR	Canadian Institutes of Health Research
CMP	Chemicals Management Plan under CEPA
CMP3	Third phase of the Chemicals Management Plan
CNF	Canadian nutrient file
COPC	Chemicals of potential concern
CRA	Collaborative research agreement
CRMN	Canadian radiological monitoring network
CSCB	Controlled Substances and Cannabis Branch

CSSP	Canadian Safety and Security Program
CSSPI	Canadian surveillance system for poison information
CSTEM	Calgary spatial and temporal exposure modelling
DAS	Drug analysis service
DEET	N,N-diethyl-m-toluamide
DIN	Drug identification number
DRDC	Defence Research and Development Canada
DQSP	Drug quality surveillance program
EEC	Estimating environmental concentration
EHSRB	Environmental Health Science and Research Bureau
ERHSD	Environmental and Radiation Health Sciences Directorate
ESRAB	Existing Substances Risk Assessment Bureau
F&DA	Food and Drugs Act
FCSAP	Federal contaminated sites action plan
FREAR	Forensic radionuclide event analysis and reconstruction
FTIR	Fourier-transform infrared
HARS	Heat alert and response systems
HHRA	Human health risk assessment
IATGA	Integrated analysis tool for genotoxicity assessment
IUM	Integrated urban models
IVIVE	*In Vitro* to *In Vivo* extrapolation
MAPLE	Microplastics air pollution laboratory and exposure
MDMA	3,4-Methylenedioxymethamphetamine
MOA	Memorandum of agreement
MIREC	Maternal-Infant Research on Environmental Chemicals
NAM	New approach method/methodology
NM	Nanomaterials
NSACB	New Substances Assessment and Control Bureau
OECD	The Organisation for Economic Co-operation and Development
ORS	Office of Research and Surveillance, Tobacco Control, Controlled Substances and Cannabis Branch
PFAM	Pesticides in flooded agriculture
PFAS	Per- and poly-fluoroalkylated substances
PI	Principal investigator (or principal contact for the project)
PM	Particulate matter (PM2.5 = fine particulate matter, < 2.5µm diameter; PM5 = particulate matter, <5µm diameter)
PMRA	Pest Management Regulatory Agency

POR	Public opinion research
PPE	Personal protective equipment
PSL	Product safety laboratory
QAPEE	Quebec air pollution exposure and epidemiology study
[Q]SAR	Quantitative / Qualitative structure–activity relationship
R-ICL	Revised in commerce list
RDT	Repeat dose toxicity
ROEB	Regional Operations and Enforcement Branch
RPB	Radiation Protection Bureau
SAQI	Subway air quality investigation
SARS	Severe acute respiratory syndrome
SED	Safe Environments Directorate
SHE-CTA	Syrian hamster embryo cell transformation assay
SMART	Systematic meta-analysis and review tools
SVOC	Semi-volatile organic compound
TCHEQ	Toronto child health evaluation questionnaire
TG	Test guideline
TRAP	Traffic related air pollution
UF	Uncertainty factor
UFP	Ultrafine particles/particulate matter (<0.1 µm diameter)
UPLC	Ultra performance liquid chromatography
UPLC-QToF HR MS	Ultra performance liquid chromatography coupled with quadrupole time of flight high resolution mass spectrometry
VFS	Vegetative filter strip
VOC	Volatile organic compound
VVWM	Variable volume water model
WAQB	Water and Air Quality Bureau
WHO	The World Health Organization
YKHEMP	Yellowknife Health Effects Monitoring Programme

Air Quality

A test system for the exposure of lung cells to microplastics under conditions that model real-life human exposures

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. The environmental prevalence of microplastics has raised questions about potential toxicity. As inhalation is a potential route of exposure, tools that realistically model human inhalation exposures are needed. Traditional toxicity testing of inhaled contaminants involves exposure of animals; growing interest in moving away from animal models (due to ethical concerns, uncertain relevance to humans, high cost) has prompted development of devices that expose human cells and tissue samples to airborne test materials. Air-liquid interface (ALI) exposures mimic lung conditions: cells/tissues more closely resemble lung cells/tissues compared to conventional submerged cell cultures, and exposures occur by air. This study aims to establish an ALI exposure system that enables reproducible testing of microplastics and other airborne contaminants under conditions that model real-life human exposures. Human cells grown at the air-liquid interface are exposed to contaminants carried by a stream of air, as occurs in the lungs. Exposure conditions are optimised through real-time monitoring of temperature, humidity, and cellular deposition of airborne microplastics in the nano- and micro- size ranges. Established conditions and protocols maintain cell viability during exposure to air, thereby ensuring that toxic and inflammatory responses are specific to test agents. The system will provide an innovative approach to assess effects of inhaled contaminants (e.g. complex mixtures of gaseous and particulate air pollutants, combustion emissions, traffic-related pollutants, secondary organic aerosols, metals, nanoparticles, microplastics, vaping products, etc.) without animal exposures. Importantly, this will provide Health Canada with the capacity to assess health-relevant biological responses in human cells to the actual atmospheres to which people are exposed, rather than using extracts or simplified model materials, thereby more closely modeling human lung toxicity and improving hazard identification and mechanistic studies in support of regulatory needs. (PI: Errol Thomson)

Acute and chronic health effects of ambient $PM_{2.5}$ oxidative potential

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. Airborne fine particulate matter ($PM_{2.5}$) is measured as the mass of particles present in the air. This measurement is used worldwide to regulate ambient air quality and is based on years of epidemiological and toxicological evidence suggesting adverse health effects. Nevertheless, it is widely recognized that particle mass concentration is merely a surrogate measure of the true underlying cause of PM-induced health effects, often termed the “biologically effective dose”. In particular, oxidative stress is known to play an important role in PM-induced health effects including both respiratory and cardiovascular outcomes. As a result, PM oxidative potential measurements have been proposed as a promising integrated measure of overall particle toxicity. This study builds on a national survey of outdoor $PM_{2.5}$ oxidative potential conducted between 2016-2018 at 40 locations across Canada with laboratory analyses completed in 2020. These data will be linked to data on emergency room visits and population-based cohorts to support epidemiological analyses. Analyses of acute health outcomes is currently underway. Publication expected in 2021. (PI: Scott Weichenthal).

Adverse birth outcomes and childhood diseases of ambient $PM_{2.5}$ oxidative potential and $PM_{2.5}$ components

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. Oxidative stress is known to play an important role in PM-induced health effects including both respiratory and cardiovascular outcomes. As a result, PM oxidative potential measurements have been proposed as a promising integrated measure of overall particle toxicity. In addition, composition elements of $PM_{2.5}$ may have differential toxicity and consequently different health impacts. This study evaluates whether $PM_{2.5}$ oxidative potential and $PM_{2.5}$ composition is associated with adverse birth outcomes and childhood diseases. The study will contribute to updating risk assessment guidelines for particulate matter and other criteria pollutants (i.e., O_3 and NO_2 [ozone and nitrogen dioxide]) and will contribute to the Air Quality Management System in identifying the most health effective approaches to improving air quality and local air zone management strategies. A scientific article was published in 2018 on the association of $PM_{2.5}$ oxidative potential and adverse birth outcomes. Another scientific article focusing on $PM_{2.5}$ components and development of childhood asthma and paediatric cancers was published in 2020. A manuscript is expected to be published on PM2.5 composition and adverse birth outcomes in 2021. (PI: Éric Lavigne).

Aerosol SARS-CoV-2 in hospitals and long-term care homes during the COVID-19 pandemic

Health Canada (HC) is responsible for assessing risks to health posed by inhaled pollutants. To support the response to the COVID-19 pandemic, HC expertise in aerosol monitoring was leveraged to help clarify transmission risks beyond close contact. Few studies have quantified aerosol concentrations of SARS-CoV-2 in hospitals and long-term care homes, and fewer still have examined samples for viability. In an effort to provide this information, this study deployed particulate air samplers in hospital ward and ICU rooms with COVID-19-positive patients, as well as in rooms in long-term care homes experiencing outbreaks. Samplers were placed between 2 and 3 meters from patients. Aerosol (small liquid particles suspended in air) samples were collected onto gelatin filters by Ultrasonic Personal Air Samplers (UPAS) fitted with size-selective nozzles, which were operated for 16 hours, after which samples were assayed for viable SARS-CoV-2 virus and for the viral genome by polymerase chain reaction (PCR). The sampling methods were validated at the National Microbiology Laboratory. In total, 138 samples were collected from 99 rooms; no viable virus was recovered, though low levels of the SARS-CoV-2 genome were detected in approximately 15% of rooms sampled. This project was conducted in collaboration with the Public Health Agency of Canada and partners from the University of Manitoba and University of Ottawa (PI: Gary Mallach). https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0258151.

Air Health Trend Indicator (AHTI): development and updates

Health Canada is responsible for assessing adverse health risks of outdoor air pollution on Canadian health to support the "Addressing Air Pollution Horizontal Initiative". The AHTI provides information on how the health risks associated with exposure to outdoor air pollution change over time. The AHTI measures day-to-day changes in non-accidental deaths including those due to heart, circulatory and respiratory conditions a few days after exposure to two major air pollutants, ground-level ozone and fine particulate matters (PM2.5). The current AHTI is based on 22-24 major urban cities across Canada, accounting for geographical differences in air pollution concentration levels and climate for 29 years (ozone) and 12 years (PM2.5). The AHTI reports and updates are posted on Environment and Climate Change Canada's website, and accessible to all Canadians since 2011. The AHTI will be updated on a regular basis in five areas: study period, number of cities, health outcomes, vulnerable subpopulations, and perspective on short-term exposure. Recent health data for 2013-2015 and additional cities have been added to the study in order to obtain more reliable and less biased estimates of public health risks.

In addition to mortality, daily hospitalizations are now being monitored, which amounts to approximately 10x the daily mortality, allowing researchers to obtain more information on specific causes of hospitalization. Subpopulation groups, such as the elderly (>65 years) will be studied by age and biological sex as these subgroups are expected to be more vulnerable to air pollution. Finally, exposure to air pollution can be short-term or long-term without consensus on the definition. As an on-going study, the project will develop new advanced statistical models to better understand deaths and hospitalizations attributable to two air pollutants concomitantly, to estimate combined health risk. The findings can be used to inform future studies on sub-populations vulnerable to outdoor air pollution. (PI: Hwashin Shin)

An online survey on kitchen ventilation in Canadian homes

Health Canada's Guidance for Particulate Matter in Residential Indoor Air identified cooking as one of the major indoor sources of fine particulate matter (PM2.5), and gas stoves have the potential to be a significant source of indoor nitrogen dioxide (NO_2). Sufficient kitchen ventilation is important to reduce cooking exposures. Published data on residential cooking and ventilation behaviors are limited. In particular, little is known in the prevalence of kitchen ventilation and use patterns in Canadian homes. Without knowing how natural and mechanical ventilation is normally used during cooking, exposure estimates could be erroneous. To fill this gap, this research conducted a nationwide online survey to collect information on the characteristics of cooking and kitchen ventilation use in Canadian homes. Sample collection was built through a probability-based method to balance each sample group across age, gender, region, and household income for representative results. The survey was conducted from January 13 to February 24, 2020 with completed responses collected for 4500 homes across Canada. The survey responses will be used to develop a profile of characteristics and usage of kitchen ventilation systems in Canadian homes and to understand people's knowledge of cooking exposures and kitchen ventilation. The results can be used to support more accurate modeling of the impact of cooking on indoor air quality and to inform risk management strategies. A report outlining the results is expected to be published on Canada.ca in 2021. (PI: Liu Sun)

Analyses of non-linear concentration-response functions for short term exposure to air

Health Canada has an interest in understanding the negative health impacts of air pollution concentration levels on human health. Traditional methods of risk assessment for outdoor air pollution have generally assumed a risk model that is a linear in shape. Many of the risk models included in the Air Quality Benefits Assessment Tool (AQBAT) make this assumption. However, new evidence is emerging that relationships between outdoor concentrations of air pollutants and health may not all be best characterized by linear risk models. In this study, new elaborated non-linear risk models have been used to assess relationships between short-term exposure and health impact. Data obtained from emergency department visits for cardiac problems and exposure to nitrogen dioxide, and respiratory diseases and ambient ozone exposure are used to develop the models. Concentration-response curves developed for a series of lagged exposures are summarized as one common parametric function. The constructed function is applied to represent risk along concentration. The study is generating knowledge on air health effects represented as concentration-response curves, and is developing a methodology to generate non-linear functions to represent the impact of air pollution on human health. (PI: Mieczysław Szyszkowicz)

AQHI updates by expanding temporal and spatial coverages

Health Canada has a mandate to assess health risks of sources and components of air pollution, identifying specific vulnerable populations, and helping Canadians maintain and improve their health.

The Air Quality Health Index (AQHI) is an important daily communication tool to provide guidance to the public on protecting their health from the adverse health effect of short-term exposure to outdoor air pollution. The current AQHI sums the individual risks associated with three major air pollutants, ground-level ozone, nitrogen dioxide (NO2) and fine particulate matter (PM2.5). This project will improve and update the current AQHI in four areas: 1) improved modelling, 2) extension of study areas, 3) reflection of more recent study periods, and 4) additional health outcomes. First, the current AQHI is based on three single pollutant models for the three air pollutants individually, which could result in under- or over-estimates depending on their correlations. It is desirable to fully represent the effect of their combined exposures on health, accounting for the interactions among the three air pollutants. Second, while the AQHI is designed for national usage, it is based on urban areas only, due to air pollution data availability so expanding to rural areas and more urban locations is desirable. In terms of time periods, the tool is based on data for 1991-2000. Recognizing that the Canadian demographic profile, air quality profile, and medical care have changed since 2000, the exposure-health outcome relationship over time may have changed and thus expansion to recent years (2001-2015) is necessary. Finally, the AQHI considers mortality but will now be extended to hospitalization. The study findings will improve daily communications with Canadians and protect Canadians from avoidable risks by providing new information on adverse health effects related to the three major air pollutants. (PI: Hwashin Shin)

Association between air pollution and COVID-19 dynamics in Canada

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. Spread of SARS-CoV-2, like other respiratory viruses, can be due to easy aerial transmissions of respiratory droplets, exposing the virus to external environmental conditions. Short term exposure to air pollution is a risk factor for respiratory infections. In fact, there is growing evidence that small particles may enhance the transport and spread of SARS-CoV-2, a finding with profound implications. In addition, air pollution may increase levels of sensitivity to being infected by depleting immune defenses. This study aims to evaluate the short term effect of air pollution on COVID-19 confirmed cases across Canadian health regions using an epidemiological case-crossover study. Specifically, environmental data will be used for each health region across Canada and evaluate whether day-to-day changes in air pollution might affect the transmission rate of COVID-19 on a daily basis. A manuscript was submitted for publication in June 2021 and expect results to be published in 2021 (PI: Éric Lavigne).

Associations between blood volatile organic compounds, and changes in hematologic and biochemical profiles, in a population-based study

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to air pollutants in the environment. In this study, Health Canada assessed the influence of volatile organic compound (VOC) exposure on hematological and serum biochemical parameters in the Canadian population. Associations between VOCs and hematogical profiles, serum tests reflecting liver and kidney function and glucose metabolism are not well known. Using generalized linear mixed models adjusting for age, sex, smoking, alcohol consumption, BMI, education and household income, the association between selected VOCs and hematogical profiles, serum tests reflecting liver and kidney function and glucose metabolism were tested in 3,950 participants of the Canadian Health Measures Survey. This study provides evidence that exposure to VOCs, at levels found in the Canadian population, may influence blood cell counts and indicators of liver and kidney function. Renal hyperfiltration is postulated to be one mechanism explaining the inverse association between serum VOC and creatinine concentrations. (PI: Sabit Cakmak)

Calgary Spatial and Temporal Exposure Modelling (CSTEM) study

Canadian air zones represent a complex mixture of urban and rural land-use impacted by diverse emissions sources. The critical challenge for local air quality management lies in determining which pollution sources have the greatest impact on human exposure and health. This study collected summer and winter air pollution measurements at 125 locations in Calgary and surrounding rural areas, as well as yearlong measurements in a subset of sampling locations. These measurements are being combined with land-use and emissions data to identify source contributions and map short term (daily and weekly) and long term (seasonal and annual) exposure to air pollutants (NO_2, VOCs, PM_{10}, $PM_{2.5}$, black carbon, and metals) across these communities. Air pollution data generated by this study will be applied in existing health cohorts to examine a variety of adverse health outcomes. Results will also be used in collaboration with local and provincial air zone managers to develop and evaluate strategies for improving local air quality and reducing health risks. An initial manuscript is expected to be published in 2021. Further land use regression modelling for NO_2 will be completed by fall 2021. (PI: Markey Johnson)

Canadian Atlantic Marine Air Pollution Study (CAMAPS)

Large marine vessels have historically used bunker fuel oil (BFO), which can significantly contribute to air pollution in areas near commercial ports and seaways and may even adversely influence air quality at inland locations through the movement of polluted air masses. Over the period 2012 to 2015, lower-sulphur marine fuel regulations were introduced for large ships operating in Canadian coastal waters and ports with the intention of reducing vessel emissions of SO_2 and $PM_{2.5}$ and thus improving ambient air quality in Canadian port cities. The *Canadian Atlantic Marine Air Pollution Study* (CAMAPS) investigates the impact these regulations have had on ambient exposures for Canadians living in Halifax, Nova Scotia. Ambient exposure sampling was carried out for criteria air pollutants (SO_2, $PM_{2.5}$, NO_2, CO, O_3) and $PM_{2.5}$ elemental composition over a one-year period downwind and upwind of the Halifax harbour (by prevailing winds), at the Bedford Basin inlet, and at select community sites to support pre- and post-Regulation comparisons, intra-urban comparisons, and source apportionment models. To further assess the potential impacts of the regulations on human health, sampling included measurement of black carbon (BC). Analysis will apply toxicity-equivalent exposure estimates for $PM_{2.5}$-associated PAHs. Field datasets have been produced. Findings to date indicate that the low-sulphur marine fuel regulations have substantially reduced ambient exposures to SO_2 and contributed to a moderate improvement in Halifax particulate air quality. Source apportionment modeling will be applied to quantify pre- and post-regulatory marine sector emission contributions to ambient $PM_{2.5}$ and $PM_{2.5}$-associated air toxics (e.g., heavy metals) relative to other transport and non-transport source types. A scientific article outlining the efficacy of the lower-sulphur marine fuel regulations was published in 2021. (PI: Angelos Anastasopolos)

CanEPIC Study - Canadian Environment, Pregnancy, Infant and Child Study

Exposure to ambient air pollution during pregnancy has been associated with low birth weight, preterm birth, maternal health outcomes and several childhood atopic diseases and neurodevelopmental outcomes. However, evidence of the impact of air pollution on these outcomes is still limited due to other factors that may be involved in this complex relationship that may not have been accounted for in previous studies (e.g. smoking and alcohol consumption during pregnancy, maternal body mass index, maternal weight gain during pregnancy, maternal comorbidities, etc.). Further evidence is also required regarding forest fire exposure during pregnancy and impacts of other important urban environmental factors (e.g. greenness, walkability, noise, heat, etc.) on adverse birth, maternal and childhood outcomes. This study aims to evaluate the risk of air pollution on birth outcomes, maternal pregnancy complications and childhood diseases while taking into consideration the complex exposures to other

environmental factors present in urban environments. The findings of this study will be used to support Health Canada's risk assessments, regulatory decision-makings and health messaging in addressing impacts of air pollution. A scientific manuscript focusing on the interelationships between urban environmental factors and maternal outcomes will be published in 2021. Results of impacts of forest fires on adverse birth outcomes across Canada will be available for presentation in 2021 (PI: Éric Lavigne)

Chronic disease and air pollution: disease trajectory and intervention (ROUTE) study

Over the past decade, there has been mounting evidence linking low levels of ambient air pollution to a higher risk of premature mortality around the world. However, important questions remain - the exact mechanism and pathways, whereby the accumulation of air pollution exposures elicits premature death, requires more precise elucidation. Because health is a dynamic state, encompassing successive episodes of good and poor health states, this information is crucial for supporting health guidance, as well as for estimating the burden of air pollution. Health Canada is conducting a study to investigate the important role of exposure to air pollution in affecting individuals' health trajectories, and how this unfolds along different physiological pathways. A better understanding of the ways in which air pollution shapes health trajectories will help identify key pathways of public health significance and inform public polices. The second objective of the ROUTE Study is to further evaluate the effectiveness of some widely-implemented or potential individual- and policy-level interventions in reducing air health effects. Air pollution has major public health and economic consequences, but considerable uncertainty exists concerning which actions can be taken to reduce its effects. To achieve the two objectives, the ROUTE Study will draw on Big Data sources, and use state-of-the-art causal inference methodologies. Results of this study will fill important gaps in air health research and support policy decisions and public actions on mitigating air pollution effects in Canada and elsewhere. (PI: Hong Chen)

Commuter air pollution intervention study

Traffic related air pollution (TRAP) is a well-recognised contributor to smog and is linked to adverse health outcomes. Although traffic pollutants can travel long distances, exposure to the highest levels of emissions occur closest to the source; e.g. in a car in dense traffic conditions. Time spent in-vehicle may contribute up to half of commuters' daily exposure to certain air pollutants. Most new cars now have, or allow for, a cabin air filter, but it is not known how well cabin air filtration can reduce exposure to TRAP. In this intervention study, Health Canada measured commuters' exposure to air pollutants in rush hour traffic during fall, 2014. Short term cardiopulmonary health indicators such as blood pressure, heart rate variability and respiratory inflammation and measured pollutant levels inside and outside vehicles were tracked. Effects on cognition (mental processing and judgement) were also measured in this real world environment where any deficit could be important to safety. Preliminary results show that participants' heart and cognitive function were found to be impacted by in-vehicle air pollution exposures. Cabin air filtration reduced in-vehicle particulate exposures by approximately one third. In-vehicle pollutant concentrations were notably elevated in tunnels. This research will contribute to the understanding of how this environment contributes to Canadians' overall air pollution exposure and potential health impacts as well as test the effectiveness of cabin filters as a direct and economical exposure reduction intervention. A scientific publication is expected to be submitted in 2021. (PI: Gary Mallach)

Effect modifiers of the associations between traffic exposure and cardiovascular, respiratory and neurological disease-related mortality in a long-term Canadian cohort (AAPHI)

National health and population-level data are considered in risk assessments carried out by Health Canada and other federal Government Departments and Agencies. The Canadian Census–Tax–Mortality

Cohort comprises 3.5 million respondents, with detailed individual and household characteristics, and includes mortality information up to 2016 including respiratory diseases, cardiovascular complications, ischemic heart disease, cerebrovascular disease, neurological diseases including Alzheimer's and Parkinson's, and chronic obstructive pulmonary disease (COPD), and diseases with known associations to traffic exposures. In this study, national traffic density data will be linked to the cohort to examine the association between traffic density and mortality due to cardiovascular, respiratory, diabetes and neurological disease causes. An assessment will then be carried out as to whether certain individual or environmental factors render individuals more or less susceptible to the adverse effects of traffic density. The factors to be investigated will include socioeconomic and sociodemographic status, weather, and the amount of neighborhood green space (vegetation). The relationship between traffic exposure and health is present within the context of a changing, warming climate, where high seasonal average temperatures and urban heat islands, urban or metropolitan areas that reach significantly warmer temperatures than surrounding rural areas, may provide additional burdens on health that disproportionately affect certain socioeconomic groups. People can be additionally stressed by limited access to green space due to urban design; socioeconomic and sociodemographic characteristics, long term seasonal average temperatures, urban heat islands, and residential greenness may modify the association between traffic exposure and mortality. The results will allow for more accurate traffic-related risk estimates for socio-economic and sociodemographic sub-populations by taking into account the complex interactions between health and exposure to traffic, socioeconomic and sociodemographic factors or characteristics (age, sex, family education and income, employment status, visible minorities, immigrants), weather, microclimates, and green space. (PI: Sabit Cakmak)

Hybrid exposure models to predict spatially and temporally resolved air pollution concentrations at local and national scales

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. Land-use regression (LUR) models provide long term estimates of air pollution at a fine spatial scale. Chemical transport models produce temporally resolved estimates of air pollution concentrations at a coarse spatial state. This study combines LUR and chemical transport models to provide spatially and temporally refined estimates of air pollution exposure at both local and national scales. Better estimates of air pollution exposure improves our ability to assess the health risks associated with both long term and short term exposure to air pollution. The results will strengthen retrospective and prospective epidemiological studies by providing more accurate exposure estimates. Hybrid models for NO_2 and $PM_{2.5}$ have been developed for a single test year. These models will be expanded to cover the period from 2000-2014, and estimate contributions of different source types (e.g., transportation, industrial, and biomass burning) to ambient NO_2, $PM_{2.5}$, and O_3. The data generated by this project will be applied in existing health cohorts to estimate the impacts of short term air pollution in urban and non-urban areas across Canada and to identify sources with stronger long term health impacts. (PI: Markey Johnson)

Ice arena air quality project

Fossil fuel powered ice resurfacers (Zambonis®) emit several pollutants, notably nitrogen dioxide (NO_2) and carbon monoxide (CO). Some segments of the population that regularly use ice arenas (including children, the elderly and those with asthma and other cardiovascular and respiratory conditions) are considered susceptible to adverse health effects after exposure to these pollutants. Provincial partners requested assistance in developing improved best practices, based upon scientific evidence, to reduce the health effects from exposure to air pollution in ice arenas. Currently, there are insufficient data on the levels of combustion-related pollutants (namely NO_2 and CO) in arenas, and insufficient evidence

supporting the effectiveness of currently recommended pollutant reduction strategies. The Indoor Air Contaminants Assessment Section (IACAS) of Health Canada designed a research study to investigate and address these issues. In the winter of 2017/2018, levels of air pollutants were measured continuously for seven days in four arenas in Ottawa and four arenas in Saskatchewan. These results are being used to better understand pollutant levels and temporal variation in the arenas, and to evaluate the use of portable monitoring equipment. The second phase of the study, conducted in winter of 2019-2020, assessed pollution reduction strategies in ice arenas, including the impact of different ice resurfacer fuel types and impact of changes in ventilation practices. The data are currently being used for development of implementable best practices for air quality in ice arenas, targeted for provincial/territorial and municipal partners. Publication of the research results and best practices is slated for FY 2021-2022. (PI: Aaron Wilson; Christie Cole; Corinne Stocco; Morgan MacNeill)

Impact of temporal variation of industrial emissions of air pollutants on asthma incidence in children of Quebec - An approach to accountability study

Industrial emissions contribute to local and regional air pollutant concentrations. In Quebec, significant reduction in industrial air pollutant emissions has been observed over the past decades, because of plant closures and government regulatory actions. Such reductions offer an opportunity to evaluate the potential emission reduction-associated health benefits. Health Canada is collaborating with the Quebec Public Health Agency (INSPQ) and the University of Toronto to conduct a study on the associations between changes over time in exposure to ambient fine particulate matter (PM2.5), nitrogen dioxide and sulphur dioxide emitted from industrial sources and childhood asthma incidence in Quebec. A birth cohort for children who resided in Quebec in 2002-2015 has been created to study asthma incidence. A chemical transport model is being used to estimate ambient air pollutant concentrations resulting from industry and transportation sectors. Yearly changes in exposure to ambient pollutants emitted from industrial sectors in each small area (census tracts in urban centres and local health service territories in rural areas) are estimated. The associations between industry emission-related concentrations of ambient pollutants and childhood asthma onset will be studied using fixed-effects regression models. Specific industrial sectors petroleum refineries, metal smelters and pulp and paper mills will be studied separately. Using the concentration-response relationship generated from this study, modelling of potential health benefits of policy scenarios may be carried out targeting emissions from various industrial sectors. This project contributes to the evidence regarding the impact of government regulatory/non-regulatory actions on industrial emissions on children's lung health. Concentration-response functions produced from this project may help estimate the costs/benefits of reducing industrial emissions, and set priorities in air quality management actions on specific industrial sectors. (PI: Ling Liu)

Indoor air quality and the effects on children's respiratory health in First Nations reserves in the Sioux Lookout Zone

According to the Canadian Paediatric Society, housing directly affects the health of children and youth. First Nations and Inuit are disproportionately affected by crowded and inadequate housing, which has been associated with increased hospital admissions of children for respiratory tract illnesses. It has been shown that Aboriginal children in communities in the Sioux Lookout Zone (Sioux Lookout First Nations Health Authority; SLZ) in northern Ontario have elevated rates of asthma, bronchiolitis and pneumonia, but there is little information on their indoor environmental quality. Working with local officials, a preliminary assessment revealed houses with issues including dampness and contaminants associated with wood stoves, as well as other problems. This study aims to evaluate Indoor Environmental Quality (IEQ) in houses of 50-100 children living in four isolated communities in this area in relation to

respiratory health and related utilisation of health care services. Community consultations with the relevant Nations Hamlet Councils and local medical officers of health are incorporated into the process. Consenting households receive a respiratory health questionnaire for their youngest child and a standardized housing inspection is being carried out in partnership with Band officials. Monitors record basic indoor environmental quality and the relationship between it and the child's respiratory health will be examined. Working more effectively with the communities, this research will help us to identify simple home improvements and other building interventions that could improve the respiratory health of this vulnerable population. The findings will also be used to inform future, similar studies/interventions in remote First Nations (FN) reserves across Canada. Field work was completed in the spring of 2019, and analysis of the data is underway. Participant reports for all four (4) First Nations communities have been completed and support given to housing authorities to support training of local technicians on air quality issues. One paper is anticipated for publication in 2021. (PI: Gary Mallach)

Integrated urban models (IUM) project

In support of the federal government's plans to take action to address air pollution in Canada, researchers from the University of Windsor, Health Canada, and Ryerson University are leading a joint effort to develop tools to support local and federal agencies in making decisions that will reduce urban air pollution and create healthier cities. Integrated Urban Models (IUM) are complex simulation platforms that act as a virtual laboratory to allow urban planners and decision makers to evaluate the impacts of development and transportation decisions and policies. This study will add air pollution exposure and health impacts, as well as other sustainability indicators to SMARTPLANS, an existing IUM. This study will provide support for evaluating alternate land use and transportation planning policies and create healthier Canadian cities. Specifically, SMARTPLANS will utilize data on local transportation, land use, economic and travel activity, as well as air pollution, health, and economic indicators, to simulate land use and transportation system infrastructure and policy changes, with the goal of assessing which decisions will maximize social and economic benefits, while minimizing negative environmental and health impacts. SMARTPLANS will help to promote healthier cities by facilitating analysis of the impacts of alternate planning and policy decisions on a variety of social, economic, environmental, and health indicators, including exposure to air pollution and health impacts of air pollution in the Canadian population. The study will culminate in the development of a user-friendly planning support tool that will be freely available to policy makers, air zone managers, researchers, public health practitioners, and other stakeholders across Canada. The SMARTPLANS platform will be developed for 5 cities across Canada: London, Halifax, Vancouver, Ottawa, and Calgary. (PI: Markey Johnson)

Interaction between gene variants and air pollution in AQHI panel studies participants

This research study addresses Health Canada's mandate regarding factors mediating vulnerability to adverse effects of air pollution, with implications for regulatory decision-making and health messaging. Research is needed to improve our understanding of the biological mechanisms of the health effects of air pollution, specifically for associations at low pollution concentrations observed in Canada. Research is also needed to better characterise and reduce health risks of air pollution for Canadians, especially vulnerable groups. Recent studies have suggested that common, heritable, genetic differences may influence susceptibility of individuals to health effects of air pollution. Specifically, genes involved in responses to oxidative stress have been investigated as possible factors that alter sensitivity to air pollution. From 2013 to 2015 saliva DNA samples were collected from 176 participants in the Air Quality Health Index (AQHI) Panel Studies. Study participants also provided 10 weeks of daily and weekly health data (lung and cardiovascular function tests, symptoms, activities). To this point, all samples have been

analyzed and study participants have been characterized with respect to the presence of 23 gene variants, and assigned an overall gene score reflecting the combined presence of multiple variants. In the next phase, analysis of health measure data will determine whether the health effects of air pollution differ between individuals with or without these gene variants, thereby evaluating the importance of oxidative stress as a mechanism for air pollution effects; and determine whether the morbidity data support the mortality-based AQHI formula (public information tool). These findings may provide important biological information about how even very low pollution levels can affect health and suggest possible mechanistic links between air pollution and health effects. This information could be useful for future development of interventions or messaging to protect individuals who have a genetic susceptibility to the effects of air pollution mediated oxidative stress. (PI: Dave Stieb)

Joint effects of exposure to aeroallergens and outdoor air pollution in the urban environment

Short term exposure to aeroallergens has been associated with the exacerbation of asthma and allergy symptoms. The joint effects of aeroallergens and outdoor air pollution on asthma exacerbation has also been investigated, however findings have been inconclusive. As well, growing evidence is showing that exposure to outdoor air pollution during gestation and early life is associated with the development of asthma and allergic symptoms among children. Little is known regarding the joint exposures of aeroallergens and air pollution among children. A major limitation of the available epidemiologic literature is that exposure has typically been assessed on the basis of pollen data from only one or few monitoring stations per city. Thus, current data do not capture intra-urban spatial heterogeneity of pollen concentrations providing less accurate data for exposure assessment when studying potential human health effects and potential interactive effects with outdoor air pollution. In this context, a land use regression (LUR) model approach based on environmental determinants will be developed for predicting the variability of pollen concentrations at fine spatial scales in the city of Toronto. Results are expected for the fall 2019 and will be published in 2021. Using the Canadian Healthy Infant Longitudinal Development (CHILD) study, a Canadian Institute of Health Research (CIHR) and Health Canada funded birth cohort, the combined effects of exposure to outdoor air pollution and aeroallergens on asthma incidence among Canadian children will be evaluated. A scientific paper based on the characterization of aeroallergens in Canada has been published in 2018. A scientific paper based on results of joint effects of aeroallergens and air pollution on atopic disease development using the CHILD Study will be published in 2021. A scientific manuscript on the spatio-temporal variations of aeroallergens in the city of Toronto will be published in 2021 (PI: Éric Lavigne)

Longitudinal effects of air pollution, aeroallergens and urban environment features in the Toronto child health evaluation questionnaire (TCHEQ) cohort

Health Canada has an interest in better understanding the multiple sources of exposure that characterize diverse features of urban environments. The Toronto Child Health Evaluation Questionnaire (TCHEQ) study established a cohort of 5,619 grades one and two (aged 5 to 9) Toronto school children in 2006, collecting detailed data on the child's and parents' health, sociodemographic characteristics and exposures in the home environment. There are few other Canadian cohorts of children of this size. In the original study, the prevalence of asthma was associated with nitrogen dioxide in those children with other allergic disease such as hay fever and eczema. In the previous round of CARA funding, TCHEQ participants were linked to Ontario health care utilization data housed at the Institute of Clinical Evaluative Sciences (ICES) to determine the incidence of new cases of asthma and other allergic disease 10 years after the original study, and to examine their associations with air pollution. To date, analyses have revealed that exposures to oxidant air pollutants (ozone and nitrogen dioxide), but not fine particulate matter, were associated with an increased risk of incident asthma and eczema. In this phase

of the study, analyses will examine the incidence of allergic disease in association with oxidative potential and aeroallergens (pollen and spores), link the cohort to other outcomes including early childhood development, and conduct updated linkage to health care data 15 years after the original study. A better understanding of longitudinal effects of air pollution and aeroallergens and the ability to control exposure sources supports Health Canada's efforts related to regulatory decision-making and health messaging. (PI: Dave Stieb)

Long-term exposure to ambient air pollution and effects on cardiovascular, respiratory and neurological health in an older population: The Canadian Longitudinal Study on Aging

The Canadian Longitudinal Study on Aging (CLSA) is a population based national study which will follow the health, lifestyle, social and economic transitions, and trajectories of 50,000 Canadians, aged 45 to 85 years old, at three-year intervals for 20 years. Health Canada's goal is to collaborate with the CLSA over the many years of follow-up to study the effects of ambient air pollution on healthy aging. The current proposal is to measure change in cognitive function measures and the incidence of cardiac, pulmonary and neurologic disease during six-years of follow-up, associated with the average neighbourhood concentrations of ozone (O_3), nitrogen dioxide (NO_2), and fine particulate matter ($PM_{2.5}$), during a six year period. Exposure will be estimated by satellite monitoring, Environment and Climate Change Canada's National Air Pollution Surveillance program (NAPS) ground monitors and land-use regression techniques, where appropriate. Traffic-related air pollution will be estimated by the proximity of residence to roadways. This project has already received AAPHI funding (2016-2019) for the first three year follow-up. This project aims to update the data linkage (air pollution and climate variables to the CLSA data base) and data analysis to include another three years of follow up for a total of six years. A longitudinal study will help clarify the health effects of air quality among the elderly, and build the foundation necessary to continue this legacy study over a twenty year period. A secondary aim is to determine if susceptible subgroups exist through stratifying results by gender, education, income, rural versus urban locations and the presence (at the time of study inception) of chronic comorbid conditions including diabetes, cardiovascular disease, and chronic obstructive lung disease. This study will be unique and provide some of the most definitive information available on the relationship between air quality and cognitive function in Canada. (PI: Bob Dales)

MAPLE: The Microplastics Air Pollution Laboratory and Exposure Project: Developing methods to detect, quantify, and characterize airborne microplastics

Microplastics are small particles of plastic measuring less than five millimeters in length. With growing concern on their ecological and human health impacts, the Government of Canada is leading international efforts to protect the environment from microplastic plastic pollution. In support of *Canada's Plastics Science Agenda*, the government has prioritized research on: a) the detection, quantification, and characterization of plastics in the environment; and b) impacts on wildlife, human health, and the environment. Very few studies have purported to measure microplastics concentrations in air, and there is a need to develop rigorous scientific protocols to strengthen future efforts. No studies to date have investigated the impact that exposure to airborne microplastics has on human health. The purpose of this study is to develop and optimise sample collection, and subsequent microscopic and analytical methods to detect, quantify and characterise different types of microplastics in both indoor and outdoor samples. As Canadians spend approximately 90% of their time indoors, data on both indoor and outdoor microplastic exposures will be required to understand their sources, pathways, fate, and distribution; and to identify and prioritize specific microplastic categories or mixtures for future research, risk assessment/management. (PI: Sabina Halappanavar)

Mobilizing changes in air quality during the COVID-19 shutdown as a guide for future sustainable development

Air pollution is one of the top global environmental health burdens, which contributes to approximately 15,300 premature deaths in Canada, and costs approximately $120 billion per year to the Canadian economy. Addressing air pollution, especially traffic related air pollution (TRAP) in urban areas, remains a priority for Health Canada. The Regulatory Operations and Enforcement Branch, Environmental Health Program in Ontario funded a research project in collaboration with the University of Toronto's Southern Ontario Centre for Atmospheric Aerosol Research to understand how different traffic emission sources affect air quality in the Greater Toronto Area. The primary goal of this study was to compare different methods to analyze the sources and levels of TRAP in the city of Toronto and parts of highway 401 during pre- and post-COVID-19 pandemic lockdown. This research also provided an understanding of the capacity of available resources to measure changes in air quality that can guide future investment in public health and sustainability. Results indicate a significant reduction of pollutants (nitrogen oxides, ultrafine particles, black carbon, carbon monoxide and carbon dioxide) during the pandemic when compared the pollution level with pre-pandemic period from 2017-2019. This study also identified substantial reductions (40-60%) of particulate matter 2.5 (PM2.5) from cooking, and tailpipe and non-tailpipe emissions from vehicles. The reduction of PM2.5 from tailpipe emissions during the pandemic was mainly due to a reduced number of trucks in the urban environment, highlighting the importance of targeted strategies to reduce heavy emitters on roadways to mitigate the levels of TRAP more effectively. Results from this study contribute to guide future policy changes that will support improved air quality and sustainable development in the Province of Ontario and in Canada. This study benefits Health Canada by providing guidance on future policy development for improving air quality. (PI: Mainul Husain; Greg Evans, University of Toronto)

New Homes Air Quality Study

Building materials have been found to release pollutants into indoor air. Recent studies suggest that, as building envelopes become even tighter, levels of volatile organic compounds (VOCs) in newly built homes may exceed health-based exposure limits. There is also concern over the concentrations of semi-volatile organic compounds (SVOCs), including flame retardants, in this environment. However, existing studies typically involve a small number of homes, usually occur at one point in time, and are not evaluated within a Canadian context. To address these knowledge gaps, this multi-year study measures concentrations of VOCs and SVOCs immediately before occupancy, as well as at multiple time points during the first year of occupancy, in 40 newly constructed homes in Ottawa. Information about factors that affect the monitoring results, including air exchange rate, occupant behaviour and housing characteristics are also being collected. The objectives of the New Homes Air Quality Study are to measure concentrations of VOCs and SVOCs in new homes; to understand how these concentrations compare to existing health-based exposure limits and/or concentrations previously measured in Canadian homes; and to examine how these concentrations change during the first year of occupancy. The study also provides the opportunity to undertake preliminary work on microplastics, an emerging issue and a priority for the Government of Canada. Results from the study will inform risk assessment and risk mitigation activities such as providing health-based guidance to organizations and individuals relating to indoor air contaminants in new homes. They may also inform the development of product standards and modifications to the national building code. The COVID-19 pandemic has had a significant impact on the duration of field work, which was initiated in 2019 and will be extended to 2023/24. (PI: Corinne Stocco)

Quebec Air Pollution Exposure and Epidemiology study (QAPEE)

Urban air pollutants such as nitrogen dioxide (NO_2), black carbon (BC), fine particulate matter (PM2.5), and ultrafine particles (UFPs) are ubiquitous in Canadian urban environments and have been suggested as factors contributing to the risk of several cardiopulmonary diseases and cancers. Past research at Health Canada has contributed to air pollution exposure modelling for several pollutants in several Canadian cities. However, Quebec City remains a major urban center with few air pollution exposure Land Use Regression (LUR) surfaces. The creation of new LUR surfaces would be beneficial for a city rich in epidemiological data from the Quebec Integrated Chronic Disease Surveillance System. As well, there is local concern that air pollution related to the Quebec City seaport and the Jean Lesage international airport pose risks to human health. Analyses that test the association of these point sources to ambient air pollutants would be valuable to developing policy around these issues. Oxidative potential can serve as an indicator the potential biological activity of particulate matter and provide a metric independent of mass concentration. Analysis of the spatial and temporal variation of oxidative potential (OP) of PM2.5 in the city and the relationship between OP and point sources will improve understanding of PM associated health risks. The source and size characteristics of different size ranges of UFPs may have distinct health effects. This study is applying novel techniques to characterise UFPs by source and test for associations with Quebec City's sea and air ports. Similarly, relating $PM_{2.5}$ OP to health effects may reveal health risks of PM2.5 independent of mass concentration. It aims to generate exposure models for several pollutants in the region that will substantially reduce exposure misclassification in the linkage of air pollution data to epidemiological cohorts in Quebec City and advance understanding of health impacts of these pollutants. Analysis is ongoing. (PI: Keith Van Ryswyk)

Short and intermediate-term exposures to ambient air pollution from biomass burning and changes in retinal microvascular responses in children

Health Canada is responsible for assessing risks to health posed by inhaled pollutants. Epidemiological studies of the cardiovascular health effects of fine particulate air pollution ($PM_{2.5}$) primarily reflect urban areas and few studies have examined non-traffic sources of particulate air pollution. Recent studies have demonstrated that biomass burning as a source of $PM_{2.5}$ may modify the acute cardiovascular health effects of this pollutant among elderly subjects; however, the components and biological mechanisms underlying this association are not entirely clear. Moreover, it is not clear how such exposures may impact cardiovascular health in children. This investigation will examine the impact of short (e.g. 24-hours) and intermediate term (e.g. 1 month) exposures to $PM_{2.5}$ from biomass burning on microvascular responses in school children over the course of a heating season in Courtenay and Cumberland, British Columbia. Few studies have evaluated the cardiovascular health effects of air pollution exposures among children; however, since microvascular dysfunction is a known contributor to the development of cardiovascular disease, it is important to understand how early life exposures may impact vascular health. In particular, retinal arteriole narrowing has been identified as a predictor of hypertension in both children and adults and may serve as a marker for similar changes in the coronary microvasculature. In this study, retinal microvascular diameter will be assessed prospectively using repeated *within-subject* measurements collected using a non-invasive retinal imaging technique. Daily mean $PM_{2.5}$ mass concentration data will be collected from fixed-site monitors and monthly mean $PM_{2.5}$ oxidative potential will also be determined. Collectively, the proposed investigation will provide important information related to the impact of $PM_{2.5}$ (and $PM_{2.5}$ oxidative potential) on cardiovascular health and will support ongoing efforts to reduce the public health impacts of air pollution from biomass burning in Canada and abroad. Data collection was completed in May 2020. Publications are expected in 2021. (PI: Scott Weichenthal)

Spatial modelling to support health studies

Several high-profile national- and local-scale air pollution health studies in Canada rely on Health Canada scientists to provide estimates of exposure to air pollution which are required to carry out epidemiologic analyses. Health Canada is working with academic partners to carry out intensive ambient air pollution monitoring, and develop land-use regression (LUR) models for Ottawa, London, Calgary, and Halifax. Such models allow for the prediction of concentrations of pollutants at a neighbourhood or household level, which reduces the error associated with obtaining data from central site monitors. LUR models are being developed by Health Canada based on data obtained to predict the concentrations of elements (such as metals) in airborne particulate matter in Calgary and Halifax. LUR models are being used to support local- and national-scale health studies investigating air pollution impacts on respiratory, cardiovascular (e.g. stroke), developmental (e.g. birth outcomes, gestational diabetes), autoimmune diseases and cancer outcomes. These LUR models support research investigating links between air pollution and a variety of adverse health outcomes including mortality, atherosclerosis, systemic autoimmune rheumatic disease, and birth outcomes. LUR models and other exposure data developed by Health Canada's Air Program are now available through several venues including The Canadian Urban Environmental Health Research Consortium (CANUE). The Halifax land use regression modelling for metals is expected to be published in 2021. (PI: Markey Johnson)

Subway air quality investigation (SAQI)

Airborne particulate matter (PM) is a global health concern, and its metallic components have been shown to have cardio pulmonary health effects. Particulate matter in subway systems has been characterized as being highly enriched in steel-based elements such as iron, chromium, manganese, zinc, and nickel as well as brake pad-related elements such as copper and tin. In Canada, the Urban Transportation Exposure Study (UTES) characterized the PM exposures in three Canadian subway systems and found that most of a typical commuter's daily exposure to particulate iron manganese and chromium would occur while in the subway and more than 20% of their daily exposure to $PM_{2.5}$ mass would result from a typical 70-minute subway ride in the Toronto subway. Similar values were found for the Montreal and Vancouver subway systems. This study returned to the Toronto Subway and has evaluated two interventions, night time tunnel vacuuming and changes in subway trains, for their potential to reduce fine particulate matter (PM2.5). Further, fine particles from the subway are being compared to that of two ambient sites in Toronto. Data from this study will be valuable towards designing air quality policy in this unique environment which is visited by millions of Canadians on a daily basis. Two papers are anticipated for publication in 2021. (PI: Keith Van Ryswyk)

The Air Quality Benefits Assessment Tool (AQBAT) - Update

The Air Quality Benefits Assessment Tool (AQBAT) is a computer application developed by Health Canada which is designed to estimate the human health impacts of changes in Canada's ambient air quality. It is used to estimate the benefits (positive impacts) or damages (negative impacts) of proposed regulatory initiatives related to outdoor air quality as mandated by the Treasury Board Cabinet Directive on Regulatory Management (when developing new regulations that affect air quality, Treasury Board requires that Health Canada quantify the human health and associated economic benefits of estimated changes in air quality). AQBAT consists of a Microsoft Excel application file which enables the user to define, run, examine and save the inputs and outputs for specific scenarios combining pollutants, health endpoints, geographic areas and scenario years. It contains historical and projected population data, pollutant concentration data, annual baseline health endpoint occurrence rates, and Health Canada endorsed concentration-response functions and health endpoint valuations. It utilizes the @Risk add-in software to perform Monte Carlo simulations, which allow the user to examine the effects of

uncertainties on estimated health impacts. AQBAT is a knowledge translation tool in that it applies findings from research studies of the health effects of air pollution to develop concentration-response functions and economic valuation estimates used in quantifying health impacts and their economic value. AQBAT has been applied to numerous regulatory and non-regulatory scenarios including impacts of vehicle electrification, impacts of wildfire smoke, assessment of climate change impacts, and Human Health Risk Assessments for Diesel Exhaust and Biodiesel. Ongoing updating of data, parameters and methodology is required to ensure that assessments of regulatory initiatives reflect the most current science such that they most effectively protect the health of Canadians and do not impose unwarranted costs to society. Version 3 of AQBAT was released in 2019. (PI: Dave Stieb)

The association between air pollution and COVID-19 related mortality in Santiago, Chile: A daily time series analysis

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to air pollutants in the environment. In this study, Health Canada and collaborators in Chile assessed the risk associated with air pollutants and COVID-19 mortality. Exposure to ambient air pollution is a risk factor for morbidity and mortality from lung and heart disease. However, it is not certain if short term exposure to ambient air pollution concentration influences COVID-19 related mortality. Using ambient air pollution (ozone, nitrogen dioxide, carbon monoxide and particulate matter) and climate data from seven air monitoring stations distributed in the nine urban centres in Santiago, Chile, along with daily deaths from laboratory confirmed or suspected COVID-19 between March 16 and August 31, 2020, an association between ambient air pollution and daily COVID-19 mortality were tested. Our findings suggest that acute increases in air pollution may be one risk factor for daily COVID-19 mortality. There were no significant differences in risk of mortality by sex, but relative risk generally increased with age. This study provides evidence that daily increases in air pollution may increase the risk of dying from COVID-19, especially in the elderly. (PIs: Sabit Cakmak and Bob Dales)

The association between air pollution and hospitalization for patients with systemic lupus erythematosus in Chile: A daily time series analysis

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to air pollutants in the environment. In this study, Health Canada and collaborators in Chile assessed the risk associated with air pollutants and systemic lupus erythematosus (SLE). SLE, characterized by humoral and cellular immune system dysregulation, loss of self-tolerance and production of auto-antibodies to self-antigens with chronic inflammation and damage to multiple organs, can be debilitating and even fatal, but its association with air pollution is not well known. Using ambient air pollution (ozone, nitrogen dioxide, sulfur dioxide, carbon monoxide and particulate matter) and climate data from seven air monitoring stations distributed in the seven urban centres in Santiago, Chile, along with daily patient hospitalization data from 2001 to 2012, an association between ambient air pollution and daily hospital admissions for SLE were tested. Our findings suggest that acute increases in air pollution may be one risk factor for hospitalization of patients with a primary diagnosis of SLE. (PI: Sabit Cakmak)

The association between air pollution and the degree of difficulty controlling sleep disordered breathing by positive airway pressure therapy (Ottawa Hospital Research Institute)

Obstructive sleep apnea (OSA) has been shown to be linked to heart disease, hypertension, diabetes and depression. Sleep disordered breathing, which is characterized by abnormal or insufficient breathing in sleep causing sleep fragmentation and a reduction in blood oxygen level, has been associated with oxidative stress and inflammatory biomarkers. Positive airway pressure (PAP) treatment which helps

keep the windpipe open during sleep is the treatment of choice for OSA. However, adherence with PAP treatment is low and multiple factors may affect PAP usage including environmental considerations. OSA and air pollution have been linked to increased cardiovascular diseases and mortality and may lead to symptoms of nervous system inflammation, including sensory discomfort and fatigue, the latter being a common manifestation of poor quality sleep. However, the association between pollution and OSA is still poorly understood and current evidence is very limited, though some human and animal studies have demonstrated that air pollution has an effect on OSA. Indoor air pollution, especially particulate matter which is small enough to be deposited in the upper airways of the respiratory tract, may potentially cause irritation and inflammation of the upper airways, reduce airway patency and consequently may lead to OSA development or worsening of existing OSA symptoms. This study aims to establish the concentration-response function for OSA by comparing day-to-day and night-to-night changes in air pollution with night-to-night changes in control of sleep apnea as measured by data from individuals'' CPAP machines. The results of this study will allow researchers to determine if air pollution aggravates sleep apnea and to what degree. This will help Federal evaluators determine the burden of illness/disease due to air pollution in the Canadian population, will be useful for determining the total economic impact of air pollution, and in the end, help with decisions about air quality standards. (PI: Bob Dales; Dr Tetyana Kendzerska [Ottawa Hospital Research Institute])

The association between pregnancy exposure to air pollution and autism in children

Health Canada is responsible for assessing public health risks of air pollution, identifying specific vulnerable populations, and reducing the negative impacts of environmental exposures on the health of Canadians. This project examines neurological effect of outdoor air pollution on children through maternal exposure during pre-pregnancy and pregnancy. The study focuses on Autism Spectrum Disorder (ASD) in young children, which is a complex developmental disorder, characterized by difficulties in social communication and interaction that can persist throughout life. In Canada, the Public Health Agency of Canada released a report of the National Autism Spectrum Disorder Surveillance System, focusing on prevalence and incidence in children (ages 5-17) from six provinces and one territory. With limited studies on the association between air pollution and childhood ASD in Canada, Health Canada is undertaking an epidemiological research study to investigate negative effects of maternal exposure to various air pollutants during pregnancy on ASD in children aged five or under; a vulnerable Canadian subpopulation in Ontario. In contrast, positive effects of neighbourhood green space and walkability are also examined. The study objective is to estimate the associations between exposure to air pollution (and/or green space and walkability) and ASD in children born between April 1, 2012 and March 31, 2020. This study examines pairs of children with ASD and their mothers based on key linkages and then estimates the association between maternal exposure to air pollution and ASD in children based on a matched case-control design with a matching ratio of 1:5. Evaluation during the perinatal period is essential since it is the period of critical brain development during which an environmental exposure can influence neurodevelopment. Study findings will help to understand potential causation or prevention of the occurrence of ASD in children and thus reduce burden of societal and family related health care and costs. (PI: Hwashin Shin)

The COVID-19 pandemic and air pollution effect (COVID-Air) study

The COVID-19 pandemic is one of the greatest health challenges in our time. Since the outbreak, it has claimed over 3.8 million lives, shut down many nations, and triggered a global socioeconomic crisis. There is unprecedented urgency to understand who are most vulnerable to COVID-19 and which factors may inflict severe illness after the infection. This information is critical for supporting population-level interventions that are essential to stem the tide of the COVID-19 crisis. Health Canada is conducting a

study to investigate whether COVID-19 patients who have been exposed to poor air quality are at greater risk for hospitalization, admission to an intensive care unit, use of a ventilator, and death. There are emerging observations linking air quality to COVID-19 mortality, but more research is needed to better understand the potential role of air pollution in affecting COVID severity. The second objective of the COVID-Air project is to further investigate whether air pollution reductions due to the lockdown may yield any health benefit. The lockdown emulates an unprecedented regulatory action that resulted in drastic traffic reductions over vast regions simultaneously. Results of this study will make unique contributions to advancing our understanding about the intersection between COVID-19 and air pollution and the potential role of air pollution mitigation in curbing the COVID-19 crisis, thereby supporting the mandate of Health Canada in the eras of COVID-19 pandemic and post-COVID recovery. (PI: Hong Chen)

The role of stress and stress reactivity in mediating impacts of air pollutants on the brain and lungs

Health Canada is responsible for assessing the health risks associated with exposure to air pollution. Even at the relatively low average pollutant levels typically experienced in Canada, exposure to air pollution is associated with increased risk of neurological and mental health disorders (e.g. cognitive decline, dementia, depression). However, underlying mechanisms are unclear. Stress may be a central unifying mechanism. Health Canada research has shown experimentally that inhaled ambient particulate matter and ozone provoke a stress response, causing the release of stress hormones that impact biological systems throughout the body. The brain is highly sensitive to stress, and chronic stress exerts profound biochemical and structural effects on the brain that contribute to local and systemic disease processes. This study investigates the role of stress responses in mediating impacts of pollutant inhalation on the brain and lungs. *In vivo* and *in vitro* models are used to examine biological pathways that link pollutant effects in the lungs and blood to the brain, and in turn feedback to impact the lungs and other organs. In collaboration with researchers at the University of British Columbia, stress biomarkers are assessed in a human diesel exhaust chamber study to extend laboratory findings to humans. Knowledge gained is being used to explore stress hormone involvement in associations between air pollution and brain development in a birth cohort in collaboration with researchers at ISGlobal (Barcelona, Spain). By linking results from experimental models to humans, this project will support the causal basis of epidemiological associations and inform effective risk assessment and management strategies. (PI: Errol Thomson)

Time-dependent vulnerability to air pollution in a pregnancy cohort (MIREC)

Identifying impacts of air pollution exposure during critical fetal developmental periods has been prioritized under Health Canada's program to address air pollution and by international air pollution regulatory programs. However, traditional approaches have had limited success in addressing this issue. This study will apply an emerging novel approach (multilevel Bayesian modeling) to identify periods of susceptibility to air pollution during fetal development in the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort. Air pollution exposures will be estimated using coupled satellite remote sensing and National Air Pollution Surveillance program (NAPS) data, an approach that Health Canada researchers have previously validated in Windsor, Ontario. The study results suggest that exposure to ambient air pollution during critical periods of pregnancy may be associated with lower birth weight among term infants. A manuscript is expected for submission to a journal in 2021. (PI: Markey Johnson)

Trainyard Neighbourhood Air Quality Study (TyNAQ)

Canada has a large railway network, with nearly 50,000 km of railway and hundreds of train yards. Train yards are nodes in the railway network that intensify polluting activity, with locomotives operating 24hr/day year-round along with transport trucks and freight-handling equipment. Railway corridors and train yards frequently intersect residential areas, including large urban cities where the majority of Canadians live and work, raising health concerns about the rail sector's significant air pollution releases. Railway-generated air pollution is complex, combining fossil fuel (diesel) combustion emissions with friction/wear emissions (steel rails/wheels, brakes) and dust resuspension. These gaseous and particulate matter (PM) releases include a suite of pollutants with known acute and chronic health effects, including nitrogen dioxide (NO2), sulphur dioxide (SO2), and respirable particles in multiple size fractions (UFP, PM2.5, PM2.5-10) and containing toxic elements (e.g., heavy metals, PAHs) that may contribute to oxidative stress. Residents exposed to railway air pollution may also experience related noise pollution with potentially cumulative health effects. Canadian train yards constitute an air health knowledge gap, lacking relevant emissions and exposure data to characterize impacts on urban air quality and health. To address this air health knowledge gap, the Trainyard Neighbourhood Air Quality (TyNAQ) research project will conduct near-source and community air quality sampling campaigns for multiple air pollutants and noise near a large Canadian urban train yard in Toronto, Canada. Field work is taking place 2020-2021. (PI: Angelos T. Anastasopolos)

Cannabis

International interlaboratory study on cannabis oil

Worldwide, governments are dealing with a wave of public interest in cannabis oil products. The legal status of these products varies significantly from country to country depending on how laws governing controlled substances and access to cannabis for different purposes are written. Canada can be regarded as an international leader in regulation of cannabis products since it is one of few jurisdictions where cannabis products can be massively produced legally, and are subject to defined quality requirements. Canada is the second country in the world and the first G20 country to have legalized cannabis for recreational purposes nationwide. Health Canada's mandate is to promote and protect the health of Canadians through leadership, partnership, innovation and action in public health. Health Canada's Health Products Laboratory Program led an international laboratory study for testing of Cannabis Oil products. The goal of this study is to conduct an inter-laboratory testing of a common set of cannabis oil products (provided by reputable legal Canadian producers) using the participants' analytical method of choice to quantify the total levels of tetrahydrocannabinol (THC) and cannabidiol (CBD) in order to verify if results are comparable and to detect trends. Ten laboratories from various countries including Canada, the USA, Singapore, Swiss, Australia and United Kingdom participated in the study. Since Canadian cannabis oil products were sent to participants, this study will also assist foreign participants to better understand the labelling requirements for these products in Canada. Participants will have the opportunity to rigorously prove their capacity and readiness in cannabis testing, e.g. for accreditation purposes. (PI : Justin Morin)

Rapid identification of visible foreign matter by FTIR spectroscopy

One of Health Canada's microbiology laboratory mandates is to evaluate the foreign matter found in health products and cannabis for the safety of Canadians. Currently, the identification of visible foreign

matter relies on microscopic observation, where the result is often inconclusive due to limitations of visual inspection. In order to improve the efficiency and accuracy of visible foreign matter identification, a novel method was developed: rapid identification of visible foreign matter by Fourier-transform infrared (FTIR) spectroscopy. This spectroscopic method obtains the unique spectrum of a sample (foreign matter) by illuminating it with a light source (infrared). Foreign matter absorbs the specific amount of energy from the light source, which is used to vibrate its unique chemical structures. Because no two different materials have the same chemical structure, a FTIR spectrum of a foreign matter is considered its fingerprint. The identity of foreign matter is then predicted within a few minutes by comparing its unique spectrum against the reference spectral database. This work included customization of the research-grade spectra analysis software into that of a "one-click, user-friendly" approach with an aim to offer a technique that no longer requires a highly trained specialist. This method provides a consistent and accurate identification of visible foreign matter in health products and cannabis within a few days. This project is funded under the Deputy Minister's Solutions Fund in support of the pharmaceutical drugs, natural health products and cannabis departmental priorities. (PI : Hayline Kim)

Validation of a rapid method for the enumeration of microorganisms in dried cannabis

One of Health Canada's mandates is to ensure that legally sold cannabis complies with cannabis regulations in terms of its microbial content. In order to be able to verify the compliance of these products, microbiological analyses are carried out. According to our service standard, results must be issued within a maximum of 21 days. The classical microbiological method used routinely in the laboratory for microbial enumeration is very time consuming and requires a lot of material. To shorten the analysis time and improve the service standard, a study was conducted to validate an automated enumeration method developed by BioMérieux for food products using a specialized device, the TEMPO. A first study was carried out on 30 dried cannabis samples to compare the results of the TEMPO with the plate enumeration method of the European Pharmacopoeia (Ph.Eur. 2.6.31) currently in use. The results demonstrated a significant difference between the two methods. It was suspected that the difference was related to the incubation time which is very different between the two methods. This led to a second study to verify this assumption. To date, a pre-study assessing the effect of incubation time on bacterial count by the automated TEMPO method has been performed. The results obtained are encouraging and a second validation study with new parameters is in preparation. The HC's Microbiology laboratory receives funds for the cannabis departmental priority. (PI : Jamile Ahmarani)

Climate Change

A qualitative and quantitative evaluation report on the Alberta Real Time Surveillance System Network (ARTSSN)

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. The evaluation of the ARTSSN completed in October of 2020 by Alberta Health Services, was the second evaluationof existing real-time syndromic surveillance systems.The purpose was to identify the key components for an effective, comprehensive real-time surveillance system to assess the health impacts of climate change. The outputs from this research, in combination with reports from previous studies, will directly address program activities Health Canada is

required to deliver on as written in the treasury board submission approved in 2016, Adapting to Climate Change Impacts. Specifically, these will inform Health Canada in the development of Pan-Canadian national monitoring and surveillance activities and provide guidance as Health Canada works with provincial and territorial partners to expand the availability of systems that collect real-time data about climate-related health issues and the public health information management systems that support them. (PI: Victor Gallant)

Building sustainable health systems: focus on climate resilience (1)

Climate change affects health through a range of pathways, including increasing frequency and intensity of hazardous extreme weather events, altering transmission of water-borne and vector-borne disease, and undermining the environmental and social determinants of health such as the quality and quantity of freshwater supplies, and of food. It therefore places stress on the infrastructure, management systems and capacity of health systems. Health Canada and the World Health Organization (WHO) have collaborated on climate change and health for approximately 20 years, resulting in publications, webinars and activities that continue to assist health authorities globally and across Canada in their efforts to prepare for the health impacts of climate change. This multi-year project will investigate and develop

1. Tools for assessing climate change vulnerability of healthcare facilities;
2. Targeted guidance for prioritization of available health adaptation options, and indicators for measuring overall health system resilience; and
3. A framework for monitoring and surveillance of climate-sensitive diseases.

Results of this research and guideline development will advance efforts to promote health system resilience to climate change around the world. (PI: Rebekka Schnitter).

Building sustainable health systems: focus on climate resilience (2)

The connections between health, economics and climate action have been less explored in policy and practice. Limited information on climate change's economic costs and stresses to health systems challenges attempts to develop climate resiliency in the health sector and to scale-up near term and longer term adaptation investments. Through this project, the World Health Organization (WHO) seeks to collaborate with economists to guide the health sector and the climate community in better understanding the economic costs and health gains and savings relating to climate change action and/or inaction. Taking action on climate change carries significant health, social and economic implications. These include benefits from the reduced risk to human health that result from adaptation to global warming, and the large health gains that can be achieved by actions that reduce greenhouse gas emissions and improve air quality. Health gains can be assigned an economic value. The social benefits of climate change can be set against the economic costs of policy interventions. Through this project, the WHO seeks to develop a more coherent approach to health, economics and climate change and a higher priority for health in climate change mitigation and adaptation policy by providing a clear common understanding of how these considerations should be jointly assessed. This will include the development of an overall health, climate change and economic framework. The organization also aims to review existing tools for health, climate and economic assessment to assist in improving global practice in selecting health adaptation options, and in promoting actions that improve health outcomes and climate change mitigation. Finally, executing a policy simulation exercise will contribute to an improvement in the global practice of analyzing the health, economic and climate change implications. (PI: Victor Gallant).

CanTEMP: National temperature-related excess mortality and morbidity estimates

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. This includes monitoring the heat-related health impacts in Canada (per 100 000 people) every 3 years, with a baseline established by the end of fiscal year 2021-2022. This project aims to establish baseline risk estimates for climate-related illness and death in Canada by cities and health regions, and project future temperature-related mortality and morbidity risk under different climate change scenarios. Mortality data will come from the Canadian Vital Statistics-Death Database for 1986 to 2015, and the morbidity data will be available from the Discharge Abstract Database for 1994 to 2015. This research takes into account demographic changes through projections made by Statistics Canada with weather data obtained from weather stations in the different cities and health regions. Investigators will obtain modeled daily temperature series for 1990-2099 for each city and health region, from five Global Circulation Models (GCM), under each Representative Concentration Pathway (RCP) and will compute health impacts by estimating exposure-response relationships between observed daily temperature and daily mortality and morbidity counts in each city and health region. The excess mortality and morbidity (with a sub-analysis investigating cause-specific mortality and morbidity, and analyses by sex and socioeconomic factors where available) for each GCM/RCP combination will subsequently be projected. This study will offer a comprehensive characterization of climate change impacts due to changes in exposure to non-optimal outdoor temperature, across various regions in Canada, and under alternative scenarios of global warming. (PI: Chris Hebbern; Éric Lavigne)

Climate change and heat vulnerabilities of Canadian workers: Focus on central and western provinces of Canada

Increases in temperature and the number of extreme heat events have been identified as key issues related to climate change for workers in Canada. Studies conducted in Quebec have highlighted that the daily compensation of workers for health problems related to excessive exposure to heat and for traumatic work-related injuries increases with outdoor temperatures in the summer. These associations have never been evaluated elsewhere in Canada and the impacts of a warming climate on these claims have not been studied in Quebec or in other Canadian provinces. This project aimed to establish associations between the summer outdoor temperatures in five provinces (Ontario, Quebec, Manitoba, Saskatchewan, and Alberta) and the compensated occupational health problems related to overexposure to heat and associated traumatic work-related injuries. In addition, it aimed to estimate the health impacts of climate warming by calculating the change in such compensation by 2050. The project, conducted by the Institut national de santé publique du Québec, was completed in November 2020. (Collaborator: Peter Berry; Monique D'Amour)

Economic analysis of climate change impacts on health and on the health system: An overview

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Although climate change could affect some countries and regions more than others, all countries are expected to be affected. The objective of this project is to provide a targeted, evidence-based (where data are available) overview of the literature published between 2000 and 2019 linked to climate change and climate-related health impacts and their attributed costs in Canada and elsewhere. This project is a first step in addressing the need to better understand increased costs on the health system (the need for costing of these impacts was identified as a priority at a February 2018 Experts Meeting on Climate Change and Health Monitoring and Surveillance that was hosted by Health Canada, as well as by HealthADAPT G&C recipients in March 2019). The report will serve as an informational tool to increase the awareness of public health officials,

planners, decision makers, and other stakeholders of the costs that climate change could pose to human health and the health system. The analysis, impacts, methods and data identified in this project may be used to inform the conduct of an in-house economic cost-benefit analysis in the future. (PI:Victor Gallant; Modjgan Alishahi, PhD Student)

Establishing evidence-based indoor temperature thresholds to protect health

Extreme heat is a major health risk in Canada resulting in a significant number of preventable illnesses and deaths annually, and is only expected to increase in severity, frequency and duration due to the changing climate. Most heat-related fatalities occur indoors where Canadians, especially vulnerable people like the elderly and the chronically ill, spend most of their time. The aim of this research is to establish evidence-based indoor temperature guidance in support of Health Canada's role in reducing negative health impacts of climate change. In 2018, the Climate Change and Innovation Bureau funded a review authored by Dr. Glen P. Kenny (University of Ottawa) that identified a need to improve understanding of how the human body responds to heat stress indoors, especially in at-risk populations. Physiological experiments are now underway to assess how individuals respond to a range of temperatures which will help determine indoor temperature conditions that are potentially dangerous for human health. This laboratory-based research was launched in early 2019 for older adults (65 to 80 years old), who have a reduced ability to adapt to heat and are therefore a population of concern. In 2019, preliminary field observations were completed for children and adolescents (10-14 years old), another population of concern. Data gathering and further literature reviews were completed as a means of building the evidence-base for this project, including for children and other potential vulnerable populations. These reviews have been completed and have been published in 2020. A final report is expected to be completed in the winter of 2022 and the results will be used in developing guidance needed to better protect Canadian health from heat risks indoors. (PI: Victor Gallant; Kerri Warner)

Extreme weather and climate change: population health and health system

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Extreme weather and disasters are among the most severe threats of climate change facing Canadians in the future. Climate change is expected to increase the frequency and severity of a number of natural hazards including extreme heat events, floods, wildfires, droughts, ice storms, and tornadoes. To inform the development of effective adaptation measures from local to national levels in Canada, greater information on links between meteorological, hydrological and climate hazards and health, including key drivers of vulnerability are needed. This research project will provide information on the latest scientific research on extreme weather in a changing climate and implications for population health and health system implications. This study was published in 2021. (PI: Peter Berry)

Greening for growth: an economic estimate of the health benefits of exposure to green spaces

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. This research project led by the Institut national de santé publique du Québec, aims to quantify certain socio-economic benefits linked to the use of green spaces in urban areas, as a tool for adapting to the challenges posed by climate change. There is currently little information on this subject worldwide. The project will focus on the main urban areas of Quebec, working to develop a methodology that can be generalized to other comparable cities here and elsewhere (other provinces of Canada, USA, etc.) in the future. The main objective of the research

project is to quantitatively document the impact of green spaces on human health and their potential for adaptation to climate change. To do this, the study will carry out a systematic review of the scientific literature on the subject, and a web survey on exposure to urban green spaces in Quebec and their use in several contexts. Next, the research project will quantify the economic benefits resulting from the current use and future establishment of additional green spaces in urban areas. It is hypothesized that these benefits will stem from the potential reduction in health costs and the improvement of future resilience in adaptation to climate change. Finally, the researchers plan to prepare recommendations for applying the quantification methodology across Canada and comparable territories. These recommendations will relate to the methodological framework, the available data, the harmonization of the parameters to be used, and the conditions for their use. (Collaborator: Monique D'Amour; Victor Gallant; Modjgan Alishahi).

Health of Canadians in a changing climate: Advancing our knowledge for action 2021

The Government of Canada is preparing a series of resources about how Canada's climate is changing. The Climate Change and Innovation Bureau (CCIB) at Health Canada is taking the lead along with a range of governmental and non-governmental partners. The development of the next climate change and health assessment that will be part of the Government of Canada Climate Change Impacts and Adaptation Knowledge Assessment to be released in 2021. This report will build on the two previous climate change and health assessments, delivered in 2008 and 2014. The objective of the assessment is to present new knowledge about climate change impacts on the health of Canadians, populations of highest concern and vulnerable regions to inform effective actions by health sector decision makers to protect health. Through consultation with partners and input from individual Canadians the resulting report, *Canada in a Changing Climate: Advancing our Knowledge for Action* will:

- Examine climate change impacts on the health of Canadians;
- Explore climate change impacts to the health system; and,
- Investigate measures to effectively adapt to a changing climate and reduce future climate change

The final assessment is expected to be released in 2021. (PI: Peter Berry)

HealthADAPT lessons learned research initiative

The HealthADAPT Program is a multi-year capacity building program introduced in 2018 to help the Canadian health sector prepare for and respond to the health impacts of climate change. The Program supports the development, testing and implementation of local and regional climate change health adaptation plans and aims to increase understanding of the impact of climate change on health systems, the health of Canadians and communities potentially at higher risk. The Program launched a call for proposals in 2018 and currently funds 10 health authorities across 5 provinces and territories until March 2022. The objective of the HealthADAPT Lessons Learned Research Initiative is to provide health authorities in Canada with practical guidance on how to address climate-driven health risks within their jurisdictions, with a specific emphasis on how to get started on a climate change and health vulnerability and adaptation (V&A) assessment. This research initiative will include: surveys with HealthADAPT funding recipients to evaluate their experiences with the program, and surveys with Canadian health authorities who have not conducted climate change and health V&As to better understand any barriers to getting started. Additionally, this research will include: key informant interviews with all HealthADAPT funding recipients to understand any challenges and opportunities they experienced getting started on their projects, and key informant interview with climate change and health experts who support health authorities with climate change and health V&As. This research will inform a guidance document that

will provide an overview of lessons learned from the HealthADAPT Program. The production and distribution of this guidance document will support the HealthADAPT Program's overarching aim of building capacity among health authorities across in Canada to prepare for and respond to the impacts of climate change. (PI: Katie Hayes)

Improving the identification of heat associated deaths in Canada: Estimating the effectiveness of medical attendance at the place of death and implications for Heat Alert and Response Systems (HARS) (Health Canada – British Columbia Centre for Disease Control MOA, 2019-21)

One of the mandates of the Climate Change and Innovation Bureau, in relation to heat hazard, is to improve the estimation of the health risks of heat. In many locations, heat associated mortality is greatly under-estimated and there are wide variances in heat-associated death estimates between jurisdictions for the same heat event. It is unclear if these differences reflect true differences or different approaches to estimation. By identifying all indirect and direct heat-associated deaths and when, where and why these deaths happen, effective and appropriate risk communication approaches and risk management actions can be informed. In 2016, the British Columbia Centre for Disease Control (BC CDC) published a unique methodology (https://doi.org/10.1186/s12940-016-0195-z) for identifying deaths associated with heat that may have otherwise been missed in traditional reports of coroners and other surveillance sources. In collaboration with local and provincial health authorities, BC CDC is examining the mortality data from past heat events and control periods in Ontario and Quebec to apply this framework. This research study will compare results from current and new methodologies to assess differenecs in deaths attributed to hot weather across jurisdictions. The results will be used to inform development of a more cohesive Canadian approach. (Collaborator: Rebecca Stranberg)

Investigation of the conditions for thermally comfortable playgrounds in Canada

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Planning and designing thermally comfortable outdoor spaces is increasingly important in the context of climate change, particularly as children are more vulnerable than adults to environmental extremes. Playground infrastructure can present some of the highest surface temperatures within an urban area and can result in unsafe heat exposure and heat-related injuries. In Canada, existing playground standards focus on equipment and surfacing to reduce trip- and fall- related injuries, but have not addressed environmental factors affecting unsafe exposure and heat stress. In partnership with the Standards Council of Canada, the goal of this project was to develop proposed guidelines for designing thermally comfortable playgrounds in Canada, for inclusion within the CAN/CSA-Z614 Children's play spaces and equipment standard. To that end, the project team conducted a detailed literature review of relevant research, standards, and design practices, conducted a needs assessment survey with a broad range of Canadian and international experts and stakeholders, and produced recommendations for an informative thermal comfort annex. This project has resulted in several important outcomes. First, the project team produced a report with design advice for improving thermal comfort at playgrounds across Canada. Second, the Canadian Standards Association has approved a six page annex with similar guidance. Third, an NGO has integrated "thermal comfort" considerations into their national school ground greening design competition. Thermally safe and comfortable play spaces will help ensure that Canada's playgrounds are designed to minimize environmental health risks for children. A summary of this work was published in the Canadian Journal of Public Health in 2021. (PI: Alexandra Rutledge; Gregory Richardson)

Potential impacts of climate change on human health risk assessments of contaminated sites in Canada (March 2021)

Health Canada has a mandate under the Federal Contaminated Sites Action Plan (FCSAP) program to provide expert scientific risk assessment/mitigation advice, technical training and other tools to assist federal custodian departments in assessing and managing human health risks for their contaminated sites. Currently, there is no guidance that specifies how Climate Change (CC) should be taken into account in the context of a Human Health Risk Assessment (HHRA). This project documented the current state of knowledge on CC considerations within the scope of an HHRA. Specific objectives included the identification of CC associated events and processes that can affect the components of HHRAs including exposure and toxicity assessments, and risk characterization of chemicals of potential concerns (COPCs). COPCs including arsenic (As), cadmium (Cd), lead (Pb), mercury (Hg), per- and polyfluoroalkyl substances (PFAS), and petroleum hydrocarbons (PHC) were used to evaluate whether the influence of CC can be incorporated into the existing HHRA framework. It is important to understand both chemical and non-chemical related human health impacts. New approaches (e.g. Adverse Outcome Pathway) that integrate the combined effects of chemical exposure and climate change are being developed for possible use in the HHRAs. The scoping review identified many data and knowledge gaps. For risk characterization, a cumulative assessment appears to appropriately address the effects of chemical and non-chemical stressors. Further evaluation of these models were recommended. The magnitude of the effect of climate change on the dose-response is not exactly known. Furthermore, a lack of methodologies were identified that can integrate the health risk associated with the direct and indirect effects of climate change. A number of follow up studies on cumulative models, receptor characterization and additional evaluation of exposure and toxicity assessments related to contaminated sites risk management were recommended. (PI: Asish Mohapatra; Dr. Laurie Chan (University of Ottawa) in association with Canada North Environmental Services Ontario)

Public perceptions of the health impacts of climate change in Canada, 2021/22

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. In order to develop effective information tools that will protect the health of Canadians from the impacts of climate change, it is important to understand their current level of awareness. This includes understanding their perceptions of climate change-related health risks as well as their knowledge of the issues affecting them now and into the future. Health Canada's Climate Change Performance Information Profile requires updated public opinion research (POR) information every 5 years. The Department undertook POR in 2008 and 2017 and therefore the next update is required by the end of March 2022. Planning for this POR survey began in 2020. In consultation with internal and external stakeholders a review of the previous POR survey questionnaires was carried out to identify those questions that remain relevant and which should be kept for the upcoming POR. The updated POR survey will also include questions related to emerging issues, such as the mental health impacts of climate change. This update will determine how public awareness and understanding of climate change has changed since 2017 and may help the department create more effective public health communication campaigns surrounding its information and training programs aimed at protecting the health of Canadians from climate change related impacts. The project is linked to Health Canada's Climate Change Program, which seeks to increase the level of awareness among Canadians of extreme heat health risks and other climate change hazards. Information on climate change, health risks and health protection advice is provided to the general public. (PI: Lubna Salman)

Urban trees and human health outcomes: A scoping review

The urban forest is a green infrastructure system that delivers multiple environmental, economic, social and health services, and functions in cities. Environmental benefits of urban trees are well understood, but no review to date has examined how urban trees affect human health. This review provides a comprehensive summary of existing literature on the health impacts of urban trees that can inform future research, policy, and nature-based public health interventions. A systematic search used keywords representing human health, environmental health, and urban forestry. Following screening and appraisal of several thousand articles, 201 studies were conceptually sorted into a three-part framework. Reducing Harm, representing 41% of studies, includes topics such as air pollution, ultraviolet radiation, heat exposure, and pollen. Restoring Capacities, at 31%, includes attention restoration, mental health, stress reduction, and clinical outcomes. Building Capacities, at 28%, includes topics such as birth outcomes, active living, and weight status. The studies that were reviewed show substantial heterogeneity in purpose and method yet indicate important health outcomes associated with people's exposure to trees. This review will help inform future research and practice, and demonstrates why urban forest planning and management should strategically promote trees as a social determinant of public health. This review was published in June 2020 and includes a list of 198 references as supplementary materials. (PI: Gregory Richardson)

Consumer Product Safety

DEET usage study

Health Canada helps to protect the health of Canadians by assessing and managing the risks associated with exposure to environmental chemicals. DEET is the common name for N,N-Diethyl-m-toluamide, an active ingredient in personal insect repellents approved by Health Canada for use by children and adults. DEET helps protect against mosquito, blackfly and tick bites. The purpose of this study is to generate biomonitoring data from DEET used by children in a camp setting. Following parental consent, about 125 children aged 7 to 13 years participating in overnight camps and who are already planning to use DEET were recruited. Urine samples were gathered over the course of one 24-hour day in the camp setting and analysed to determine the amount of DEET and two metabolites in the body. The study, which complements other studies by Health Canada that measure chemical exposures in children from typical use, will provide a better understanding of Canadian children's exposure to DEET and inform any future recommendations. (PI: Jennifer Gibson; Kim Irwin)

Dermal absorption of flame retardants in a survey of consumer products

The Chemicals Management Plan (CMP) is a Government of Canada initiative aimed at reducing the risks posed by chemicals to Canadians and their environment. Organic flame retardants were among the chemicals identified as priorities for action in the second and third phases of CMP. In 2019-20, in order to support risk assessment and risk management strategies for flame retardants, the Product Safety Laboratory (PSL) tested a series of polymeric foam consumer products for the total concentration of five flame retardants: tris(1-chloro-2-propyl)phosphate (TCPP), tris(1,3-dichloro-2-propyl) phosphate (TDCPP), 1,3,5-Triazine-2,4,6-triamine (melamine), triethyl phosphate (TEP), and isopropylphenyl phosphate (IPPP). The current project expands on the work from 2019-20, by examining the dermal absorption of TEP, IPPP, and melamine using a simulated sweat system. PSL developed and validated test methods for the dermal absorption of TEP, IPPP and melamine, and tested a subset of consumer products from the 2019-20 project. A total of 27 specimens were tested for the dermal absorption of melamine, and 30 specimens were tested for the dermal absorption of TEP and IPPP. In addition to

dermal absorption, this project examined loss of flame retardant concentration over time in storage, by testing the identified subset of consumer products for total concentration following 20 months in storage. The dataset generated from this project will further support risk assessment and risk management strategies for TEP, IPPP and melamine. (PI: Nathalie Ritchot; Katrina Griffiths)

Development of a high throughput chamber test method for the determination of semi-volatile organic compounds from consumer products

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Consumer products are major indoor sources of many chemicals including semi-volatile organic compounds (SVOCs) such as plasticizers and flame retardants. SVOCs in these products can enter indoor environments through evaporation if they are not chemically bound to the materials. The rate of evaporation, also called emission rate, is a critical piece of information in estimating SVOC levels indoors in order to assess human exposure to SVOCs from products. Due to relatively low vapour pressure and great tendency to be absorbed on surface materials, emission rates of SVOCs are difficult to measure using traditional environmental chamber tests. Further, when temperature increases, the emission rate also increases and desorption tendency decreases. The relationship between temperature and emission rates can be established through an empirical model. This project uses chamber tests at elevated temperatures to develop high-throughput methods to generate emission rates of selected bulk SVOCs, including plasticizers and flame retardants, and of SVOC-containing products. The emission rates are then used to predict levels of SVOCs in indoor air as a result of using SVOC-containing products indoors through available indoor air fate models. Prediction of SVOC levels in indoor air will support human exposure assessment and development of indoor air policies and guidelines. (PI: Jiping Zhu)

Development of methodology for home dust microbiome analysis towards Canadian exposure assessments of biotechnology microbes

Health Canada assesses and manages risks of biotechnology microorganisms under CEPA (Canadian Environmental Protection Act, 1999). The scope of management includes microorganisms on the Domestic Substance List (DSL) that are contained as active ingredients in some types of microbe-based cleaning products (MBCPs). These products are used as alternatives, or additives, to chemicals-based cleaners and likely contribute to the biomass found in house dust. The exposure patterns of MBCPs in home environments are unknown and without this information, risk cannot be accurately evaluated. In recent years, initiatives have taken place to analyze Canadian house dust ((Canadian House Dust Survey and Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort study)) and these initiatives have helped provide an understanding of Canadian house dust composition. This project examines metagenomic DNA extracted from dust samples from Canadian homes in order to inform the assessment of MBCPs derived from biotechnology microbes. Metagenomic DNA analysis is necessary because microbial cultivation methods can only support the growth of a fraction of microbial flora. The overall objectives are to develop methodology for estimation of DSL microbial presence in house dust and provide insight into the microbial content of homes where MBCPs are used, versus those homes where chemicals-based cleaning products are used. (PI: Phil Shwed)

Development of methods for identification and hazard assessment of biotechnology-related microorganisms: Assessment of virulence of opportunistic human pathogens in microbial mixtures

Microorganisms formulated as heterogeneous mixtures (i.e., microbial mixtures, consortia) must undergo a detailed screening for human pathogenicity and environmental impact by manufacturers. Under current regulations, each microorganism within the mixture must be screened separately which can be costly and time-consuming. Towards understanding if pathogenic characteristics would be masked in mixtures of microorganisms compared to pure cultures, this project aims to compare virulence characteristics (e.g., growth temperature, antibiotic resistance, cellular toxicity) of several known pathogens in pure cultures compared to within a mixture of microorganisms used in biotechnology. The goal is to develop and adapt methods so that they can be applied to any type of heterogeneous microbial mixture being considered for commercial biotechnology applications. (PI: Azam Tayabali)

Development of pathogenicity test methods for assessing the hazard of microorganisms used in biotechnology

Microorganisms routinely used in biotechnology for industrial (e.g., biofuel production), consumer (e.g., cleaning products), or emerging applications (e.g., synthetic biology) can be related to those capable of causing infections, especially in people with compromised immunity. Pathogens that can infect people with compromised immune systems are known as opportunistic pathogens. These opportunistic pathogens may share traits with biotechnology-related microbes, which could be a serious problem for risk management. Therefore, it is critical that reliable pathogenicity testing protocols are established to ensure that risk assessments are carried out with the best available data. This project will develop clear, stepwise methods to test the pathogenicity of new microorganisms considered for biotechnology applications. Standardized pathogenicity laboratory methods for opportunistic pathogens do not currently exist, but are needed in order to reduce the regulatory burden associated with non-standardized industry submissions. These methods will enable regulators to guide the biotechnology industry when they notify Health Canada of new microorganisms to be imported into or manufactured in Canada. Examples of these novel methods are advanced intercellular communication toxicity assays, simultaneously screening for multiple indicators of toxicity, and methods to eventually eliminate the need for animal testing. Ultimately, microbial test methods and new laboratory models will greatly advance science-based decision-making for regulators/evaluators, ensure risk assessments take into consideration the most sensitive people in our population, and ultimately result in safer biotechnology products available to the consumer. (PI: Azam Tayabali)

Environmental concentration of veterinary and human drug substances in surface water

The *Food and Drugs Act* (F&DA) Substances Assessment Division within the New Substances Assessment and Control Bureau has been established to conduct assessments of the potential environmental and health risk to the general population associated with environmental exposure to substances in F&DA products such as human drugs, biologics, veterinary drugs, cosmetics, novel foods, food additives, natural health products and medical devices. The goals of this research project were to: (a) develop and validate additional methodologies required to analyze a panel of drug substances; and (b) characterize environmental concentrations of 16 R-ICL (Revised In Commerce List) drug substances used in high volume in Canada from sites impacted by agricultural activities and waste water treatment plant (WWTP) effluents across six watersheds in Ontario/Quebec. A total of 228 water samples were analyzed by Liquid Chromatography Mass Spectroscopy (LC-MS), resulting in detections for 11 of the 16 compounds. Venlafaxine was the most detected with 158 hits, while tazobactam and fluvoxamine were

only reported from 2 and 1 sites, respectively. Although only detected in 34 surface water samples, guanylurea, the breakdown product of metformin, was detected in the highest concentrations. These data will be used directly in the environmental assessments of substances listed on the Revised In Commerce List and new substances in products regulated by the F&DA notified under the New Substances Notification Regulations of the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Dianne Hughes; Jean Grundy)

Identification of unknown substances in e-cigarette refill fluids and vapors

Electronic vaping products (EVPs), or e-cigarettes, are battery powered devices that are used to create an aerosol which is inhaled by the user. EVPs are used by hundreds of thousands of Canadians to obtain nicotine. An aerosol is created from a liquid, known as e-liquid, that is housed in a tank or cartridge and usually consists of propylene glycol, glycerol, nicotine, and various flavorings. When used, the devices vaporize the e-liquid by way of a heating element or coil, housed in an atomizer. This vapor then quickly condenses into an aerosol that is inhaled. Many of the substances found in e-liquids, as part of a review conducted by Health Canada's Tobacco Control - Office of Research and Surveillance (ORS), are well-known harmful chemicals also found in tobacco. However, very little is known on the full composition of the thousands of e-liquid formulations available on the Canadian market. The objective of this study is to build Health Canada's capacity in the analysis of complex mixtures of e-liquids. The results of the open characterization will complement the existing body of knowledge on components of e-liquids. It will also support decision making and regulatory activities in providing TORS with data on the chemical composition of electronic cigarettes refill fluids and their aerosols, from products available in the Canadian market. (PI: Cariton Kubwabo)

In vitro toxicity screening of nanoforms of zinc oxide

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. Engineered nanomaterials (NMs) including nanoforms of zinc oxides (ZnO) are incorporated into various consumer products. Nano zinc oxide, for instance, has wide ranging applications in paints, coatings, building materials, antibacterial agents, sunscreens, moisturizers, food packaging, etc. These NMs thus can have human health implications and furthermore are problematic in terms of hazard identification and risk evaluation due to lack of reliable physico-chemical and toxicity data, creating a challenge for government agencies towards establishing effective hazard evaluation guidelines. The recent data gap analysis of nanoscale forms of substances on the Domestic Substances List (DSL) of the New Substances Assessment and Control Bureau (NSACB) of Health Canada has identified the nano ZnO (CAS RN 1314-13-2) as one of the 53 nanomaterials in commerce in Canada under the CMP that requires information to help tailor assessment and management approaches. This work is designed to conduct *in vitro* cytotoxicity screening of nano-zinc oxide forms in two types of lung cells to determine their relative toxicities, using various toxicity testing approaches. Oxidative stress changes and secreted proteins were measured to gain information on toxicity pathways. In addition, association between nano ZnO potencies and their physico-chemical properties is also studied. Toxicity information obtained from this work will support advance the risk assessment processes by NSACB will also support Health Canada’s commitments to the Organisation for Economic Cooperation and Development (OECD)- Working Party on Manufactured Nanomaterials (WPMN). (PI: Premkumari Kumarathasan; Azam Tayabali)

Increases in exposure calls related to selected cleaners and disinfectants at the onset of the COVID-19 pandemic: data from Canadian poison centres

The Canadian Surveillance System for Poison Information (CSSPI) led by Health Canada is a developing network of poison centres, health authorities and regulatory agencies that facilitates early detection of poisoning incidents and alerting at the national level to inform harm reduction interventions. In response to the COVID-19 pandemic, concerns were raised over the potential for misuse of cleaning products and disinfectants; the CSSPI network monitored and assessed these concerns. An overall increase in calls about select cleaning products and disinfectants occurred concurrently with the pandemic, with percentage increases for selected products as high as 400% compared to the same period in the previous year. (PI: Abdool Yasseen)

Portable automated biosensing of potential dual-use biological threats to critical water systems (DRDC-CSSP)

New genetic engineering and synthetic biology technologies are generating unknown threats that need to be assessed and countered. This project aims to advance a biological sensor to detect specific bacteria (*Bacillus* species) commonly used in biotechnology applications, but that could be manipulated to function as agents of bioterrorism. These bacteria are termed 'dual-use' because of their capacity to be used for both beneficial and malicious activities. The proposed device is envisaged to be physically linked to water systems (e.g., potable water supplies, dams, pipelines, treatment plants, and recreational sites), and repeatedly (i.e., daily) concentrate and sample bacteria without user intervention. This project also aims to provide fundamental knowledge on the pathogenic potential of bacteria used in biotechnology applications. This will be done by developing a method to mimic an infectious mechanism shared by close relatives of the known biological threat, *Bacillus anthracis*, which is the etiological agent of anthrax. More specifically, *Bacillus anthracis* infects specific white blood cells called macrophages, so testing whether other biotechnology bacteria can infect macrophages will provide a functional method to assess pathogenicity. Furthermore, this project will investigate whether biotechnology-related *Bacillus* species can be detected in natural surface waters. Ultimately, the project aims to develop an innovative biological sensor for automated detection of potential dual-use Bacillus strains, and generate important information on the pathogenic potential and environmental occurrence of biotechnology-related *Bacillus* species that are close relatives to known human pathogens. (PI: Azam Tayabali)

Controlled Substances

Addition of benzodiazepines to opioid identification method by ultra performance liquid chromatography coupled with quadrupole time of flight high resolution mass spectrometry (UPLC-QToF HR MS^E)

The mandate of Health Canada's Drug Analysis Service (DAS) laboratory is to identify controlled substances to support public safety and law enforcement. Benzodiazepines are a class of drugs that are among the highest prescribed in the pharmaceutical market. Recent trends in seized drugs indicate the addition of new designer benzodiazepines that are often mixed with other harmful drugs, such as opioids. Since Benzodiazepines are potent abused drugs and studies have shown there are increased risks with its dependence and withdrawal, the detection of such compounds is crucial in the protection of the health of Canadians. Historically in DAS, the methods used to detect benzodiazepines required extra work with labor intensive extractions using less sensitive instrumentation. Therefore, the creation of a new analytical method to detect and certify these compounds in an accurate and efficient manner

was required. This project, led by the DAS Laboratory, aims to correctly detect and identify these compounds using highly sensitive instrumentation: Time of Flight Mass Spectrometry. Through the addition of benzodiazepines to the scope of the previously validated opioid identification method by UPLC-QToF HR MS^E, these analytes can be quickly and effectively reported. The overall process required to certify these compounds is now simplified and more samples can be accurately analyzed in a shorter amount of time. The DAS is funded under the Canadian Drugs and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI : Stephanie Dubland)

Collaborative harm reduction initiative between Health Canada and British Columbia Centre on Substance Use for accurate community based drug checking

In British Columbia, where nearly 90% of opioid overdoses occur indoors, making it difficult for first responders to respond, the implementation of drug checking programs has had a positive impact. A pilot project was implemented to check the contents of street drugs in British Columbia using methods that could be used in point-of-care facilities, enabling clients to have their drugs tested in real-time and providing an opportunity for immediate feedback in the community. Health Canada's Drug Analysis Service (DAS) and British Columbia Centre on Substance Use (BCCSU) have worked together to better understand gaps in detection of the FTIR and test strip method used in the community. Where gaps are identified, other methods for detection have been explored. Current gaps in community detection include carfentanil, etizolam, synthetic cannabinoids and potent benzodiazepines. A quantitative Nuclear Magnetic Resonance method for opioids has been used to provide relative % composition of the components in street drug mixtures. In addition, other sensitive techniques including a Liquid Chromatographic Mass Spectrometry assay of the opioid(s) and potent benzodiazepine mixtures are also performed where needed for dilute mixtures. As of July 2021, 13 knowledge products have been published or accepted and 5 more manuscripts are in preparation based on data from this collaborative agreement. The DAS is funded under the Canadian Drugs and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI : Richard Laing)

d,l-Methamphetamine survey in looking for synthesis route specific information

The Drug Analysis Service's (DAS) mandate is to provide quality scientific and technical services to assist with the enforcement of the Controlled Drugs and Substances Act and Regulations. For forensic intelligence purposes, analysis residues from methamphetamine samples were analyzed by the DAS to obtain further chemical profiling information. While both methamphetamine enantiomers (*d* and *l*) are scheduled in Canada under the Controlled Drugs and Substances Act (CDSA), the distinction between the two enantiomers has important implication for law enforcement in monitoring trends associated with methamphetamine manufacturing, specifically synthetic routes and precursors used. It is hypothesized that the ban on precursor pseudoephedrine and ephedrine by Canada, US and Mexico drove illicit producers to use phenyl-2-propanone (P2P) process in Mexico, while in Canada access to health product supplements and decongestants has permitted a steady domestic supply. Samples were quantitated using an internal standard solution containing maleic acid in deuterated water. To differentiate between the two enantiomers, NMR experiments were performed under a chiral environment by using chiral resolving reagent (R)-(+)-1,1'-bi(2-naphthol) or BINOL. All the sample residuals were found to be *d*-methamphetamine. These results are consistent with methamphetamine profiling reports from the U.S. Drug Enforcement Agency (DEA) special testing laboratory. Presently, DAS is unable to differentiate the source of the *d*-methamphetamine produced from either the ephedrine method or the enantiomeric enrichment of *d*-methamphetamine from the P2P method, until, if or when, more specific techniques and methods are developed in DAS to achieve this goal. The DAS is funded under the Canadian Drugs

and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI : Richard Laing)

Identification and quantitation of cocaine, heroin, methamphetamine, and MDMA by ultra performance liquid chromatography (UPLC) triple quadrupole mass spectrometry

The Drug Analysis Service's (DAS) mandate is to provide quality scientific and technical services to assist with the enforcement of the Controlled Drugs and Substances Act and Regulations. The level of purity of a drug is important for investigative and sentencing purposes. Previous methods used by DAS focused on the quantitation of one specific compound at a time. This project involves the development of a new method to measure effectively the concentration of cocaine, heroin, methamphetamine and MDMA within an exhibit. Besides simultaneous quantitation of multiple drugs of interest, the method utilizes a Triple Quadruple Mass Spectrometer, an instrument that is able to identify accurately compounds at low concentrations. Statistics of seized drug exhibits show that there is a trend towards the mixing of drugs. Unlike in research environments, where samples are relatively pure or mixed in simple matrices, seized drugs are often present in complicated mixtures. The technology used in the method is able to effectively separate the compounds of interest from complicated mixtures, and accurately identify and measure the individual purity of these compounds. Various testing in the validation phase ensured the applicability of the method to real samples. Since the implementation of the method, it has been applied to a large number of exhibits and is greatly beneficial for the efficient and accurate testing of these compounds. The DAS is funded under the Canadian Drugs and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI : Stephanie Dubland)

Impact of filtering pharmaceutical opiates as a replacement for street opioids during COVID

In March 2020, Vancouver Coastal Health and the British Columbia Centre on Substance Use released a new risk mitigation interim clinical guidance that promotes the prescription of pharmaceutical alternatives to the toxic drug supply as a means of reducing overdose risk. It is suspected that a considerable proportion of those receiving prescribed pharmaceutical alternatives in the form of oral tablets or capsules will likely inject them. As oral formulations of tablets and capsules are intended for ingestion, they contain binders, fillers, coatings, waxes, and dyes that can cause a number of health issues if injected, but there is a lack of published studies on the efficacy of filters prior to injection. The BC Center for Disease Control has approached Health Canada's Drug Analysis Service (DAS) and a study on the effect of filters on the recovery of active ingredients, namely morphine sulfate and hydromorphone hydrochloride, using three different filters and in hot and cold water preparations was carried out. Based on DAS' results, no single approach is consistently better for each formulation. Hot preparation does not consistently produce higher recovery of active ingredient as initially expected. DAS's study is strictly focusing on the effect of filters on the recovery of active ingredients and not on the potential risks that may be associated with the route of administration. It cannot be used to develop guidance on how to reduce harm associated with dissolving and injecting oral pharmaceutical formulations. The DAS is funded under the Canadian Drugs and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI: Richard Laing)

Metformin environmental fate and effects study

The *Food and Drugs Act* (F&DA) Substances Assessment Division within the New Substances Assessment and Control Bureau has been established to conduct assessments of the potential environmental and health risk to the general population associated with environmental exposure to substances in F&DA products such as human drugs, biologics, veterinary drugs, cosmetics, novel foods, food additives, natural health products and medical devices. Currently, one of the most prevalent contaminants is the

type-2 diabetic drug, metformin, prescribed to ~120 million people globally, often detected in the ng-µg/L concentration range in surface waters and wastewater effluents. However, there is very little in the scientific literature describing metformin's fate and effects in the aquatic environment. Recent laboratory research observed significant effects on larval growth and metabolite profiling and a shift in hepatic sex steroid levels were seen in adult medaka. This raised concern regarding metformin's effects on wild fish, but also on its fate and potential effects in the aquatic ecosystem as a whole. To address these concerns, Health Canada partnered with Environment and Climate Change Canada, Aquatic Contaminants Research Division. An 8-week mesocosm study was conducted at the IISD-Experimental Lakes Area to investigate the fate of metformin in the aquatic environment and the effects of the compound on aquatic biota via a food web-analysis. As metformin was fairly stable in the mesocosms, the study was extended to follow degradation of metformin through the fall and winter of 2019 and through the following spring and summer of 2020. In addition to observing the fate of metformin through additional seasons, engineered floating wetlands were deployed in mesocosms to assess their ability to take up metformin, removing it from the aquatic system. These data will be used directly in the environmental assessments of substances listed on the Revised In Commerce List and new substances in products regulated by the F&DA notified under the New Substances Notification Regulations of the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Dianne Hughes; Jean Grundy)

Method validation for the analysis of 14 drugs of concern and metabolites in wastewater

Health Canada has a mandate to reduce the harms to Canadians associated with the use of opioids and other psychoactive substances. Wastewater based epidemiology for drugs of concern and their metabolites is a developing scientific field that allows for establishing temporal and geographical trends for drug consumption. In collaboration with Statistics Canada, a method was validated to measure drugs in wastewater for the Canadian Wastewater Survey. A method of analysis involving the quantitation for the following 14 drugs of concern and metabolites was developed for wastewater analysis: amphetamine, benzoylecogonine, cocaine, codeine, fentanyl, heroin, 6-monoacetylmorphine (6-MAM), MDMA, methadone, methamphetamine, morphine, 11-Nor-9-carboxyl-D9-tetrahydrocannabinol (THC-COOH). The method has a method detection limit ranging from 0.2 ng/L to 16ng/L and a method quantitation limit ranging from 0.6 ng/L to 53.3 ng/L. Assessment of accuracy and precision demonstrated that the method has a % recovery ranging from 80% to 115% and a % relative standard of deviation (%RSD) ranging from 3% to 25% across the three spike levels. This validated method will be used to determine levels of drugs of concern from various wastewater treatment plants across five Canadian cities. HC's Food Laboratory receives funding from Statistics Canada, Centre for Population Health Data, for this project in support of the controlled substances departmental priority. (PI: Kerry Kwong)

qNMR multicomponent identification and quantification of street drugs presented

In 2018, the Drug Analysis Service (DAS) received funding under the Canadian Drugs and Substances Strategy to provide expanded analysis for project work for non-traditional clients such as provincial health authorities, regional or community based drug checking programs. Drug mixtures are often comprised of known molecules of interest – such as drug molecules and cutting agents for which high quality reference NMR spectra exist. However, when significant resonance overlap occurs, the analysis and interpretation of NMR spectra can become prohibitively time consuming or entirely infeasible. This obstacle provides a significant challenge for the implementation of NMR as a routine, high-throughput instrument in a forensic laboratory. To overcome this, DAS has developed a novel multi-component, multi-resonance algorithm to analyze complex drug mixtures using quantitative nuclear magnetic resonance (qNMR) spectroscopy, a powerful analytical technique in the identification and quantitation

of components present in a sample. The ^{1}H NMR spectrum of the drug mixture can be reduced to a linear combination of reference spectra, and the analysis of the drug mixture becomes a signal decomposition problem to find the weights for each of the reference spectra to reconstruct the mixture spectrum. The NMRquant algorithm can identify, separate, and quantitate overlapping resonances from different components in commonly encountered drug matrices. This turnkey solution has allowed for the successful implementation of for the analysis of hard drugs and cannabis resin. Key strengths of the method include simple sample preparation, quick analysis time, high specificity, and flexible library that allows for adaptation to new compounds. The DAS is funded under the Canadian Drugs and Substances Strategy (CDSS) in support of the controlled substances departmental priority. (PI: Richard Laing)

Food & Nutrition

Method development and validation of vitamin K (K1 and K2 subtype MK4) in retail foods to support the Canadian nutrient file

The Canadian Nutrient File (CNF) is a comprehensive food composition database for reporting amounts of nutrients in foods commonly consumed in Canada. There is currently very little information on the levels of vitamin K in foods from Canadian sources. The data that are available are typically limited to levels of K1, one of the two naturally occurring vitamin K subtypes. Vitamin K is a group of fat-soluble vitamins found in foods, which perform several essential functions in the human body, including production of blood-clotting proteins. Vitamin K1 occurs naturally in plants, especially dark green leafy vegetables like spinach and kale. In animals, K1 is converted to MK4 (a subtype of vitamin K2), so it is found in foods of animal origin. Determination of both K1 and MK4 in the foods we eat is therefore critical to understanding our dietary intake of vitamin K. The Food Lab has developed and validated a method to determine vitamin K in a variety of food samples collected for SNAP-CAN. This will be the first time that Canadian generated data for vitamin K1 and MK4 will be reported in the CNF. Briefly, the method uses enzyme digestion to break down proteins, followed by extraction with hexane to isolate the fat-soluble vitamins. This extract is purified and concentrated, and levels of K1 and MK4 are determined using ultra-high performance liquid chromatography and tandem mass spectrometry. Detection levels are 0.05 µg/100 g for K1, and 0.06 µg/100 g for MK4. (PI: Monica Dyck)

Health Impacts of Chemicals

An integrated testing strategy to assess somatic and germ cell mutations using the OECD's transgenic rodent test guideline TG 488 and the MutaMouse model

Health Canada contributes to the development and standardization of internationally accepted test guidelines (TGs) for the Organisation for Economic Cooperation and Development (OECD). TGs are routinely used for assessing the safety of chemicals before they come on the market. HC has played a fundamental role in developing TG 488 (Transgenic Rodent Mutation Assay) for evaluating the induction of mutations (i.e., changes in the DNA sequence) in germ cells (sperm and eggs) or in somatic cells (all other cell types in the body). Mutations in germ cells may be transmitted to offspring resulting in heritable genetic effects that impact both the individual and population; mutations in somatic cells increase the risk that an individual will develop cancer. Despite these distinct implications, regulatory testing is done almost exclusively in somatic cells. A significant hurdle is the need for a second set of animals for germ cell testing, because of the duration of spermatogenesis, the process producing sperm. Previous work conducted under this project has generated critical data that has recently lead the OECD

to update TG 488 on the recommended design for germ cell mutagenicity. This work suggested that it may be possible to select a single time-point for analyzing mutations in somatic and germ cells of the same animals with comparable sensitivity. However, more data is needed to demonstrate the impact of the germ-cell specific time point for detecting mutations in somatic tissues. In new work, data has been generated demonstrating the suitability of this single time-point for mutagenicity testing in somatic tissues. This integrated approach will significantly reduce the number of animals that are needed for testing. (PI: Francesco Marchetti)

Assessment of the carcinogenic potential of CMP-chemicals through the application and investigation of the Syrian Hamster Embryo Cell Transformation Assay (SHE-CTA)

The Organisation for Economic Co-operation and Development (OECD), in which Canada is a member country, and the European Centre for the Validation of Alternative Methods (ECVAM), are international agencies collaborating to set standards to be used by industries worldwide to identify toxic chemicals. Among evaluated cell transformation assays, the "Syrian Hamster Embryo Cell Transformation Assay" (SHE-CTA), was found to be the most accurate CTA to identify chemicals with the ability to induce cancer. In contrast to other tests, the SHE-CTA detects both the chemicals that induce cancer by damaging DNA and those that do not damage DNA (which are difficult to identify). Some OECD-member countries raised concerns that the molecular mechanisms in the SHE-CTA may not be relevant to those in humans. Nevertheless, the advantages of this test, and its consideration in proposed chemical testing strategies by the U.S. Environmental Protection Agency's (Office of Chemical Safety and Pollution Prevention), may influence companies to generate SHE-CTA data, which will also eventually be submitted for review by Health Canada. The initial research plan involved the development of the SHE-CTA in the laboratory to: (1) gain expertise in conducting this assay and test priority chemicals, (2) investigate mechanisms of cell transformation, and (3) identify endpoints that can improve this assay. The chronology of DNA changes were demonstrated starting from normal cells up to the time at which they become potential cancer cells. Based on these findings, methods to improve the assay can be suggested and tested. Collectively, these *in vitro* data will assist HC in the development of chemical testing strategies, in strengthening predictions of chemicals that can increase the risk of developing cancers, and in providing alternatives to reduce dependence on *in vivo* rodent cancer bioassays. (PI: Daniel Desaulniers)

Assessment of the performance and predictiveness of an optimized *in vitro* developmental neurotoxicity assay using proven developmental neurotoxicants and negative controls

Many *in vitro* assays have been proposed for Developmental Neurotoxicity Testing (DNT). However, the reliability and reproducibility of these assays will need to be properly validated before they can be used to inform chemical health risk assessments by Health Canada and other regulatory agencies. Cerebellar Granule Cells (CGCs) harvested from rat pup brains are a popular experimental *in vitro* model used to study neurodevelopment and neurotoxicity. CGCs are easy to grow and can recapitulate neuron differentiation and maturation processes observed *in vivo*. Genes associated with CGCs neuro development have been identified and used to screen chemicals for potential developmental neurotoxicity. Unfortunately, replication of these findings at Health Canada proved challenging, as gene expression measurement protocols were often poorly described, quality controls infrequently reported and CGCs themselves presented significant batch-to-batch variability. In spite of these issues, a reliable *in vitro* DNT protocol based on commercially-sourced CGCs and reagents was optimized and a subset of developmentally-regulated genes presenting reproducible expression patterns across different laboratories was identified. Promising preliminary results suggest that proven developmental neurotoxicants can be differentiated from non-neurotoxic controls based on the expression of this

subset of key genes involved in neuron differentiation and maturation. The complete and transparent description of a reliable *in vitro* DNT assay using well-characterised CGCs and neurodevelopmental biomarker genes will facilitate future investigations and inter-laboratory comparisons. Further validation of this CGC-based assay may lead to its inclusion in a yet-to-be-determined battery of *in vitro* DNT assays that will support the screening and prioritization of potential developmental neurotoxicants. (PI: Guillaume Pelletier)

Associations among urinary triclosan and bisphenol A concentrations and serum sex steroid hormone measures in the Canadian and U.S. populations (CMP M&S)

Health Canada helps to protect the health of Canadians by assessing and managing the risks associated with exposure to environmental chemicals. People are commonly exposed to triclosan, an antimicrobial agent, and bisphenol A (BPA), the basis of polycarbonate plastics. There is some evidence that these chemicals can disrupt the endocrine system, such as the levels and functions of reproductive hormones. Concentrations of triclosan and BPA were compared in urine in the Canadian and U.S. populations using nationally-representative data from the 2012–2015 Canadian Health Measures Survey (CHMS) and the 2013–2016 National Health and Nutrition Examination Survey (NHANES). The relationship between triclosan or BPA and reproductive hormones was also examined, such as estrogen and testosterone. We found that levels of triclosan were higher in some Canadians and the levels of BPA were higher in some Americans. Higher levels of triclosan or BPA found were related to changes in the levels of estrogen and testosterone, especially in children and adolescents. Additional research is necessary to confirm these findings and determine their potential public health significance. Link: https://doi.org/10.1016/j.envint.2020.106229 (PI: Annie St-Amand)

Automated workflows for chemical scoping and data mining: Advance approaches to prioritization and problem formulation

Health Canada has a mandate to assess the health risks of chemicals to which Canadians are exposed. Modernization of approaches to prioritization and assessment is fundamental to advance the manner by which complex and emerging issues of concern such as endocrine disrupting chemicals, regrettable substitution and cumulative risk are considered. Emerging existing substances are currently identified through the 2014 Approach For the Identification of Risk Assessment Priorities (IRAP) process; problem formulation (PF) provides a mechanism through which computational tools and innovative approaches can be used to define substance groupings, describe the data landscape and triage substances. PF defines the gap between a problem and a solution, and makes a plan that teases out what is needed to close the gap, which may include data collection or generation, risk assessment or monitoring, as examples. Following IRAP, further scoping is needed to identify chemicals that may also be of concern but not captured due to the paucity of data for a large number of chemicals. There is also a desire to rapidly mine data to inform PF outcomes. This project explores automated workflows to avoid resource intensive manual tasks and expedite early steps in PF. A computational algorithm was developed to scan inventories to identify chemicals with a common moiety (e.g. a phenol ring) or belonging to a class (e.g. bisphenol). Chemicals that lack defined chemical structures such as UVCB's (substances of unknown or variable composition, complex reaction products, or biological materials) are searched using key phrases, e.g. "bisphenol". Another computational program was developed, which cross-references chemical lists with online databases (e.g. PubChem, CompTox, and ChemIDplus), to gather information such as physical-chemical properties, toxicity and exposure data as available. The aim of this work is to develop and implement automated workflows to gain efficiencies and enhance the robustness of early scoping activities. This work should allow for the refinement of chemical groups based on evolving

science and for information to be collected that will be useful for decision making in the context of PF and assessment. (PI: Sean Collins)

Characterization and toxicological testing of metal oxide nanoparticles and nanocellulose (CMP)

Manufactured nanomaterials (NMs) are being widely used in industrial applications as well as in consumer products, leading to concerns regarding increased exposure and associated human health risks. Health Canada (HC) is responsible for risk assessment of NMs which are regulated under the Canadian Environmental Protection Act, 1999 (CEPA). As part of Canada's Chemicals Management Plan (CMP), HC has developed strategies to address NMs that are listed on the Domestic Substances List (DSL) and has identified a number of priority NMs for which data on physico-chemical characterization and toxicity are required for regulatory human health risk assessment. To fill these data needs, HC collaborated with the National Research Council's (NRC) Nanoscale Measurement group of the Metrology Research Centre on a project to characterize the physico-chemical properties (e.g. size, shape, size distribution, surface area, surface charge, and surface chemistry) of representative nanoforms of prioritized NMs, including titanium dioxide (TiO2), copper oxide (CuO), and nanocellulose. This project also investigated the potential toxicological effects of TiO2 and CuO NMs on selected cultured cells to examine their effects on cell viability, membrane integrity, and ability to induce cellular stress. Data obtained from this project will not only inform Health Canada's regulatory decisions on the priority DSL NMs but also give better understanding of the relationships between toxicological potentials of the representative nanoforms and available physico-chemical properties to permit read-across for risk assessment of these prioritized NMs (PIs: Kathy Nguyen; Djordje Vladisavljevic)

Characterization of residential exposures to CMP metals and organics

Health Canada assesses potential exposures of the general population to chemical substances through all routes (inhalation, ingestion and contact on the skin) and all possible sources (including ambient and indoor air, food, soil, dust, and consumer products). As Canadians spend more than 90% of their time indoors, there is an increasing demand for information on indoor environmental exposures. This research examines settled house dust samples collected from 1025 homes in 13 cities under the Canadian House Dust Study (CHDS), which was designed to provide a representative national baseline. This study focuses on metals, but also considers synthetic organic compounds including bisphenol A, pesticides, flame retardants, synthetic musks, bactericides, surfactants, and plasticizers. Metals enter the home by residents tracking in outside dirt and by infiltration of airborne particles which settle on hard surfaces, carpets and in crevices. In addition, metal and synthetic organic compounds in consumer products and building materials, such as plasticizers and drying agents in surface coatings, also accumulate in indoor particles as products deteriorate with age and wear. Nationally representative levels of contaminants will be reported as both concentrations and loadings to accommodate various approaches to estimating exposures. Correlations between house characteristics (such as house age, construction materials and environmental setting) and the chemical datasets will help to identify exposure sources and trends. The study focuses primarily on childhood exposures to house dust through normal hand-to-mouth ingestion behaviour. The study also looks at potential inhalation exposures by characterizing re-suspended dust in carpeted versus non-carpeted homes. Dust particles undergo physical and chemical transformations in the indoor environment, which may increase their bioaccessibility (solubility in the lung and gastrointestinal tract), and therefore metal bioaccessibility will be measured. This research supports Health Canada's risk assessment and management activities, with particular focus on mitigation of childhood residential exposures to chemical substances. (PI: Pat Rasmussen; Suzanne Beauchemin)

Cohort profile: health effects monitoring programme in Ndilǫ, Dettah and Yellowknife (YKHEMP)

The Yellowknife Health Effects Monitoring Programme (YKHEMP) was established to examine the relationship between exposure to arsenic and other chemicals of potential concern (such as antimony, cadmium, lead, manganese and vanadium) and health outcomes. A total of 2037 individuals were recruited, including children (age 3–19) and adults (age 20+) residing in Dettah, Ndilǫ, and Yellowknife, Northwest Territories, Canada, in two waves: Fall 2017; and Spring 2018. In Yellowknife, there were 891 (675 adults, 216 children) randomly selected participants with a participation rate of 64%. In addition, 875 (669 adults, 206 children) volunteer participants were recruited. A total of 225 (137 adults, 88 children) of the Yellowknife Dene First Nation (YKDFN), and 46 (33 adults, 13 children) of the North Slave Métis Alliance participated in the study. Each participant answered a lifestyle questionnaire as well as provided toenail clippings and urine for contaminant testing, and saliva samples for testing of genetic polymorphisms associated with arsenic metabolism. Participants also provided consent to have their medical records reviewed by the research team for the past 5 years to allow for the investigation between exposure and health outcomes. The adult YKHEMP participants had lower urinary total arsenic but the children had higher inorganic arsenic than the general Canadian population. There was no difference in urinary total arsenic concentrations between adults and children; however, urinary inorganic arsenic concentrations were generally higher in children than in adults in all four YKHEMP sampling groups. The adult YKDFN participants had lower urinary total arsenic and inorganic arsenic concentrations compared with the random selected and volunteer participants. YKHEMP is designed as a prospective cohort study; the children participants will be re examined in 2022 and both adult and children participants in 2027. Article published in *BMJ Open* in 2020. (PI: Asish Mohapatra; Dr. Laurie Chan (University of Ottawa)).

Creation of a master database of mercury and methylmercury levels in top country foods contributing to exposure among Indigenous communities

Health Canada has a mandate, in the context of major projects subject to federal impact/environmental assessments, to provide advice regarding the human health risk assessment (HHRA) of contaminants found in country/traditional foods, including mercury (Hg). Health Canada's current HHRA framework assumes that 100% of Hg in country foods is present as methylmercury (MeHg), the form that is readily absorbed. However, recent science indicates that this assumption and resulting risk assessments may be overly conservative, potentially leading to unnecessary consumption advisories and causing Indigenous communities to turn to less nutritious commercial foods. The objective of this project is to create a master database of Hg and MeHg levels in the country food items that contribute the most to Hg exposure among Indigenous communities across Canada, in order to identify potentially more realistic MeHg-to-Total Hg (THg) ratios. Eighty-five top contributing country food items were identified based on the Inuit Health Survey (2007-2008), the First Nations Food, Nutrition and Environment Study (2017-2019), and through consultations with experts in the field. A critical review of the published and grey literature was carried out to document the existing knowledge on the concentrations of Hg species reported/measured in the key country food items identified. Means and standard deviations of THg and MeHg concentrations (µg/g wet weight) and mean MeHg:THg ratios (%MeHg) (for country food items for which there is sufficient data) will be integrated into the database. This data will be used to identify food items with significantly less than 100% MeHg and to conduct more realistic HHRAs. Additional information gathered in the database (e.g., sample location, age) will be used to identify factors that may influence the %MeHg and to create a geographic information systems-based database that would allow risk assessors to find associations between pollution hotspots of Hg and levels in country foods. (PI: Laurie Chan (University of Ottawa); Alexandra Iliescu; Gregory Kaminski)

Derivation of biomonitoring equivalents for organics and inorganics for interpreting biomonitoring data to support chemical risk assessment

Biomonitoring can provide valuable data on the presence of trace levels of chemicals in human blood, urine or breast milk. Determining the presence of a chemical, however, is not enough to establish the potential risk to human health. A biomonitoring equivalent (BE) is the concentration of a chemical in human tissue or fluid that corresponds to an allowable exposure guidance value, such as a reference dose (RfD) or tolerable daily intake (TDI), that is considered safe. BEs are an integral part of the hazard and risk characterization and resulting data are used to inform the health risk assessment for many chemicals. As a part of the third phase of the CMP, risk assessments of inorganic chemical groups are being conducted. The overall research objective is to derive biomonitoring equivalents (BE) for metals to interpret biomonitoring data in support of the chemical risk assessments. BEs for additional chemicals were also generated for corresponding biomonitoring data as a part of a CHMS Biobank project. Risk assessments for the latest metals began in FY 2018/2019. Over a dozen open access scientific publications, two science approach documents and a final screening assessment report have been released since then. The list of published works on inorganic metals includes molybdenum, silver, titanium, lithium, aluminium, bismuth, cyanide, zinc, beryllium, barium, tin, antimony, iodine, neodymium, yttrium, cerium, praseodymium, and thallium. A database was produced to help analyze different biomonitoring values from various health agencies. (PI: Andy Nong)

Determination of risk assessment UFs (uncertainty factors) for estimation of exposure limits to environmental mutagens

Genetic damage is associated with numerous human diseases, and chemical screening programs routinely assess genetic toxicity. The results of genetic toxicity tests have traditionally been evaluated using qualitative binning (i.e., yes or no) that merely identifies agents that can damage genetic material (i.e., DNA). However, there is increasing interest in quantitative analyses of genetic toxicity test results, and estimation of human exposure limits that effectively minimise the likelihood of adverse health effects associated with genetic damage (e.g., cancer and human genetic diseases). Estimation of exposure limits requires use of uncertainty factors (UF) that account for differences between humans and experimental animals, for inter-individual differences in human sensitivity, for the short treatments of experimental animals, and for the severity of genetic damage. This work is employing analysis of published data to evaluate the UFs for inter-individual human variability and treatment duration that are currently being used to calculate exposure limits to genotoxic substances. To critically evaluate the currently-used inter-individual sensitivity UF of 10, analyses of over 800 datasets extracted from the scientific literature is assessing the effect of eliminating a cultured cell's ability to repair damaged DNA. Analyses of published human epidemiological data are assessing variability in humans' ability to repair damaged DNA, i.e., human DNA repair capacity. Additional analysis of epidemiological data is evaluating the effect of genetic differences in the ability to repair DNA on the risk of developing cancer. Finally, analysis of published animal experiment results is evaluating the effect of treatment duration on the level of adverse genetic effects caused by long-term chemical exposures. The results obtained to date indicate that the default UFs of 10 might be appropriate for calculation of exposure limits that can effectively minimise the risk of the adverse health effects associated with genetic damage. (PI: Paul White)

Developing *in vitro* screening methods for metabolic disruptors in adipocytes

Evidence from animal and human studies suggests that exposure to commercial chemicals is associated with adverse health outcomes including diabetes, cardiovascular disease, endocrine cancers and obesity which are afflicting the human population in the developed world. The fat tissue and the fat cells are not

only responsible for storage of excess caloric consumption but also potently influence the metabolism of the entire organism via the secretion into the blood stream of hormones and other factors that affect the function of other organs. It is hypothesised that one of the ways by which the fat tissue affects cardiovascular disease, high blood pressure and diabetes is through an imbalance in the factors secreted by this tissue. This makes the fat tissue a likely target for chemical effects. A hormone known to contribute to cardiovascular and metabolic disease, including diabetes, is the stress hormone cortisol. Increased cortisol level is associated with increased mid body fat accumulation and an increase in cardiovascular disease and type 2 diabetes. It has been postulated that chronic exposure to cortisol leads to a change in the metabolic function of the fat cells. As previously shown in cell models, chemicals such as bisphenols and flame retardants can act through the same pathway as the stress hormone in fat cell formation. However, it is unclear whether the resulting fat cell is healthy or contributes to disease through imbalanced secretion of soluble factors. To date, there is limited information and no high content or validated screening method for the functionality of the fat cells exposed to chemicals. This project is working to develop a screening method which can both identify substances that drive fat cell formation and determine if they contribute to metabolic disease. (PI: Ella Atlas)

Development and application of fit-for-purpose, adverse outcome pathway-based testing strategies to enhance hazard and risk assessment of chemicals causing genomic damage

The *Canadian Environmental Protection Act, 1999,* requires the evaluation of the health effects of chemicals that are in the Canadian marketplace. However, conventional toxicology tests are time consuming, expensive, and require large numbers of animals. Health Canada (HC) regulators are in urgent need of new tests to meet legislated mandates. New methods proposed to identify toxicological hazards are based on measuring a chemical's ability to disrupt critical biological processes. Genomics is a powerful tool to identify biological changes because it surveys effects across all of the genes in tissues/cells following a challenge. The use human cells in culture offers considerable advantages including increased throughput, reduced animal use, and cost savings. The need to modernize regulatory toxicology tests by making greater use of human cells in culture (instead of animals) and genomic methodologies has been emphasized internationally, but practical examples of use in human health risk assessment are required. This project works toward the unifying purpose of providing genomic solutions to support Canadian regulatory sciences and the challenges/needs noted above. The overarching objective of the project is to develop and implement practical genomic methods in human cells in culture for hazard identification and risk assessment of environmental chemicals in the area of genetic toxicology (damage to DNA). This project harnesses the adverse outcome pathways (AOP) knowledge base towards its objectives; AOPs catalogue cellular perturbations that are associated with detrimental health outcomes following chemical exposures. The project is building expert-informed AOPs to develop testing strategies implementing state-of-the-science genomic methods to predict genetic diseases like cancer. The methods, data, and analytical tools will be made publicly available to enable widespread use of the technologies/approaches. Case studies applying the modern test strategies are being applied to evaluate the effectiveness of the proposed approaches, assess feasibility to regulatory adoption, and provide data for human health risk assessment. (PI: Carole Yauk (University of Ottawa); Francesco Marchetti)

Development and application of novel next generation sequencing approaches for mutagenicity testing in the 21st century

The *Canadian Environmental Protection Act, 1999,* mandates that chemicals coming into commerce must be tested for the ability to induce mutations (changes in DNA sequence). Mutations occur at each

cell division either because of random errors or because of exposure to a toxic agent. When mutations happen in tissues, they may generate cancer. When mutations happen in sperm or eggs, they can be transmitted to the offspring and result in a variety of genetic diseases. Existing mutagenicity tests have limitations. Specifically, they measure mutations in a single gene (the human genome has ~20,000 genes) or use genetically modified laboratory rodents where mutations are measured in a bacterial gene. Also, these methods are not suited for studying transmitted mutations in the offspring because they would require large numbers of animals. Recently, significant improvements in DNA sequencing technologies enabled the identification of mutations over the entire genome. These methodologies were used to analyze the genomes from human families to identify environmental exposures that increase the number of transmitted mutations to future generations. In addition, a new sequencing approach as a replacement of existing methods for mutation testing is being evaluated. This new method allows the analysis of mutations in many genes in parallel without the need for genetically modified rodents, and, it provides information on the mechanism of mutation induction. Lastly, computational approaches are being used to analyze mutations induced by chemicals and have shown that each chemical produces specific patterns, some of which are observed in cancers with known environmental causes (e.g., lung cancer and tobacco smoking). This approach provides a venue to identify novel environmental causes of cancer. Overall, this project will generate foundational data to modernize and improve regulatory testing for mutagenicity. This project is linked to Health Canada's priority of effectively and efficiently assessing the potential adverse health effects of chemicals and is expected to provide regulatory knowledge to help prevent cancer and other genetic diseases. (PI: Francesco Marchetti).

Development and validation of rapid methods to assess endocrine toxicity

There are growing concerns that exposures to commercial chemicals cause harm by interfering with the hormonal control of growth and development of the brain, reproductive tract and lead to metabolic and stress-related problems. Developing rapid methods to identify chemicals posing these hazards is a critical need for safety assessment. Building on experience gained in previous studies, the current project seeks to 1) develop rapid methods to detect chemical toxicity to thyroid hormone signalling (very important to early brain development) and 2) identify, characterize and develop assays for the enzymes that are inhibited by some organophosphate flame retardants (OPFR) leading to toxicity to the ovary and adrenal gland. Separate assays based on molecular targets of thyroid hormone disruptors will be refined and further validated using a robust list of substances known or suspected of interfering with TH signalling. High-throughput assays based on these molecules will be developed into protocols fit for toxicity test guideline development through the Organization of Economic Cooperation and Development (OECD). Health Canada is collaborating with the US EPA to further develop and validate a high throughput assay of to screen chemicals for thyroid peroxidase inhibition. Secondly, innovative methods will be employed to identify proteins that react with the flame retardant molecules. Early results show that these are enzymes involved in cholesterol metabolism. Assays for these enzymes are currently being developed and these will be used to compare the potency across all phosphate flame retardants that are used in Canada. These studies will help inform risk assessment activities and support assessment and minimization of the risks of chemical use. (PI: Mike Wade)

Development of a screening approach to assess endocrine disrupting activity of chemicals using (Quantitative) Structure Activity Relationship ([Q]SAR) approaches and *in vitro* high throughput data

In the follow up report to the review of the *Canadian Environmental Protection Act, 1999* (CEPA), the Government of Canada is committed to continuously improving its ability to address endocrine disrupting substances and to keep pace with scientific developments including new approach methodologies (NAM). In line with this commitment, the current study begins to advance the development of a tiered strategy that proposes to incorporate predictive models and a sequential testing strategy involving the consideration of NAMs. In this pilot analysis a group of bisphenols and related substances are being evaluated to determine the relevance and reliability of a suite of models to predict the endocrine disrupting potential of these select chemicals. It is well known that endocrine disrupting chemicals act through interaction with receptors to interfere with hormonal signalling leading to health effects. Accordingly, this study aims to assess a chemical's binding potential to a series of receptors using both *in silico* models and high throughput *in vitro* data generated by the US Environmental Protection Agency ToxCast™ Program in order to determine endocrine activity for our set of chemicals. Models under evaluation include Oasis TIMES, VEGA, CASE Ultratox, USEPA rtER Expert System, P&G's DART scheme, ChemProp models as well as Endocrine Disruptome. To begin to incorporate the next tier of information, data available from various endocrine related assays from the ToxCast™ and Tox21™ programs will be integrated. The information acquired from the analysis and integration of the *in silico* and *in vitro* data sources will support the early development of a proposed tiered approach to screen chemicals for potential endocrine disrupting activity. (PI: Sunil Kulkarni)

Development of an integrated analysis tool for genotoxicity assessment (IATGA)

Genetic damage is associated with a variety of human diseases; routine toxicological screening of chemicals in commerce requires identification of substances that can damage genetic material (i.e., genetic toxicity assessment). A related CMP-funded project is developing an efficient, effective, high(er) throughput genetic toxicity assessment platform based on analysis of cultured cells; the platform is known as GeneTox21. Compound screening using the GeneTox21 platform generates large amounts of complex data; the regulatory utility of the data depends on the user's (e.g., clients and stakeholders) ability to organize, browse, analyse, display and interpret the information in an intuitive and user-friendly fashion. A recent research endeavour established an innovative, user-friendly bioinformatic tool known as DREAM-TK; the tool allows users to browse, analyse and interpret complex toxicological test results. DREAM-TK constitutes a foundation for the development of a related tool for efficient interpretation of test results generated using the GeneTox21 platform; a tool to facilitate essential interpretation of genetic toxicity screening data in a regulatory context. This work is building on the DREAM-TK paradigm, and developing a bioinformatic platform to browse, visualise, analyze, and interpret GeneTox21 results; the tool being delevlooped is called the *Integrated Analysis Tool for Genotoxicity Assessment* or IATGA. Work conducted to date has built a *beta* test version of IATGA; interactions with regulatory group have highlighted avenues for improving functionality. Bioinformtic tools such as IATGA are essential for effective and efficient chemical safety assessments based on simultaneous interpretation of results generated using several (geno)toxicity assessment tools. (PI: Paul White)

Development of non-targeted screening analysis approaches for identifying emerging metabolites and chemicals in human fluids as exposure biomarkers using high-resolution mass spectrometry

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Over the past decade, the sensitivity of biomonitoring approaches have considerably improved as it relates to human exposure assessment of some targeted chemicals. However, there is still a gap between pre-selected targets and our capability of qualitatively and quantitatively determining unknown and new substances of emerging concern (also known as emerging substances) in human biofluids (e.g. urine, follicular fluids and blood). As a result, non-targeted approaches have gained much attention in risk assessment of human exposure to unknown and emerging chemical contaminants. The proposed four-year project plan, as a proof of concept study, is using high-resolution mass spectrometry to develop new non-targeted analytical methods, which aims to rapidly screen and identify new metabolites of these chemicals and some parent compounds in human biofluids as potential biomarkers for assessment of human exposure to substances, including CMP priority chemicals and other emerging chemicals. Suspected, unknown, and emerging contaminants will be screened and identified based on accurate mass measurements with high-resolution mass spectrometry, fragmentation patterns, retention time with prediction models, and the structural similarity of known chemical groups. These newly developed analytical methods will provide valuable screening information for metabolites and parent compounds as to the identification of potential emerging contaminants for future assessments under CMP; models will be developed to provide semi-quantitative information of identified unknown chemicals without using standards; they will also generate meaningful knowledge regarding metabolites derived from emerging chemicals in human biofluids. The developed methods may be applied to analysis of samples collected in the Canadian Health Measures Study and Ontario Health Study and will also be beneficial to broader scientific communities. Method development and validation will include metabolites of selected CMP priority chemicals, but not necessarily limited to flame-retardants, BPA analogues, plasticizers, UV filters and stabilizers, their alternative or replacement chemicals, and mercapturic acids in various environmental samples and human biofluids such as urine, serum, plasma, and follicular fluids. (PI: Yong-Lai Feng)

Direct comparison of the sub-acute toxicities of Bisphenol A, F and S using a standardized OECD exposure protocol

Bisphenols are chemicals produced in large quantities for use primarily in the production of polycarbonate plastics and epoxy resins. Bisphenol F (BPF) and bisphenol S (BPS) are bisphenol A (BPA) substitutes prioritized for measurement in the cycles 7 and 8 of the Canadian Health Measures Survey (CHMS). BPF and BPS both present structural similarities to BPA and their levels in environmental and human samples are increasing. Information on BPF and BPS toxicities is much more limited than for BPA, making it difficult to properly evaluate the potential health consequences of BPA substitution by BPF and BPS. In this study, the toxicities of BPA, BPF and BPS were directly compared when administered to rats over a wide dose range according to a regulatory toxicology protocol based on OECD 407 Guidelines (Repeated Dose 28-Day Oral Toxicity Study in Rodents). Given the relatively limited effects of BPA on the parameters prescribed by the OECD 407 Guidelines, perturbations of endocrine functions were further investigated. Based on published information on the *in vivo* and *in vitro* toxicities of BPA, BPF and BPS, additional serum hormone levels were measured, while the expression of specific genes involved in their biosynthesis and degradation will be assessed in the liver. By directly comparing the *in vivo* toxicities of BPA, BPF and BPS, this project will allow a better assessment of the potential human health risks

associated with the substitution of BPA by BPF and BPS. It will also contribute to a better interpretation of CHMS biomonitoring data. (PI: Guillaume Pelletier)

Effect of country food preparation on concentrations and bioaccessibility of mercury and associated metals

Country/traditional foods are defined as foods sourced outside of commercial food systems. These include food that is trapped, fished, hunted, harvested or grown for subsistence or medicinal purposes. Mercury (Hg) found in country foods, which are consumed more frequently by Indigenous communities, can pose health risks to Canadians in communities that rely on fishing and hunting to complete their diet. Health Canada's approach to estimating human exposure to Hg from country foods consumption assumes that: (1) all Hg is present as methylmercury (MeHg), the neurotoxic form; (2) Hg levels remain constant during food preparation; (3) all MeHg in country food is absorbed by humans; and, (4) Hg interactions with selenium (Se) and arsenic (As) do not alter human exposure. However, these assumptions and resulting human health risk assessments may be overly conservative, potentially leading to unnecessary consumption advisories and causing Indigenous communities to turn to less nutritious commercial foods. To test these assumptions, concentrations of Hg, MeHg, As and Se will be measured in fresh, frozen and cooked samples of grey seal liver, muscle and kidney, and of whitefish muscle. Country food samples will be prepared according to traditional methods, and methods with contrasting cooking temperatures. The resulting changes in metal speciation, including changes in %MeHg (i.e., percent of total Hg present as MeHg), will be documented. To evaluate whether all Hg in country foods consumed is absorbed by humans, simulated human digestion experiments will be conducted on 'prepared' versus 'unprepared' country food items. This will be done using a modified *in vitro* physiologically-based extraction test to estimate how the bioaccessibility of Hg, MeHg, As and Se is altered following both the gastric and gastro-intestinal phases of digestion. The study results could contribute to the refinement of Health Canada advice regarding human health risk assessments of Hg exposure from country food consumption, and to better inform potential risk management measures. (PI: Marc Amyot (University of Montreal); Alexandra Iliescu; Gregory Kaminski)

Endocrine disrupting chemicals: Towards responsible replacements (CIHR Team Grant McGill University)

Scientific and public concern mount about the potential health impacts due to widespread use of chemicals suspected of causing endocrine disruption and Health Canada has a mandate to regulate chemicals to which Canadians are exposed. Regulatory action and/or consumer pressure have caused a reduction in the use of a number of suspected endocrine disruptors including pentabromodiphenyl ethers (PBDE; flame retardants), bisphenol A (BPA) and diethylhexyl phthalate (DEHP). In response, a large number of chemicals have been introduced into the marketplace as substitutes; some of which may pose similar risks due to structural or functional similarities. In this study, chemicals used as replacements for PBDE, BPA and DEHP are screened with *in vitro* assays to determine effects on thyroid hormone or steroid hormone production. In particular, large number of structurally similar compounds that are potential replacements for bisphenol have been screened for effects on steroidogenesis (20) and thyroid peroxidase inhibition (38). Results will inform the potential hazards of use of these replacements and help identify less toxic alternatives. (PIs: Dr Barbara Hales [McGill University]; Tara Barton McLaren. Collaborators: Mike Wade; Ella Atlas; Cariton Kubwabo)

Endocrine disrupting chemicals: Towards responsible replacements - Determination of organophosphate esters (OPEs) and their metabolites in breast milk, food and water samples

Health Canada has a mandate to regulate chemicals to which Canadians are exposed. Several chemicals that have been banned from the Canadian marketplace due to their toxicity, have been replaced by alternate chemicals for which there is limited knowledge. Health Canada is collaborating on a CIHR (Canadian Institutes of Health Research) Team Grant project to investigate the exposure and hazards of substances used as replacements for polybrominated diphenyl ethers (PBDEs) flame retardants. PBDEs, initially used in home furnishings, were removed from commerce in 2008 in Canada due to their persistence in the environment and their tendency to accumulate in human and animal tissues. Manufacturers are increasingly using organophosphate esters (OPEs) as a replacement to PBDEs to ensure that their products continue to meet the flammability standards in a variety of home furnishings, fabrics, clothing, electronics, and motor vehicles. Health Canada's Biomonitoring Laboratory has developed and validated analytical methods for OPEs and their metabolites in food, water and breast milk.This study examined dietary exposures to OPE flame retardants and plasticizers as well as other chemicals in 3 locations: 1) Montreal, Canada (urban developed world), 2) Pretoria, South Africa (urban less developed), and 3) the Vhembe region of Limpopo province of South Africa (rural, poorly developed). The data will support epidemiological analysis and contribute to the dietary assessment of exposure to these chemicals. This dataset is the first assessment of breast milk that allows comparison between the levels of these substances in Canada and in less developed countries, using identical sample collection and analytical methods. (PI: Cariton Kubwabo; in collaboration with McGill University)

Estimating the number of cases of male infertility due to prenatal dioxin and furan exposures in Canada

The Performance Measurement Division of the Risk Management Bureau conducts performance measurement evaluations on the risk management of toxic substances to determine whether actions taken to help protect Canadians and their environment are meaningful and effective. This study is in support of the performance measurement and evaluation of dioxins and furans. Dioxins and furans are two groups of persistent organic pollutants that were declared toxic to human health in 1990 under the *Canadian Environmental Protection Act*, 1988. The Government of Canada has implemented several risk management actions since the early 1990s to reduce exposures to these chemicals. One of the more sensitive health endpoints is reduced fertility in males born to mothers exposed to high levels of dioxins and furans. The objectives of this study are to help assess the performance of risk management actions by estimating the number of cases of male infertility in Canada that may have occurred due to dioxin and furan exposures over time. Estimates of dioxin and furan concentrations will be obtained using several Canadian human milk surveys conducted over the years. The number of cases of male infertility attributed to dioxin and furan exposures will be estimated, then compared to estimates in a scenario where exposures to these chemicals did not decrease over time. This will then provide an idea of the number of cases of male infertility that may have been prevented by risk management actions. (PI: Michael Elten)

Evaluation of dermal decontamination to reduce firefighters' exposures to combustion-derived PAHs (polycyclic aromatic hydrocarbons) (Ottawa Fire Services, Canadian Forces Fire Marshall, Ottawa Professional Firefighters Association, Association des pompiers de Montréal, International Association of Firefighters, and Institut de protection contre les incendies du Québec)

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Firefighters face serious risks on the job,

including heat, physical and mental stress, as well as exposure to a toxic environment both in and around fires. In recent years, statistics have shown that these exposures have taken their toll on firefighters. For example, it has been shown that firefighters have an increased cancer risk compared to the general population. Previous studies have shown skin to be a major route of exposure. Skin cleaning wipes are the most practical and suggested method for dermal decontamination for firefighters yet little research has been done to assess if this is effective, and whether or not different types of wipes or other skin cleaning methods (e.g., soap and water) are better at removing dermally-deposited contaminants. This project is specifically designed to collect the necessary information to make sound, evidence-based decisions on how to optimally protect firefighters from dermal exposure to combustion emissions. An intervention study at training fire events in Ottawa has been designed to assess the effectiveness of the use of skin cleaning protocols. Exposures to PAHs are measured and compared between participants following current decontamination protocols (i.e., the control group), and those who add an additional dermal decontamination step using skin cleaning wipes or a wash cloth with soap and water (i.e., the intervention groups). These research activities are conducted at training fires, where exposures are relatively uniform across the participants. Ultimately, the research will contribute to a greater understanding of the effectiveness of skin cleaning procedures and furthermore, whether different protocols are superior to others in removing hazardous contaminants deposited on the skin. The results will be used to develop new protocols, or modify existing practices, to minimize dermal absorption of contaminants among firefighters. (PI: Jules Blais [University of Ottawa], and Collaborator: Paul White)

Evaluation of *in vitro* methodologies to resolve the differences in toxicity characteristics of newly synthesized nanosilica particle (SiNP) variants optimally to assist read-across in risk assessment of nanoparticles

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. Cellular respiration is a critical aspect of cell health and thus functioning of mitochondria, the power-house of the cell, can be of importance in terms of toxicity testing of nanosilica particles (SiNPs). Typically, *in vitro* cell viability assays incorporate assessment of mitochondrial performance. Previous observations indicated subcellular localization of SiNPs in the mitochondria by transmission electron microscopy (TEM) analyses and others have reported mitochondrial oxidative stress in response to nanoparticle exposure. Mitochondrial protein changes were measured after exposure to nonporous SiNPs following mass spectrometry analysis. Association between physicochemical properties of the SiNPs and mitochondrial protein changes were tested. Suitability of this methodology for screening nanoparticles for mitochondrial toxicity is tested in this work. These findings can support OECD test guideline development, provide a mechanistic basis to rank and prioritize SiNPs that are on the Domestic Substances List (DSL) for further toxicological testing as well as support the activities on risk assessment of these materials by the New Substances Assessment and Control Bureau. (PI: Premkumari Kumarathasan)

Evaluation of select ADME models to determine suitability and performance for existing substances and for broader implementation in chemicals risk assessment

Absorption, Distribution, Metabolism, and Excretion (ADME) characteristics of a chemical are important for understanding (toxico) kinetics and the mode of action for predicting toxicity. These parameters provide important insight into how a chemical behaves inside the body following exposure. *In vitro* and/or *in vivo* toxicokinetic data are often not available for the large number of chemicals that require assessment. Since prediction and simulation of various ADME properties is considerably more resource efficient than generating *in vitro* or *in vivo* data there is an emphasis on the development of methods such as those based upon quantitative structure–activity relationship (QSAR) and molecular modeling to

complement or replace the need for empirical data when sufficient confidence can be demonstrated. To ensure applicability of the ADME predictive tools to environmental chemicals in Canada, there is the need to carry out internal validation of these *in silico* models in a focused manner to support priority setting and assessment of chemicals of greatest interest for human health risk assessment under the ongoing and future Chemicals Management Program. In this project, available published experimental ADME data on chemicals is being collected. Through statistical analysis on the predictions obtained for known chemicals the performance of select *in silico* ADME prediction models will be evaluated. Further, using chemical similarity analysis (clustering analysis) it will be determined how many of these chemicals (with ADME data) are structurally similar (or identical) to chemicals on the Canadian Domestic Substances List (DSL). This exercise will provide an approach to assess confidence in the ADME predictions both from the perspective of model reliability as well as model suitability for the DSL chemical space. (PI: Sunil Kulkarni)

Expanding high-throughput toxicokinetics chemical space to increase its applicability to existing substances

There is increased interest in the use of new approach methodologies (NAMs) in risk assessment, including bioactive concentrations (µM) measured in *in vitro* toxicology assays. In order to translate bioactivity concentrations to human relevant doses (mg/kg/bw) for hazard assessment, *in vitro* to *in vivo* extrapolation (IVIVE) methods are required. The US Environmental Protection Agency developed a high-throughput toxicokinetics (HTTK) model for IVIVE that is being explored at Health Canada. The model has been paired with ToxCast™ data to enhance chemical screening through determination of Bioactivity Exposure Ratios. However, the HTTK chemical space is primarily comprised of pesticides and pharmaceuticals, with limited data for industrial or environmental compounds. Furthermore, there are few comparisons between *in vitro* predictions with the model and *in vivo* toxicokinetics analyses. This study aims to identify and compile available toxicokinetics data to understand the chemical space covered by HTTK models and how this compares to the chemical space of interest (i.e., Canada's Domestic Substance List). This will allow for the establishment of the applicability domain for current HTTK models and the identification of environmental compounds to which the models can be appropriately applied. Also, this project seeks to establish and provide recommendations for addressing the uncertainty when applying HTTK methods to chemicals outside this defined applicability domain. The findings will guide future research into expanding on the coverage of HTTK chemical space through the targeting of chemical features or properties, currently inadequately covered by HTTK models, for future toxicokinetics analyses. (PI: Marc Beal; Sunil Kulkarni)

Exposure Load: Using biomonitoring data to quantify multi-chemical exposure burden in a population (CMP M&S)

Assessing the impacts of multiple chemical exposures from different sources has long been a challenge for scientists and regulators. The Exposure Load method has been developed to quantify multi-chemical exposures and understand how chemical burdens vary within a population by taking advantage of human biomonitoring data. Biomonitoring is the measurement of chemicals in urine, blood or other tissues, reflecting real-world exposures from all sources and routes. For this analysis data was used from the Canadian Health Measures Survey (CHMS), a national survey led by Statistics Canada in partnership with Health Canada and the Public Health Agency of Canada. Exposure Load counts the number of chemicals measured in the blood or urine of individuals above a defined concentration threshold (which indicates exposure), and then sums the counts for multiple chemicals of interest and expresses the result for a population. 44 blood and urine biomarkers were used representing 26 chemical groups for

1,858 participants aged 12 to 79 years from cycles 3 and 4 of the CHMS. Initial findings support that Canadians are concurrently exposed to many chemicals at lower concentrations, and to fewer chemicals at high concentrations. It was also found that the youngest age group (12–19 year olds) had a significantly lower Exposure Load than older individuals, smokers incurred a much higher Exposure Load than nonsmokers, but males and females did not substantially differ. Health Canada protects the health of Canadians by assessing and managing the risks associated with exposure to environmental chemicals, and Exposure Load analysis supports and informs this mandate by providing valuable nationally-representative information about multi-chemical exposure burdens in the Canadian population. Additional Exposure Load analysis is planned. Link: https://doi.org/10.1016/j.ijheh.2021.113704 (PI: Jeff Willey)

GeneTox21 – An integrated platform for *in vitro* genetic toxicity assessment and regulatory evaluation of new and existing substances

Genetic damage is associated with numerous human diseases, and chemical screening programs routinely assess a chemical's ability to damage DNA (i.e., genetic toxicity). Traditional assessment tools (i.e., bioassays) are laborious and not conducive to high-throughput (HT), high-content chemical screening using tools that employ cultured cells (i.e., *in vitro* bioassays). Physical manifestation of genetic damage (e.g., mutations and chromosome damage) requires cellular replication; thus, no *in vitro* genetic toxicity assay can truly be considered HT. Even the most rapid assays require 24+ hours from cell exposure to data acquisition; consequently, no *in vitro*, HT, multi-endpoint system for genetic toxicity screening has been established. However, HT scoring technologies (e.g., flow cytometry) can be employed to increase the throughput and precision of some traditional *in vitro* genetic toxicity assays. Assays using such newer scoring technologies can be considered higher throughput in comparison with the traditional approach (e.g., manual microscopy). This project aims to establish an integrated, multi-assay, higher throughput platform for the assessment of chemically-induced genetic toxicity. The system includes multi-measurement, per-cell assays for an array of effects (i.e., MicroFlow® and MultiFlow™ tools), the high-throughput CometChip® assay for DNA breaks, a miniaturized version of the Salmonella fluctuation test (i.e., Ames II), a gene expression profiling assay for cellular responses to DNA damage, and high-throughput microscopy for per-cell *in situ* imaging. The performance of the higher throughput system is being evaluated by analysis of 35 reference compounds and 20 data-poor compounds prioritized for regulatory screening. The overall performance of the assay is being evaluated; it will subsequently be deployed for routine generation of genetic toxicity profiles for prioritized substances. The platform, termed GeneTox21, will be internationally promoted to encourage its adoption for routine genetic toxicity assessment of new and existing substances. (PI: Paul White)

Health risk assessment of arsenic exposure among the residents in Ndilǫ, Dettah, and Yellowknife, Northwest Territories, Canada

There are concerns in Yellowknife, Northwest Territories, Canada, about arsenic (As) exposure due to past mining operations, particularly the former Giant Mine. The objective of this study was to characterize the risk of arsenic exposure, and associated risk factors among the local residents. Arsenic and its species were quantified in urine (n = 1966) using inductively coupled mass spectrometry. Children in the study were found to have significantly higher ($p < 0.05$) urinary inorganic-related As (uiAs) concentrations than children in the general Canadian population, as well as higher levels than adults in the study. Additionally, uiAs concentrations in children, particularly those above the 95th percentile, are above the Biomonitoring Equivalents (BE) levels that are associated with dermal effects, vascular problems and cancer risks. Multiple linear regression results showed that market seafood (fish

and shellfish), and rice consumption frequency were significantly positively associated with uiAs. Specific to children, drinking lake water was positively associated with uiAs. Specific to adults, consumption of local mushrooms and berries was significantly positively associated with uiAs while there was a significant negative association with age, smoking and recreational water activities. The risk factors identified in this research can be used for public health education to lower arsenic intake. Overall, these results support the need for an ongoing monitoring program. Article published in *International Journal of Hygiene and Environmental Health* in 2020. (PI: Asish Mohapatra; Dr. Laurie Chan (University of Ottawa))

Impacts of major projects on traditional foods and implications for food security of Indigenous peoples: A current state of practice in Canada

Traditional food is a nutritionally high-quality food resource that helps combat food insecurity, influences (directly or indirectly) all dimensions of the holistic definition of health, and is closely tied to the culture and identity of Indigenous peoples. This work will summarize the principles, current practices and methodologies, and basic information that Health Canada will seek during its review of traditional food and food security assessments, submitted by proponents of major projects under the *Impact Assessment Act*. Relevant and targeted methods gathered from the literature can be adapted to enhance current practices for evaluating traditional food security for Indigenous peoples. The work builds on a previous product titled "Methods for Determining Impacts on Traditional Food Security in Indigenous Communities", which were specifically developed by three First Nations in the Athabasca oil sands region of Alberta. This document will be appended to the final published product. (PI: Aurelia Thevenot) Dataset not expected.

Implementing *in vitro* bioactivity data to modernize priority setting of chemical inventories

Internationally, there are thousands of existing and newly introduced chemicals in commerce, highlighting the ongoing importance of innovative approaches to identify emerging chemicals of concern. For many chemicals, there is a paucity of hazard and exposure data. Thus, there is a crucial need for efficient and robust approaches to address data gaps and support risk-based prioritization. Several studies have demonstrated the utility of *in vitro* bioactivity data from the ToxCast program in deriving points of departure (PODs). ToxCast contains data for nearly 1,400 endpoints per chemical, and the bioactivity concentrations, indicative of potential adverse outcomes, can be converted to human-equivalent PODs using high-throughput toxicokinetics (HTTK) modeling. However, data gaps need to be addressed for broader application: the limited chemical space of HTTK and quantitative high-throughput screening data. Here the applicability of in silico models to address these data needs was explored. Specifically, ADMET predictor for HTTK predictions and a generalized read-across approach to predict ToxCast bioactivity potency was used. These models were applied to profile 5,801 chemicals on Canada's Domestic Substance List (DSL). To evaluate the approach's performance, bioactivity PODs were compared with *in vivo* results from the EPA Toxicity Values database for 1,042 DSL chemicals. Comparisons demonstrated that the bioactivity PODs, based on ToxCast data or read-across, were conservative for 95% of the chemicals. Comparing bioactivity PODs to human exposure estimates supports the identification of chemicals of potential interest for further work. The bioactivity workflow shows promise as a powerful screening tool to support effective triaging of chemical inventories. (PI: Marc Beal; Tara Barton-Maclaren)

In vitro pharmacokinetics for high throughput data interpretation (Part 2)

Health Canada is responsible for assessing the risk to human health of thousands of substances present in the environment. The assessment of individual substances is tedious and unrealistic for a holistic risk assessment therefore, the use of high throughput screening (HTS), a combination of multiple signals

from various sources and substances is increasing. Under a research project funded through the CMP, Health Canada researchers and regulatory scientists are collaboratively investigating the utility of integrating *in vitro* toxicity tools for human health risk assessment. The generation of pharmacokinetic parameters is crucial to the interpretation of the HTS data and the estimation of levels of human exposure that will provide a better basis for informed decision on a chemical's potential for toxicity. The aim of this project is to conduct *in vitro* experiments in order to generate required pharmacokinetic parameters for a series of chemical classes such as complex phenols, glycols, plasticizers, perfluorinated compounds and flame retardants identified by risk assessors. More than 200 chemicals were analyzed by an external company and results will be used by Health Canada scientists to develop a science approach document on the application of *in vitro* HTS data for regulatory purposes. (PI: Andy Nong)

In Vitro to *In Vivo* extrapolation (IVIVE) toxicokinetics of CMP chemicals

Advances in toxicity testing have led to a rise in *in vitro* and high-throughput approaches to predict potential biological effects following chemical exposures. Health Canada is responsible for assessing the risk to human health of thousands of substances present in the environment. The challenge remains to relate these screening results with exposure guidance values based on actual animal or human effects. To address this challenge, new exposure and *in-silico* methods were developed to help interpret and extrapolate the *in vitro* measures. The latest development in translating the *in vitro* measures has been the use of drug metabolism pharmacokinetic tests, also known as *in vitro* toxicokinetics (TK), to generate critical data for computer models to incorporate when predicting the fate of a chemical *in vivo* based on *in vitro* toxicity assays concentrations (*in vitro* to *in vivo* extrapolation – IVIVE). However, current *in vitro* TK studies and models used to extrapolate the concentrations observed from *in vitro* toxicity tests are made on basic assumptions that are not necessarily true *in vivo* for all environmental chemicals. Other biological processes such as gut absorption and metabolic activation have yet to be accounted for in past modeling efforts. The resulting omission may result in misinterpreting human dose exposures based on *in vitro* measures. The goal of this research is to develop better *in vitro* toxicokinetic data and consistent biological extrapolation models to predict realistic doses *in vivo* where potential toxicological effects would be anticipated based on measures from high throughput *in vitro* assay toxicity database. These tests and models will explore the largest family of substances recently used as replacements to plasticizers, flame retardants and perfluorinated chemicals that are identified on the Health Canada CMP priority list and found in the US Environmental Protection Agency ToxCast™ program. This effort will help Health Canada develop tools, including a database, and supporting data to predict toxicity of chemicals for high throughput risk assessments with IVIVE and help identify chemicals to be considered safe or alternatively trigger additional testing for the health of Canadians. (PI: Andy Nong)

In vitro toxicity testing of TiO_2 nanoforms

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. Nano-sized titanium dioxide (TiO_2) is valued for its high tensile strength, electronic, optical and catalytic properties, with annual production exceeding four million tons per year. Due to this prevalence, these nanomaterials are on a priority list developed by New Substances Assessment and Control Bureau (NSACB) that need to be thoroughly assessed for health and environmental hazard. Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. TiO_2 can be manufactured with various chemical modifications, which are known as nanoforms. Since there is no information available on the comparative toxicity of these nanoforms, the current project aims to screen 11 nanoforms of TiO_2 using cultured lung cells (i.e., epithelial cells) and immune cells (i.e., macrophage) to determine their relative toxicities. Cellular toxicity was measured by assessing cell viability, cellular metabolic activity, and membrane integrity. Also, certain cellular stress

pathways were measured following exposure to these nanoparticles. The association between these toxicity indicators and their physical (e.g., size, shape) and chemical (e.g., surface charge, reactivity) properties will reveal the most important nanoform characteristics contributing to toxicity. This data will be provided to our regulatory colleagues to support risk assessment of TiO_2 and support HC's commitment to the Organisation for Economic Cooperation and Development (OECD) - Working Party on Manufactured Nanomaterials (WPMN). (PI: Premkumari Kumarathasan; Azam Tayabali)

In vitro toxicokinetics for data interpretation

Health Canada has been exploring the use of new approach methodologies to evaluate health risks from chemicals. This study develops computer models and applications to help interpret and relate new testing data and approaches into population daily exposure levels for regulatory purposes. An abundance of toxicity data known as high throughput screening is now available thanks to large international testing initiatives. These tests screen thousands of chemicals over various biological responses measured in cells, tissues or even small organisms. As a joint effort between Health Canada and the US Environmental Protection Agency, additional experimental chemical kinetic information, also known as *in vitro* toxicokinetics, are generated to aid with the computer models to predict exposure levels. Web applications that combine all this knowledge and help predict the potential harm from chemicals are also being designed for regulatory end users. By investigating different categories of environmental chemicals, case studies are being prepared to address key elements and considerations in the use of computer application with high throughput screening data to predict and evaluate health concerns. Eventually, the computing research will provide a better basis for informed decision making to prioritize and evaluate chemicals from potential health risks in the next cycle of Health Canada Chemicals Management Plan. (PI: Andy Nong)

Incorporating computational workflows for the identification of risk assessment priorities under the *Canadian Environmental Protection Act*

Since 2006, priorities for risk assessment of chemicals and other substances under the Canadian Environmental Protection Act, 1999 (CEPA) have largely been based on the results of categorization of the Domestic Substances List (DSL). The categorization process was a multi-year initiative that relied upon the manual curation of chemical hazard and exposure information in order to make prioritization decisions. Moreover, the process mainly relied on toxicity testing results available at the time to prioritize chemicals. Data poor chemicals, while potentially hazardous, were generally not prioritized for assessment due to lack of data. In the 15 years since categorization, there has been a tremendous increase in both the availability of public toxicity datasets as well as the development of *in silico* and *in vitro* screening technologies for hazard assessment. Furthermore, proposed amendments to CEPA include the establishment of a new plan to identify chemicals management priorities that reflect the evolving science in the field. As a result, the Existing Substances Risk Assessment Bureau has been developing computational workflows that automate the collection and weighing of evidence related to *in vivo*, *in vitro* and in silico outcomes across the 28,000 chemicals on the DSL. For *in vivo* and *in vitro* data collection, the workflow makes use of scripts for web-scraping and other methods (e.g. API calls) to rapidly query electronic sources of information. Moreover, for data poor chemicals, several in silico models have been developed that make use of machine learning technologies to predict toxicity. The workflow applies rule-based algorithms to weigh the collected data/information across multiple regulatory endpoints in order to prioritize chemicals for further assessment or information gathering activities. The computational workflow is being developed using open source software (KNIME, R, Python) to increase methodology sharing opportunities. (PI: Matthew Gagné)

Investigating the effects of dissolution rates of metal-based nanoparticles on cellular responses (CMP)

Metal-base nanomaterials (NMs) are extensively incorporated in consumer products, including cosmetics, sunscreens, textiles, personal care products, therapeutic products, and paints. As a result, likelihood of human exposure to these materials has also increased. Health Canada (HC) is responsible for conducting human health risk assessments of manufactured NMs whose Chemical Abstracts Service Registry Numbers (CASRNs) appear on the Domestic Substances List (DSL). The variety of NM forms which may be manufactured with the same CASRN is very broad, and there is uncertainty whether all such forms pose similar hazards to human health and whether NM physico-chemical properties, including dissolution, have effects on their toxicity. To fill existing data gaps for nanoforms, HC collaborated with the Health and Environments Research Centre (HERC) Laboratory at Dalhousie University on a project to study the solubility and to determine the toxicological profiling of seven nanoforms of zinc oxide (ZnO) NM to establish the relationship between dissolution rates of these nanoforms and their cellular responses. The dissolution rates of the representative nanoforms were measured in different biological solutions and matrices and the cultured lung cells were exposed to the test nanoforms through an air-liquid interface system, an exposure system that mimics realistic exposure conditions to NMs through inhalation. The toxicological profiles of ZnO nanoforms were compared based on their effects on cell viability and membrane integrity, as well as the ability to induce cellular stress and inflammatory responses. The data obtained from this project will be used directly in nanomaterial risk assessments and will also allow evaluators at HC to determine how this particular property of nanomaterials affects the cellular responses from NM exposure and will allow for refinement of tools and approaches that HC evaluators are able to use for assessment of risk of nanomaterials on the DSL (PI: Kathy Nguyen; Djordje Vladisavljevic)

Machine learning models for predicting endocrine disrupting chemicals

There are ongoing efforts in the regulatory community to identify and assess chemicals with the potential for endocrine disrupting activity. Endocrine disrupting chemicals (EDCs) have been linked to effects on reproduction and development, learning disabilities, cognitive and brain development, thyroid effects as well as cancer. A majority of commercial chemicals have very limited data and conventional toxicity testing methods are time consuming and require significant resources, both in cost and animals. These methodologies are less feasible given the rapidly changing chemical landscape including a continual stream of new and complex chemistries. Further, the resource intensive approach may not always be needed when screening for a particular mode of action such as endocrine disruption when in fact a large number of chemicals on the market are not EDCs. To gain efficiencies in screening and identifying chemicals of greater potential concern, new approach methodologies are being developed and employed which can perform rapid screening to focus priority setting and assessment activities. Current methodologies for this field were found to only cover a limited number of substances. In this project, multiple machine learning models were developed which predict endocrine disruption activity of a chemical. This is accomplished by using simple structural information and training the model to predict the activity in a process known as (quantitative or qualitative) structural-activity relationship ([Q]SAR). The aim of this work is to develop and implement the machine learning models to screen the Domestic Substances List for substances of potential concern as a result of endocrine activity to allow for more focused prioritization and evaluation of potentially harmful chemicals. A manuscript highlighting the methodology and models developed for this work is currently in preparation. (PI: Sean Collins)

Maternal-Infant Research on Environmental Chemicals (MIREC) research platform

The Maternal-Infant Research on Environmental Chemicals (MIREC) Research Platform encompasses the original MIREC Study of Canadian pregnant women and the follow-up studies of some of their infants (MIREC-Infant Development: MIREC-ID) and young children (MIREC-Child Development at age 3: MIREC-CD3 and MIREC- Early Childhood Biomonitoring and Neurodevelopment: MIREC-CD Plus) and is designed to obtain pan-Canadian data on maternal and fetal/early life exposure to priority environmental chemicals and potential adverse health effects on the pregnancy, and newborn and infant/childhood growth and development. For the original MIREC Study, co-led by Health Canada researchers, approximately 2,000 women were recruited in the 1st trimester of pregnancy from 10 cities across Canada and followed through to delivery. Questionnaires administered during pregnancy and post-delivery collected information on occupation, lifestyle, medical history, environmental exposures and diet. Information on the pregnancy and the infant were collected from medical charts. Maternal blood, urine, hair and milk as well as cord blood and infant meconium were collected and analyzed for numerous environmental chemicals and nutrients. Subsequent follow-up studies of the infants and young children were designed to examine the potential association between prenatal exposure to various chemicals and the risk of adverse effects on infant growth, and potential markers of reproductive toxicity (MIREC-ID), child behaviour (MIREC-CD3) and neurodevelopment (MIREC-CD Plus). Child blood and urine samples were analyzed to address gaps in data for young children on several metals/elements and non-persistent chemicals (phthalates, phenols, pyrethroids) (MIREC-CD Plus). The Platform also includes the MIREC Biobank of biospecimens collected for future research on the health of mothers and their children. The project continues to generate new knowledge on early life cumulative exposure to endocrine disrupting chemicals and potential health risks in vulnerable populations of pregnant women, fetuses, infants, and young children that contributes to risk assessment and management of chemicals. (PI: Jillian Ashley-Martin)

MIREC ENDO: pubertal timing, endocrine and metabolic function

MIREC ENDO is a new longitudinal component of the Maternal-Infant Research on Environmental Chemicals (MIREC) Research Platform studying the metabolic health of MIREC mothers over time and the pubertal growth and development and metabolic health of the MIREC children. The results of this study will address critical information gaps for Health Canada on the potential role of early life and childhood exposures to endocrine disrupting chemicals on children's metabolic function, growth (e.g., obesity) and the onset and progression of puberty, as well as whether maternal health status and chemical exposures during pregnancy have any long-term health impacts on the women. To do this, researchers are collecting and analyzing biospecimens for hormones and chemicals, conducting clinical health assessments of mothers and children and collecting questionnaire-based data from the cohort at key ages relevant to pubertal onset, namely 7-9 years of age, 10-12 years of age, 13-15 years of age and from the MIREC mothers. The first phase of the study recruited over 500 mothers and children and successfully responded to the challenges of the COVID-19 by adopting at-home based data collection tools. In addition, 1st trimester maternal urine samples from the MIREC Biobank have been analysed for a number of emerging chemicals including organophosphate flame retardants, glyphosate, and bisphenol analogues. Planning for the second phase of the study – recruitment of 10-12 year old children – is underway. This study incorporates sex- and gender-based analysis. The project has resulted in new analytical methods for emerging chemicals and will generate new knowledge on cumulative exposure to chemical mixtures and potential health effects in vulnerable populations through various critical life stages that will support risk assessment and risk management policies. (PI: Jillian Ashley-Martin)

Modelling and assessment of short-duration exposures to lead in soil

Lead is a naturally occurring substance found at contaminated sites, and scientific research on human health effects from lead is continuously evolving. Young children are sensitive to harmful effects of lead on their developing neurological systems with effects from childhood exposures lasting a lifetime. To support management of lead at these sites, Health Canada (HC) is investigating methods to assess health risks from lead exposure. As a Federal Contaminated Sites Action Plan (FCSAP) expert support department, HC provides guidance to federal departments on potential risks to human health. Using FCSAP funding, one ongoing effort has been the development of scientific guidance to assess non-cancer effects from short-duration (less-than-chronic) exposures to chemicals. Lead, given its prevalence and the technical challenges with assessing associated risks, proves an interesting candidate for investigation from a short-duration assessment perspective. Preliminary investigation into the applicability of mathematical models to determine blood lead level (BLL) changes was undertaken. This exercise was based on a comparison of varying levels of lead in soil, and subsequent health effects on various age groups. Two pharmacokinetic models from the US EPA (Integrated Exposure Uptake Biokinetic and All-Ages Lead Model) were used to simulate BLLs. The starting lead soil concentration of 140 mg/kg (a withdrawn Soil Quality Guideline), a concentration similar to background soil concentrations in Ontario, was assumed. Keeping total exposure constant (1 or 2 weeks), soil concentrations were increased in increments proportional to the reduction in frequency, with daily exposure assumed as baseline. Modelled changes in BLLs were compared to reference values from European Food Safety Authority (2010), which are based on 1 IQ decrement in children. Preliminary results indicate some dose averaging over a week may be acceptable within certain soil concentration ranges however, further peer review is planned to refine the findings of this study. (PI: Sue-Jin An; Nicole Somers (Inrinsik Corp.))

Multimedia exposure to replacement chemicals of emerging concern and selected CMP3 chemicals

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Several jurisdictions around the world have begun regulating the production, use and importation of various specific chemical compounds [e.g. bisphenol A (BPA), polybrominated diphenyl ether (PBDE) flame retardants, phthalates, parabens and triclosan] that have been shown to exhibit a range of health effects including endocrine disrupting properties. Consequently, many alternative chemicals have been introduced into the market as replacement chemicals; however, their exposure and potential health risks have not yet been assessed in Canada. The goal of this 4-year project is to generate Canadian exposure data for compounds including selected flame retardants, quaternary ammonium compounds, BPA analogues, alternative plasticizers, and alternatives to parabens and triclosan, in environmental and biological matrices, as well as children's products (baby bottles). Where unavailable, new analytical methods will be developed for quantitative analysis. This will be achieved by using archived specimens or new samples of dust, water, urine, serum, follicular amniotic fluid, and placental tissues collected from a variety of populations and residential homes across Canada. Furthermore, biological modeling of some of these chemicals will provide an insight into the relationship between the measured levels in different matrices and estimated daily exposure. The data generated will inform the risk assessment and/or risk management of those chemicals, and may be used to assess potential health outcomes. It can also be used to support the planning of future biomonitoring initiatives including the CHMS. (PI: Cariton Kubwabo)

National Biomonitoring Program under the Canadian Health Measures Survey (CHMS) – Cycles 5-6 (2016-2019) and cycles 7-8 (2022-2025) (CMP M&S)

The National Biomonitoring Program is conducted as a component of the Canadian Health Measures Survey (CHMS), which is a national survey led by Statistics Canada, in partnership with Health Canada and the Public Health Agency of Canada. Through personal interviews and the collection of physical measurements, this ongoing survey provides nationally-representative data on indicators of environmental exposures, chronic and infectious diseases, fitness, and nutritional status. The physical measurements include biomonitoring, the measurement of environmental chemicals or their metabolites in blood, urine and/or hair samples. Health Canada's Population Studies Division is responsible for the National Biomonitoring Program that encompasses planning, collection, quality control, reporting and dissemination, as well as analysis and interpretation of national biomonitoring data. The program establishes baseline concentrations and trends for environmental chemicals of concern in Canadians and help meet the regulatory and public health data needs. Key milestones for the national biomonitoring program during FY 2020-2021 included: 1) publication of the first Report on Human Biomonitoring of Environmental Chemicals in Pooled Samples that included data for persistent environmental chemicals such as dioxins and furans measured in cycles 1, 3, 4 and 5 of the CHMS; 2) drafting of the Sixth Report of Human Biomonitoring of Environmental Chemicals in Canada that includes data for 79 environmental chemicals (e.g. alternate plasticizers and pesticides) collected from CHMS cycle 6 (2018-2019); 3) publication of a key paper introducing exposure load as an approach to quantifying multi-chemical exposure burden at the population level, and another describing associations between exposure to triclosan or bisphenol A and serum sex steroid hormones in Canadians; 4); publication of an online biomonitoring guidance value database and comparison tool (https://biomonitoring.shinyapps.io/guidance/); 5) Refinement of analytical methods for certain chemicals prioritized for biomonitoring in CHMS cycle 7, including a novel method that captures 28 chlorinated paraffin congeners; and 6) Initiation of analysis of the CHMS biobank samples during the CHMS gap year (Jan - Dec 2020) to meet near-term data needs of stakeholders.

Northern Contaminants Program (NCP)

The Northern Contaminants Program (NCP) was established in response to concerns about human exposure to elevated levels of contaminants in wildlife species that are important to the traditional diets of northern indigenous people. The program's main objective is to work towards reducing and, where possible, eliminating contaminants in traditional/country foods, while providing information that assists individuals and communities in making informed decisions about their food use. Biomonitoring and health outcome studies continue to be undertaken to characterize human exposures to, and the health impacts of, environmental chemicals in the northern population. In 2020-2021, five human health project proposals were funded to address exposure to contaminants and links to country foods and nutritional status and the development and evaluation of health communication tools. Along with colleagues in the Health Products and Food Branch (HPFB), staff from the Population Studies Division is leading the human health component of the NCP. The NCP currently provides Canada's main contribution to the contaminants component of the Arctic Monitoring Assessment Programme (AMAP) under the Arctic Council. A Human Health Assessment Group (HHAG) was established under AMAP, through which trend monitoring and assessment of implications and impacts of pollutants on the health of Arctic residents is undertaken. (PI: Cheryl Khoury)

Phase identification of metal oxide nanopowders purchased from on-line distributors

Health Canada is responsible for assessing and managing risks associated with engineered nanomaterials (materials in a size range of 1-100 nanometers). As part of their risk assessment activities,

New Substances Assessment and Control Bureau (NSACB) purchased commercially available metal oxide nanopowders to characterize their physical-chemical and toxicological properties. For metal oxide nanomaterials, identifying the mineral phase and crystallinity is critical for their risk assessment because distinct phases exhibit different solubility and toxicity. Mineral phase identification is usually achieved using powder X-ray diffraction (XRD). This research assists NSACB in their physical-chemical characterization of eight groups of metal oxides (Cu, Ni, Ce, Al, Fe, Mn, Ti and Zn) to complement on-going toxicological studies on the same nanomaterials. The goal is to use powder X-Ray diffraction to identify the mineral phases (crystalline and amorphous) of several nanoforms of each of the priority metal oxides, and estimate crystallite size based on XRD spectral features. By confirming mineral phases, purity and particle size of these nanomaterials, the results of the proposed research will bring to completion the full physical-chemical characterization of the initial 54 nanopowders listed for investigation by NSACB and add value to the toxicological investigations conducted on these nanomaterials. (PI: Suzanne Beauchemin; Pat Rasmussen)

Project Apollo: Assessment of game-based learning digital solutions for optimized environmental health outreach targeting youth

The COVID-19 pandemic has posed challenges for traditional methods of outreach that serve to help people maintain and improve their health. “Building Back Better” is a priority across the federal Government, and expanding digital capacity through use of modern technologies is one of the ways that outreach delivery is being adapted. In particular, game-based learning on digital platforms has been shown to increase user engagement and comprehension. This may offer an effective method for the outreach to youth, which the Government has identified as a priority group. The Regulatory Operations and Enforcement Branch, Environmental Health Program in Ontario, the Transformation Office, and the Canada School of Public Service are collaborating on a project under the Solutions Fund Initiative that will explore the effectiveness and feasibility of game-based learning digital solutions as a tool to increase awareness and motivate behaviour change about environmental health hazards among youth. Digital solution technologies under examination include web-based applications, 360^{o} 3D video production, augmented reality, virtual reality, and mixed-reality. The effectiveness of a solution considers user engagement, and behaviour change; feasibility is evaluated based on financial costs, accessibility, and learning resource supports. The project adopts a human-centred design approach which optimizes system development by focusing on user needs. Methods involve a review of literature and identification of market trends on game-based learning, consultation with behavioural specialists regarding behaviour change measurement, and facilitated group discussions with stakeholders on digital solutions. The assessment will provide suggestions on game-based learning designs and platforms for new and improved outreach to youth. Potential next steps will be to develop digital solution prototype(s) informed by the results of this study. (PI: Joel Kaushansky; Phoebe Tung)

Putting databases together: a study of association between environmental chemical exposure levels and health outcomes

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Chemicals management around the globe has mainly focused on individual or groups of chemicals based on the hazards associated with their chemical properties, and the degree to which individuals or the environment are exposed to those chemicals. Information that has so far been available does not provide sufficient understanding of the impact of exposure to certain chemicals (or groups of chemicals) and the link with specific human disease outcomes. Consideration of an approach beyond looking at chemical exposures but rather looking to links between exposures (single chemical and in combination) and diseases within a

framework that also considers other health factors is therefore warranted. In this study two databases will be linked together by Statistics Canada for the first time: the Canadian Health Measures Survey biomonitoring data for all 5 cycles from 2007-2017 and the Canadian Cancer Registry. Results will be analyzed and recommendations for further study will be made. (PI: Mary Lysyk)

Quantitative read-across using cheminformatics approaches

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Read-across is a common data-gap filling method used in risk assessment of substances that lack data regarding toxicological properties. Generally, it is easier to carry out qualitative read-across for well-defined toxicity endpoints such as mutagenicity and skin sensitization. The challenge begins when one needs to read-across endpoints such as repeat dose toxicity (RDT) or developmental and reproductive toxicity due to the complexity of the mechanism of actions leading to a diversity of adverse outcomes. In a recent collaborative effort, a cheminformatics-based approach was developed through the incorporation of toxicity endpoint-specific information to estimate confidence bounds for the NOAEL (no observed adverse effect level) of a target substance to support read across for RDT in the absence of empirical test data (Yang et al. 2020). This method incorporates not only structural similarity but also biological similarity as well as endpoint specific information. Examples presented in this initial investigation using a database enriched with antimicrobials illustrated reliability of the approach for this chemical space however further work is needed to refine NOEL (no observed effect level) bound estimates and improve the broader applicability. The main objective of this study is to determine how this method performs when applied to a larger set of compounds that are dissimilar to the previous chemical space; bisphenols will be explored as an initial chemical subset. Demonstrating accuracy and characterizing uncertainties of this methodology when applied to diverse groups of chemicals is a critical step toward gaining confidence for further use to support quantitative reading across to complex toxicity endpoints. (PI: Sunil Kulkarni; Chihae Yang)

Refining and deploying a quantitative framework for the analysis and regulatory interpretation of genetic toxicity dose-response data

Genetic damage is associated with numerous human diseases, and chemical screening programs routinely assess genetic toxicity. The results of genetic toxicity tests have traditionally been evaluated using qualitative binning (i.e., yes or no) that merely identifies DNA-damaging agents. However, there is increasing interest in quantitative analyses of genetic toxicity test results, and the use of chemical-specific potency values (i.e., Point-of-Departure or PoD metrics) to determine human exposure limits and assess the likelihood of adverse health effects. Earlier work determined the most suitable PoD metric for routine analyses of genetic toxicity test data and developed a preliminary approach to determine human exposure limits that correspond with negligible likelihood of adverse effect. This research study addresses issues that hinder routine use of PoD metrics, such as the Benchmark Dose (BMD), to assess the likelihood of chemically-induced genetic effects. More specifically, the project uses dose-response data collected from the scientific literature to determine test-specific Critical Effect Size (CES) values. These values, which are also known as Benchmark Response (BMR) values, are required to determine the dose associated with a toxicologically meaningful response; and moreover, to determine the exposure limit associated with minimal risk of adverse human health effects. Analyses of published data is also being used to empirically-determine values for the uncertainty factors used to interpret experimental toxicity assessment data for human health risk assessment. Related analyses of published test data are being used to compare regulatory assessments based on genetic toxicity data with those based on carcinogenicity data (i.e., case studies). The results obtained will be used to develop a

framework for routine quantitative use of genetic toxicity data for regulatory evaluations of new and existing chemicals. Interactions with stakeholders will permit an evaluation of the proposed framework, and international promotion of quantitative methods for regulatory evaluations of genotoxic chemicals. (PI: Paul White)

Regional analysis of CHMS biomonitoring data

The Canadian Health Measures Survey (CHMS), an ongoing national health survey conducted in two-year cycles, collects extensive data on blood and urinary concentration of environmental chemicals that are used to assess chemical exposures in Canadians. Although the data collected is only nationally representative within each cycle of CHMS, combining data from multiple cycles of the CHMS allows calculation of chemical concentrations that are representative at the regional level for the 5 different CHMS regions: Atlantic, Quebec, Ontario, Prairies, and British Columbia. The aim of this ongoing project is to develop statistically robust estimates of concentrations of chemicals at the regional level and secondarily, to explore opportunities for calculation of valid estimates at smaller geographical scales. In the first-ever regional analysis of CHMS data published in FY 2019-2020, blood and/or urinary concentrations of several environmental chemicals for the provinces of Quebec and Ontario, as well as the entire CHMS (representing Canada) minus Quebec, and the entire CHMS minus Ontario were compared. The analysis showed several regional differences in exposures to chemicals and helped assessment of contributing factors. Continued regional-scale assessments under this project will involve additional CHMS regions (e.g. British Columbia), and help relating exposures to regional or point sources of pollutants and/or sociodemographic or lifestyle factors unique to a region. Ultimately, these data may contribute to a regional-scale prioritization of control measures to reduce chemical exposures in Canadians. (PI: Annie St-Amand)

Relative toxic potency of silica and titanium dioxide nanoparticle variants

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. Manufactured nanomaterials (NMs) provide challenges in hazard identification and risk evaluation due to lack of reliable physico-chemical and toxicity data, creating a difficulty for government agencies to establish effective safety evaluation guidelines. Furthermore, engineered NMs are reaching the market through consumer products and applications such as paints, sealants and cosmetics, there are also new reports suggesting that these NMs are found in ambient atmospheres and consequently can have public health implications. The project is designed to address the needs of the risk assessment process for NMs, specifically nanosilica and nanotitanium dioxide, which exhibit the potential to reach the atmosphere and may potentially be harmful to human health and environment. Understanding the toxicity of NMs can also help understand the health outcomes due to components of air pollutants that are in nano size range. In this work, Health Canada investigators, in collaboration with academic and Environment and Climate Change Canada partners, are probing toxicity characteristics of these NMs with varying physical and chemical properties. Influence of composition, size and surface coating characteristics of these NMs on their toxicity in lung epithelial cells and macrophages, and in cells from biopsy samples from healthy and pulmonary diseases (e.g. cystic fibrosis) are being assessed. Oxidizing ability of these particles were determined. Also, uptake of amorphous silica nanoparticles into the macrophage cells were examined. The information obtained from this work will advance our understanding on the health consequences of exposure to NMs, in providing toxicity information to contribute to the risk assessment of these materials (e.g. NSACB), and also can assist in the design of less toxic NMs. (PI: Premkumari Kumarathasan)

Review of available human biomonitoring data to improve the understanding of firefighters' exposures to combustion-derived toxicants of concern

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Firefighters experience elevated risks of cancer and other serious illnesses. Their exposures to chemicals in combustion emissions, including polycyclic aromatic hydrocarbons (PAHs), flame retardants, and PFAS (per- and polyfluoroalkyl substances) are of concern. Some of these substances are known to be able to cause adverse health effects in exposed cells and experimental animals, i.e., they are toxic. To date, the precise levels and routes of firefighters' exposures to these substances is not well understood. This work is collecting and analysing firefighter exposure data from the scientific literature; more specifically, biomonitoring data on the levels of the aforementioned substances in firefighter blood, and/or the levels of substance metabolites in firefighter urine. The work is also collecting and analysing published data on the levels of the aforementioned substances in the firefighters' occupational environment, more specifically, the levels of substances in fire hall dust, in air collected at the fire suppression scene, and on the surfaces of firefighter PPE (Personal Protective Equipment). The data collected to date confirmed that firefighter blood and urine contain the prioritised toxicants and toxicant metabolites, respectively; moreover, that the prioritised substances are present in the firefighting occupational environment. The biomonitoring data are being compared to national biomonitoring surveys in Canada (Canadian Health Measures Survey) and the United States (National Health and Nutrition Examination Survey). Most of the data reflecting the levels of the prioritized substances in the firefighting occupational environment comprise fire hall dust contamination data; these data are being compared with worldwide house dust contamination data. Levels of toxicants in air collected at the fire suppression scene are being compared with urban air contamination values. Analyses of all collected data are currently underway; the results will form the basis for design of a follow-up biomonitoring study of Canadian firefighters. (PIs: Paul White; Rocio Aranda-Rodriguez; Leona MacKinnon; Elyse Bernard; Peter Mochungong; Virginie Bergeron; Catherine Campbell)

Sublethal effects of selective serotonin reuptake inhibitors (SSRIs) in the freshwater snail Planorbella pilsbryi and amphipod Hyalella azteca

The *Food and Drugs Act* (F&DA) Substances Assessment Division within the New Substances Assessment and Control Bureau has been established to conduct assessments of the potential environmental and health risk to the general population associated with environmental exposure to substances in F&DA products such as human drugs, biologics, veterinary drugs, cosmetics, novel foods, food additives, natural health products and medical devices. The goals of this research project were: (1) to develop methods for the extraction and analysis of SSRIs citalopram, paroxetine, fluoxetine, and sertraline; (2) to complete a fate study to determine the stability of the compounds in 6 L aquaria; and (3) to complete short-term studies to determine the toxicity of citalopram, paroxetine, fluoxetine, and sertraline in two native freshwater invertebrates, the File Ramshorn snail *Planorbella pilsbryi* and the amphipod *Hyalella azteca*. To achieve these goals, analytical methods were developed for the analysis of SSRIs in aqueous samples, a 2-week fate study with a mixture of SSRIs of interest was completed, and short-term testing with individual chemicals on snail embryos and juvenile amphipods was completed. These data will be used directly in the environmental assessments of substances listed on the Revised In Commerce List and new substances in products regulated by the F&DA notified under the New Substances Notification Regulations of the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Jane Pappas; Dianne Hughes; Jean Grundy)

Systematic characterisation and preliminary validation of genomics-guided non-animal test models (*in vitro*/*ex vivo*) and methods for nanomaterial safety assessment

Broadly defined, nanomaterials (NMs) are a novel class of man-made substances that exhibit a size range of 1-100 nanometers (one nanometer is one billionth of a meter). While their nano size-associated physical and chemical properties make them attractive for various industrial and consumer product applications, the same properties can complicate their safety assessments. Health Canada (HC) is responsible for regulating products containing NMs in Canada however, an effective risk assessment strategy and appropriate tools for evaluating NM-induced toxicity are not available. While the 'gold standard' for evaluating toxicity of substances involves testing in animals, owing to their time and resource intensiveness, animal-reliant methods are not optimal for NM testing. Thus, the overarching objective of the proposal is to identify and optimise animal alternatives (involving cells derived from animal or human tissues) that are already in development at HC and in other organisations internationally, and demonstrate their relevance and sensitivity to assess NM-induced responses in animal tissues. The optimised tools will be used to generate toxicological data for the effective risk assessment of NMs at HC. The study is conducted in collaboration with New Substances Assessment and Control Bureau of HC, and the results will enhance HC's ability to assess and manage the risks of adverse effects from exposure to NMs in products and the environment. (PI: Sabina Halappanavar)

Systematic meta-analysis and review tools (SMART) in support of science assessments

Science assessments involve the review of large amounts of research data with a view to evaluate the existence of a causal relationship between the exposure and response in question. Like the assessment process, systematic reviews formalize the review process by identifying, determining the relevance of, critically appraising, and extracting data from relevant literature according to a standard protocol. In a meta-analysis, results from individual studies are quantitatively pooled to provide an overall quantitative estimate of the magnitude of association between an exposure and response. Systematic reviews and meta-analyses provide a powerful summary of the weight of evidence which may be particularly informative in assessing the existence of a causal association. In this study, a standard protocol, data management and analysis tools were developed, and as a test case, these tools were applied to evidence from 86 studies linking short-term nitrogen dioxide (NO_2) exposure to ischemic heart disease (IHD) morbidity, and 76 studies of long-term exposure and mortality. Pooling results across these studies showed that short term NO_2 exposure was significantly associated with IHD morbidity, while long term exposure was significantly associated with mortality from all causes as well as specific causes including cardiovascular disease, respiratory disease and lung cancer. The evidence was considered sufficient to infer a likely causal relationship between short term NO_2 exposure and IHD morbidity, while the evidence was considered suggestive of, but not sufficient to infer, a causal relationship between long term NO_2 exposure and mortality. The results highlight the need for additional research to understand physiological mechanisms through which NO_2 contributes to both morbidity and mortality, and to evaluate the role of confounding factors such as other air pollutants, noise and stress. The synthesis tools should prove valuable in future risk assessments. (PI: Dave Stieb)

Testing the effects of selective serotonin reuptake inhibitors (SSRIs) on zebrafish (*Brachydanio rerio*)

The *Food and Drugs Act* (F&DA) Substances Assessment Division within the New Substances Assessment and Control Bureau has been established to conduct assessments of the potential environmental and health risk to the general population associated with environmental exposure to substances in F&DA products, and to integrate innovative science into the risk assessment and risk management of new substances. There are eleven Selective Serotonin Reuptake Inhibitors (SSRIs) on the Revised In

Commerce List (R-ICL) which have been identified as priorities for risk assessment and grouped together as they are known to have the same mode of action. The goals of this research study are to evaluate zebrafish models that, when combined, could provide information on the potential consequences of long-term exposure to environmentally-relevant levels of five different SSRIs from a higher (systems) perspective. A robust model that tests multiple physiological parameters has been developed, including growth, behaviour, fecundity, bioaccumulation and changes in gene expression that can be used to assess the fitness of juvenile and adult fish following chemical substance exposure. These data will be used directly in the environmental assessments of substances listed on the R-ICL and will be used to scope the feasibility of a cumulative risk assessment process for substances notified under the New Substances Notification Regulations of the *Canadian Environmental Protection Act, 1999* (CEPA), in support of a Chemicals Management Plan Post-2020 initiative. (PI: Dianne Hughes; Jane Pappas; Jean Grundy)

The impact of dissolution behaviour of metal oxide nanomaterials on toxicological response

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials (materials in a size range of 1-100 nanometers). The New Substances Assessment and Control Bureau (NSACB) has identified metal oxide nanomaterials as high priority for assessment under the CMP. The toxicological behavior of nanomaterials (NMs) is closely associated with their distinct physical-chemical properties. This research is investigating the influence of dissolution behaviour of NMs on their toxic potential. The term "dissolution behaviour" includes solubility as well as changes in suspension stability (e.g. size, agglomeration/aggregation, surface area, and surface charge) of NMs dispersed in different aqueous media. Although NM solubility has been recognized as one of the key properties that must be determined for accurate categorization of toxicological potential, standardized solubility test methods for nanomaterials are lacking. This study focuses on eight groups of metal oxides determined by NSACB to be in commerce in Canada (copper, nickel, zinc, titanium, iron, manganese, cerium and aluminum), many of which are used in consumer products to which Canadians are regularly exposed. The study investigates solubility of eight individual metal oxide NMs and determine the impact of solubility on their toxicity using toxicogenomics tools (to investigate the changes in the expression of all genes simultaneously). In addition, environmental releases of metal oxide and metallic NMs used in the automobile industry (e.g. iron oxides and platinum) will be investigated using road dust samples collected from the expressway network in the City of Toronto, providing a realistic exposure scenario. The results of the proposed research will inform HC risk assessments and will help HC meet its commitments associated with the Organisation for Economic Cooperation and Development (OECD) Working Party on Manufactured Nanomaterials (WPMN). (PI: Pat Rasmussen; Sabina Halappanavar; Suzanne Beauchemin)

Toward risk assessment modernization - A new approach methodology based integrated approach for screening potential genotoxic chemicals

New Approach Methodologies (NAMs) are emerging approaches or tests, considered to be synonymous with alternative test strategies, that can inform chemical risk assessments in the absence of traditional toxicity data. Currently, there are substantial international efforts to develop NAM-based approaches that provide information related to regulatory endpoints. The aims of this project are to provide support for applying *in vitro* genetic toxicity data, with a novel data analysis and interpretation framework, in future priority setting initiatives and quantitative risk assessments of organic chemicals. In this study, assessment will be based on the results of a high throughput *in vitro* test battery currently being developed by collaborators within Environmental Health Science and Research Bureau. The test battery consists of higher throughput versions of well-established genetic toxicity assays, some of which are functionally related to established OECD test guidelines. The development of this NAM-based approach

will begin with the assessment of over 30 data-rich reference compounds with *in vitro* genetic toxicology data made available by international collaborators. An in-depth case-study is being conducted to scrutinize the utility of the NAM-based approach for risk assessment and regulatory decision-making. Specifically, *in vitro* to *in vivo* extrapolation will be coupled with assay results to establish administered dose equivalents, which will be compared to human exposure estimates and points of departure from traditional animal studies. Once established, this integrated approach could be used for routine chemical screening and future risk assessments. (PI: Marc Beal; Paul White)

Uptake rates of silicone based personal sampling devices – Proof of principle

The Chemicals Management Plan (CMP) aims to assess the risks to human health posed by thousands of chemicals but only a fraction of these chemicals have known human exposure data. It has been evident from previous assessment cycles that changes to priority setting paradigm must be made in order to assess chemicals more effectively and to identify potential triggers for future assessments. There has been extensive work in the environmental analysis and biomonitoring front, but personal exposure has been overlooked. Unlike biomonitoring, personal exposure can provide dosimetry data. The use of personal passive sampling devices (PSDs) are limited to those compounds that can be measured at environmental concentrations but often require longer sampling periods, thus limiting the practical wear time or number of subjects that can be monitored. In recent years, there has been a growing interest in using silicone PSDs for monitoring indoor air and water. In a study carried out at Oregon State University, a wide range of chemicals absorbed on silicone wristbands (SWs) worn by 22 participants were identified. However, the main limitation in the published work was the lack of uptake rate values, the constant contact between SW and skin, surfaces and clothing. Without the uptake rate, the concentration found in the SW cannot be translated to the environmental concentration or exposure estimation, which restricts the use of these data for risk assessment. Our project aims to fill current data gaps in the determination of uptake rates in different sorbent materials: silicone (use as wristbands, SW); and new material developed at North Caroline State University (CIPS). In addition, silicone wristbands will be deployed during firefighters training exercises in order to assess their exposure to polycyclic aromatic hydrocarbons (PAHs). (PI: Rocio Aranda-Rodriguez)

Use of gene expression profiles to facilitate read-across for 24 priority PFAS

Per- and poly-fluoroalkylated substances (PFAS) are a large class of man-made chemicals that are ubiquitously found in the environment due to their wide variety of industrial and commercial uses, their persistence and their high mobility. There are concerns for PFAS exposure through environmental media (e.g., water, soil, foods) to cause potential adverse health effects including liver and kidney toxicity, increased cholesterol levels and delays in mammary gland development. Although there is a growing body of knowledge on PFOS (perfluorooctanesulfonic acid) and PFOA (perfluorooctanoic acid) toxicity, there is little known about the many other PFAS. Health Canada has identified toxicity testing for PFAS as a research priority. To date, >3,000 PFAS have been identified; it is recognized that not all PFAS can be tested to develop health-based values. Therefore, Health Canada compiled a list of 24 PFAS that best represent variability in chemical composition across PFAS and importantly, have been found in Canadian drinking water or have analytical methods for detection in drinking water. Acquiring information on data poor substances for risk assessment has been challenging for regulatory agencies worldwide, including Health Canada, due to the cost and length of traditional toxicological research. In an effort to accelerate the pace of risk assessments, the international toxicology and risk assessment communities are investing in case studies to demonstrate the utility of new approach methodologies (NAMs) that are cost/time effective in chemical evaluations. This research employs gene expression profiling in human liver cells in culture to facilitate assessment of various PFAS. Objectives include: 1) applying gene expression data to

acquire mode of action and potency information on poorly studied PFAS ; 2) to explore how PFAS behave in mixtures; 3) to use the data as a case-study for the use of NAMs in risk assessment. (PI: Carole Yauk (University of Ottawa); Ella Atlas)

Use of new approach methodologies to facilitate potency ranking and evalute mode of action for 25 bisphenols

BPA is an endocrine disrupting chemical (EDC) that is the topic of both regulatory and public concern. Its use has been banned from products available to consumers, including baby bottles (Canada) and thermal paper (European Union). These bans have led to increased use of BPA alternatives as replacements, many of which are chemically similar. BPA and alternatives were examined using New Approach Methodologies (NAMs) that integrate *in silico* and *in vitro* methods. BPA's cellular effects occur primarily through its interaction with the estrogen receptor (ER). When active, the ER interacts with the DNA to modify gene expression. Therefore, changes in gene expression represent BPA's earliest toxicological effect on the cell that can be reliably measured. Here, 25 BPA alternatives, were assessed for: i) general systemic toxicity (hazard-independent) that does not predict the potential of specific adverse effects; and ii) estrogen receptor (ER) pathway-specific expression of genes related to the ER pathway. The objectives are: (1) to expose human mammary epithelial cells (MCF7 cells) to an extended dose range of known BPA alternatives; (2) to measure changes in gene expression; (3) to perform dose response modeling and potency ranking of these substances relative to BPA and estradiol; and (4) compare these outcomes to current estimates from *in vivo* (i.e., animal) studies. In doing so, a weight of evidence approach combining both *in silico* predictions and *in vitro* data will be used to characterize the potential hazards and compare relative potencies within this group of 25 substances. These data have contributed to the development of an Integrated Approach to Testing and Assessment under the OECD Working Party for Hazard Assessment (WPHA), which has the overarching goal to advance the application of New Approach Methods (NAMs) in prioritization and risk assessment. (PI: Tara Barton-Maclaren; Ella Atlas).

Validation of the zebrafish (Brachydanio rerio) model as an *in vitro* NAM for the assessment of chemicals for endocrine disruption and general toxicity

The *Food and Drugs Act* (F&DA) Substances Assessment Division within the New Substances Assessment and Control Bureau has been established to conduct assessments of the potential environmental and health risk to the general population associated with environmental exposure to substances in F&DA products, and to integrate innovative science into the risk assessment and risk management of new substances. In 2018, given the momentum of the international regulatory community to eliminate animal testing in chemical risk assessment, Health Canada, in partnership with National Research Council (NRC) Canada, initiated research to develop the zebrafish model as a potential alternative to the rodent model for generating data for chemical risk assessments. Using 20 test compounds, the goal of this research project is to: develop a model to evaluate general toxicity using traditional biomarkers (e.g., morphological, tissue and behavioral changes) as well as novel markers such as changes in gene expression (transcriptomics). Additionally, methods to assess the kinetics of absorption, distribution, metabolism and excretion (ADME) have been developed and 10/20 test compounds have been evaluated. In order to further develop the model to evaluate chemicals for endocrine disruption, a platform was developed using traditional tissue markers (melatonin, cortisol, norepinephrine) and an evaluation of gene expression changes using transcriptomic testing. Integral to this work is collaboration with the international zebrafish research and regulatory community. These data will be used to validate the zebrafish New Approach Methods (NAMs) as predictive tools in assessing the toxicity of substances

notified under the *New Substances Notification Regulations* of the *Canadian Environmental Protection Act, 1999* (CEPA). It will also be used to facilitate the 3Rs (reduction, refinement, and/or replacement of animals in toxicity testing) in chemical risk assessment. (PI: Cindy Woodland; Jean Grundy)

Pesticides

Estimating pesticide concentrations in cranberry flood water

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for pesticide regulation in Canada under authority of the *Pest Control Products Act* (PCPA). Cranberry production in Canada has been increasing, and, with it, requests for registering pesticides for use on cranberries. Cranberry production is a unique combination of relatively wet and dry processes. Cranberry bogs must be well-drained, but also occasionally flooded, as most are harvested by flooding. Thus, cranberry bogs are usually constructed in layered structure - peat over sand with drainage tiles on the bottom. Cranberries also require highly acidic soil (pH 4-5). With high organic carbon contents, desorption, particularly after aging, becomes an important factor to consider. Common methods used for estimating environmental concentrations (EECs) of pesticides in surface waters from runoff from agricultural lands are not suitable for estimating concentrations in cranberry floodwater. The PMRA developed a simple model to estimate pesticide concentrations in cranberry floodwater and post-flood drainage. The model uses the calculations found in the US EPA's Variable Volume Water Model (VVWM) and Pesticides in Flooded Agriculture (PFAM) models. It considers degradation in soil and floodwater, transfer of pesticide from soil to floodwater and pesticide in post-flood drainage, and allows routing the floodwater through several cranberry bogs. Furthermore, using azoxystrobin and chlorantraniliprole as representative pesticides and in collaboration with a cranberry farm, the PMRA conducted aged sorption/desorption laboratory studies and analyzed soil and water samples throughout the 2019 growing season. Water samples were collected daily during flooding and from drainage pipes during growth and after flooding. The model was tested using the measured desorption parameters and soil pesticide concentrations prior to flooding. Other model parameters were set to default values, which are the same as those used in VVWM and PFAM for surface water estimations. The model predicts a transfer of pesticide from field to floodwater comparable to that measured in the field. (PI: I. Kennedy; L. Gui; C. Hart)

Health Canada's Pest Management Regulatory Agency: Results of a multi-year analysis on dermal absorption

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for pesticide regulation under authority of the *Pest Control Products Act* (PCPA). Using a multi-stakeholder and collaborative approach, the PMRA has been involved in a multi-year analysis related to dermal absorption. The onset of this initiative led to the development of a position paper on the use of *in vitro* dermal absorption data for health risk assessments. This paper also outlined the Triple Pack approach of combining data from *in vivo* rat, *in vitro* rat, and *in vitro* human data and using this to estimate a human dermal absorption factor for health risk assessments. Subsequent work resulted in a streamlined *in vivo* dermal absorption test guideline that detailed how to reduce animal use and cost, while maintaining scientific integrity and utility for risk assessment purposes. Standardization of the data requirements resulted in the submission of studies that were of better quality, thereby allowing the PMRA and other experts to undertake a retrospective analysis. The outcome of this analysis was published in the Journal ALTEX: Alternatives to Animal Experimentation, and has now demonstrated that the routine requirement of an *in vivo* study to characterize dermal absorption may be replaced by *in vitro* data. (PI: K. Irwin; S. Ramji)

Modelling efficiency of a vegetative filter strip at mitigating pesticides in surface runoff

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for pesticide regulation in Canada under authority of the *Pest Control Products Act* (PCPA). General guidance to mitigate pesticide runoff from treated areas into aquatic habitats appears on all product labels with outdoor uses, with the exception of registered uses where exposure from runoff is not expected (for example, insect baits and greenhouses). The PMRA recognizes the potential for a Vegetative Filter Strip (VFS) to help protect aquatic organisms in waterbodies from exposure to certain pesticides through runoff. Vegetative filter strips are bands of non-cropped grassy land (that may also include shrubs, trees, or other vegetation) between treated fields and water bodies. A computer model for simulating a VFS was integrated into current models used to estimate pesticide exposures through runoff. The ability to model the effectiveness of a VFS allows rapid initial assessments without the burden of expensive and time consuming field experiments. Computer simulations, which estimate the effectiveness of a VFS to reduce pesticides in runoff for a range of agricultural regions in Canada, have demonstrated the importance of strip width and soil properties. Most commercial and domestic class pesticide labels for products used outdoors recommend including a VFS between the treated area and the edge of a water body to reduce contamination through runoff. For certain pesticides, commercial class product labels include the requirement for a mandatory VFS of at least 10 metres wide that must be constructed between the field edge and adjacent, downhill aquatic habitats to protect aquatic organisms from pesticide runoff. The decision to make the VFS mandatory on certain products includes consideration of the physicochemical properties of the pesticide. Currently, the presence of a VFS is not considered during evaluation of the amount of a pesticide that may enter drinking water sources. (PI: J.N. Westgate; M. Whiteside)

Refining pesticide health risk assessments for workers in the greenhouse environment

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for the federal regulation of pesticides in Canada. The *Pest Control Products Act* provides the legislative framework and corresponding policies, and guidance documents provide additional details on the data requirements for determining the safety of these products to both human health and the environment, and also that these products have value when used according to label directions. Only pest control products that have acceptable risk are registered for use in Canada, which includes products that will be used in a greenhouse. In a greenhouse environment and after a pesticide is applied to a crop, greenhouse workers can be exposed to the pesticide residue that remains, due to crop contact from post-application hand labour activities such as pruning, thinning, or harvesting. In turn, PMRA collaborated with the Agriculture and Agrifood Canada's Pest Management Centre and industry to determine if a standardized daily rate of residue decline could be established for greenhouse crops. This rate of decline value could then be used in pesticide risk assessments for greenhouse workers, to more accurately assess their exposure to a pesticide following application to either ornamental and vegetable crops. Having this value is an important aspect in determining the length of time that must elapse before a worker can safely conduct the necessary hand labour tasks on treated crops. (PI: K. Parsons; J. Selwyn; C. Moase)

Regulatory use of exposure task force data

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for the federal regulation of pesticides in Canada. The *Pest Control Products Act* provides the legislative framework, and corresponding policies and guidance documents provide additional details on the data requirements for determining the safety of these products to both human health and the environment, and also that these products have value when used according to label directions. Only pest control products that have acceptable risk are registered for use in Canada. The PMRA data requirements for human health risk

assessments includes studies to assess the degree and nature of exposure to specific human populations, such as workers and children. These data requirements can be addressed using chemical-specific exposure studies. On the other hand, scientific methodology that allows exposure studies conducted with one pesticide to be used for the assessment of many pesticide active ingredients in a generic manner, such as handler exposure studies, is another option. Much of the generic exposure data has been developed by experts who have formed exposure task forces. The regulatory input on the various protocols is incorporated throughout the process in a collaborative and scientific manner. Overall, this has resulted in a large, comprehensive, and modern collection of data, and has been an efficient mechanism for developing data required for pesticide submissions. It has also allowed pesticide regulatory authorities, such as the PMRA, to use these studies, when applicable, in lieu of chemical-specific data. (PI: C. Vizena; T. Satchwill; S. Ramji; I. Pilote)

Update on the Pest Management Regulatory Agency's approach to non-animal testing

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for the federal regulation of pesticides in Canada. The regulatory review of pesticides, in Canada and internationally, currently relies primarily upon animal studies. Over the years and as a means to reduce, refine and/or replace existing animal studies, non-animal based alternative approaches have and continue to be developed. The Canadian regulatory framework for pest control products has sufficient flexibility to allow for incorporation of validated alternative approaches such as: in silico methods ([quantitative] structure activity relationship ([Q]SAR) models), integrated approaches to testing and assessment (IATA), adverse outcome pathways (AOPs), and Tox21 and RISK21 approaches. More recently, consideration of new approach methodologies (NAMs) has also come to the forefront and this has reignited discussions on the current pace of incorporation of alternative methods in existing regulatory approaches for chemicals, which includes pesticides. As global acceptance of such approaches highlights the importance of having internationally recognized technical guidelines, such as those developed by the Organisation for Economic Co-operation and Development (OECD), the PMRA continues to be actively involved in several, ongoing multi-stakeholder initiatives. Given the importance of human safety and protection, when considering alternative approaches, robust scientific scrutiny of these methods is necessary so to help facilitate their adoption for regulatory purposes. (PI: Y. Bhuller; D. Ramsingh)

Pharmaceutical Drugs

DQSP: A program that monitors quality of pharmaceutical products on the Canadian market

As part of Health Canada's mandate to ensure the health and safety of Canadians, every year the Health Products (HP) Laboratory Program collects and tests pharmaceutical products that have a Drug Identification Number (DIN) under the Drug Quality Surveillance Program (DQSP). The purpose of the DQSP is to ensure the quality of pharmaceutical products on the Canadian market through testing the quality of the products, and by verifying the methods used by the company to control product quality. Besides ensuring the health and safety of Canadians, the DQSP is required to fulfill Health Canada's obligations to conduct drug quality surveillance under our Mutual Recognition Agreements with other countries. The program has operated for decades, with the selection strategy for products to be tested more recently transitioning to a risk-based approach. The new risk-based selection criteria consider newly marketed products (75%), risk intelligence from partners (15%), and random selection (10%) to ensure that any marketed DIN product could potentially be sampled and tested. It covers risk factors that are hidden or not otherwise explicitly included in the other models. This new model is similar to the US FDA's DQST Drug Quality Sampling and Testing Program and includes practices from the European

Medicine Evaluation Agency (EMEA). Over the last seven years, the HP laboratories have tested more than 580 finished products and active pharmaceutical ingredients. When a product is found to have deficiency (5% of them), work is done in close collaboration with ROEB inspectors to implement compliance and enforcement activities. HC's Health Products Laboratories receive funds through cost recovery fees (DELS) in support of the pharmaceutical drugs departmental priority. (PI: Josée Trudel)

Inter-laboratory study of nitroso-compound determination in angiotensin II receptor blocker (ARB) drugs

Health Canada has a mandate to ensure the health and safety of Canadians and provide regulatory oversight of the Canadian pharmaceutical drug supply. In fulfilling this role, the Department and its international regulatory partners became aware of high levels of nitrosamine impurities in Angiotensin II Receptor Blockers (ARB) products (which relax veins and arteries to lower blood pressure) in the global supply chain. Since then, nitrosamine impurities have been found in several other drugs on the Canadian market including ranitidine, metformin, varenicline, amitriptyline, etc.. As nitrosamines are generally considered quite toxic, their presence in human pharmaceutical products are a major concern for international regulators. For example, the nitrosamine impurity N-nitrosodimethylamine (NDMA) which was detected above acceptable limits in multiple products on the Canadian market is classified as "probably carcinogenic to humans". This study was proposed by the US FDA and was presented to the Nitrosamine International Strategic Group. Six laboratories from various countries (Australia, Switzerland, Ireland, France, Germany, US, and Canada) agreed to participate in the study; the goal of which is for each participating laboratory to test an identical set of samples using their own analytical methods in order to: i) assess the observed variation in results generated by their different analytical methods; ii) identify the factors that contribute to these variations, and; establish performance criteria for measuring nitrosamines in ARB Drugs. The results of this study should prove useful to manufacturers of pharmaceutical products and the regulatory community by helping them development sensitive, accurate and robust methods (or improve current methods) for testing of toxic nitrosamine impurities in potentially any human pharmaceutical. Hence, this project is directly related to Health Canada's mandate and aims to prevent and reduce risk to individual health by helping to ensure that the method of analysis for nitrosamines are suitable for their intended use. HC's Health Products Laboratories receive funds through cost recovery fees (DELS) in support of the pharmaceutical drugs departmental priority. (PI: Y. Su)

Rapid confirmation of Burkholderia cepacia complex by molecular method

One of the mandates of Health Canada is to be a leader in compliance and law enforcement by protecting and informing Canadians against associated health risks with products, substances and the environment. One of which is post-marketing surveillance that is carried out in chemistry and microbiology laboratories. In recent years, health products have been recalled in Canada and the United States following microbial contamination by a group of bacteria called Burkholderia cepacia complex (Bcc). Bcc is a group of bacteria that are commonly found in the environment (soil, water, plants). Member strains of this complex can be opportunistic pathogens primarily affecting immunosuppressed individuals, especially people with cystic fibrosis. The Bcc complex so far includes 23 genetically closely related species. Members of the Bcc group are capable of forming biofilms, are resistant to disinfectants and are frequent contaminants of water systems. They are therefore problematic for liquid pharmaceutical products. No rapid method has yet been developed to detect these microorganisms in health products. The microbiology laboratory project consisted of validating a proposed rapid confirmation protocol by molecular method (PCR) of member isolates of Burkholderia cepacia complex. The method has been tested and validated on 59 isolates from various clinical and environmental

sources. The developed method will be submitted for scientific publication. The HC's Microbiology Laboratory receive funds through cost recovery fees (DELS) and A-Base in support of the pharmaceutical drugs, natural health products and cannabis priorities. (PI: Karine Lebel)

Radiation Protection

A better understanding of radon dosimetry through indoor aerosol characterisation and computational simulation

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Radon is the second leading cause of lung cancer, after smoking. Although the guideline for radon exposure in homes is expressed as the concentration of radon gas, it is actually the short-lived radon progenies that deposit most of the energy that contributes to the radiation dose. The majority of the radon progenies attach to particulate matter; deposition in the lung, therefore, is dependent upon particle concentration and relative size distribution. In this study, measurements of indoor aerosol characteristics relevant to radon dosimetry, such as radon progeny concentration, equilibrium factor, unattached fraction, and radon progeny particle size distribution will be carried out. These characteristic parameters will be used in conjunction with a radon dosimetry computational simulation tool to calculate radiation dose to lung. The knowledge generated from this project will improve our ability to assess residential radon dose and associated risk. (PI: Baki Sadi)

An assessment of uncertainty using two different modelling techniques to estimate the cost effectiveness of mitigating radon in existing housing in Canada

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Long-term exposure to radon gas is the second leading cause of lung cancer, after smoking. In Canada, it was estimated for 2016 that 34% of lung cancer deaths attributed to radon in women and 27% in men. A previous analysis demonstrated that mitigation of high radon levels in existing housing in addition to reducing radon ingress in new housing is only cost effective where regional radon levels are high; therefore, it was important to assess the sensitivity of the cost effectiveness estimate to parameter uncertainty. The cost-utility analysis is a secondary analysis that incorporates many different published datasets to model the costs and the benefits of a health intervention. This analysis was focussed on evaluating the uncertainty associated with the estimates of cost effectiveness of interventions to reduce residential radon in existing housing only, according to the choice of model used, the rate of radon testing and mitigation in existing housing, the renewal rate of the housing stock, and the distribution of the number of residents per dwelling. The results showed that the cost effectiveness would improve at increased rates of testing and mitigation of existing housing. The estimates were not sensitive to the choice of model used, nor to the housing renewal rate, nor to the increase in one person households and decrease in two-person households reported recently for Canada. Based on the study findings, recommendations to home owners to test and mitigate high radon concentrations in existing housing are strengthened. Policy options and communication of these results to the public will be explored to encourage homeowners and thereby increase the rates of radon testing and mitigation. (PI: Janet Gaskin, NRC; Jeff Whyte, University of Ottawa; Doug Coyle)

Assay development for biological dosimetry

Health Canada has a mandate to support emergency response and the National Biological Dosimetry Response Plan, linked to the Federal Nuclear Emergency Plan. In the case of a nuclear/radiological event it is imperative to quickly identify exposed individuals for the purpose of medical intervention, and to identify first responders who must be restricted from further exposure. Even for a lesser-scale event, many concerned members of the public will seek an assessment of their radiation exposure. The assessment of radiation dose is called dosimetry and when biological material is used for this dose assessment, it is termed biological dosimetry. This research involves the development of imaging flow cytometry methods for high throughput biological dosimetry. In addition, genomic, proteomic and metabolomic endpoints are being examined as new biomarkers for radiation damage to estimate the dose of ionizing radiation absorbed by an individual. (PI: Lindsay Beaton)

Assessing the impact of new strategies for communicating radon gas health risk, testing, and mitigation information to Canada's younger age demographic

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. This study, conducted by Evict Radon, involves the development, execution, and evaluation of multiple new communication strategies designed to increase radon awareness, promote radon testing, and encourage mitigation of radon risk for Canadians between the ages of 25-38. Evidence suggests that current radon awareness strategies are not effectively reaching younger Canadians. Data collected in previous studies indicate that communication tactics such as print media, and/or media cycle approaches work well with older age groups, but not well with younger populations (ages 25-38). There is a need to find the best communication strategy for these demographics that can help Health Canada to enhance the effectiveness of radon education and awareness. Younger Canadians are more likely to respond to advice obtained via peer-to-peer recommendations, delivered through transitory stories, and posts on social media platforms. A minimum of three different communication strategies will be piloted during the fall of 2020 and 2021. For each communication strategy, awareness uptake, psychosocial, and behavioural data will be complied, and a detailed demographic survey of participants will be completed. This study will contribute the on-going task of informing Canadians about the health risk of radon gas. It will also contribute to developing awareness campaigns in the future. (PI: Madison Pecoskie (Evict Radon); Dr. Goodarzi (University of Calgary))

Assessment of radon mitigation strategies in the Canadian environment

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Exposure to indoor radon is the leading cause of lung cancer among non-smokers, and the second-leading cause among smokers. Radon enters a home as radon gas and quickly decays through a series of short-lived radioisotopes. Health Canada and the National Research Council's (NRC) Ventilation and Indoor Air Quality Group of the Construction Portfolio collaborate closely on radon mitigation studies. Ongoing work focuses on evaluating the performance of full vertical passive stack mitigation systems in specialized testing facilities and in homes ("field studies"). Preliminary results, including field studies conducted in the National Capital Region, indicate that these are effective radon reduction solutions under test conditions. In this study, field studies will be conducted in different regions in Canada to investigate the impacts of different climatic factors (e.g., indoor and outdoor temperature, relative humidity, air pressure), geographic conditions and construction patterns on the performance of the systems. Testing will be conducted in both the summer and winter seasons. This research supports national radon mitigation guidance and standards and will

inform future revisions to the National Building Code. (PI: Zhou Liang Grace [National Research Council] Michel Gauthier; Adelene Gaw)

Atmospheric nuclear forensics capability advancement project (ANFCAP)

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities of a nuclear emergency. In a collaborative effort to improve Canada's ability to deduce the origin and nature of global nuclear activities, eight partner institutions have launched a multi-faceted project to address any gaps in Canada's nuclear forensic capabilities. Under the ANFCAP project, Health Canada (HC) leads the measurement and instrumentation stream that will commission state-of-the-art radiation detection systems in three different laboratories, each specializing in the measurement of specific types of radioactivity. These include: (1) a multi-detector system at Health Canada specializing in the measurement of radioactive noble gases, (2) a dual-detector system at the Canadian Nuclear Safety Commission (CNSC) Laboratory aiming to unscramble the complex signals from special nuclear materials, and (3) a dual-detector system at the Sudbury Neutrino Observatory Laboratory (SNOLAB), where the deep underground location enables the detection of the smallest traces of radioactivity. These systems aim to push the limits of detection of rare radioisotopes indicative of nuclear events and provide crucial information on the licit or illicit nature of the underlying activities. These advancements will dramatically enhance Canada's capability to monitor for any indications of nuclear activity, fulfilling Health Canada's mandate to protect Canadians from the radiation exposure risks posed by global nuclear threats, and further support Health Canada's obligations under the Comprehensive Nuclear-Test-Ban Treaty) (PI: Pawel Mekarski; Nadereh St-Amant [CNSC]; Jeter Hall [SNOLAB])

Biomarkers for exposure to low doses of ionizing radiation

Health Canada acts, on request, as the principal health advisor to other federal departments and agencies on occupational and public health matters related to radiation safety as part of Health Canada's mandate to protect the health and safety of Canadians. CCRPB (Consumer and Clinical Radiation Protection Bureau) conducts research to support Health Canada's advice on radiation health impacts based on state-of-the-art science. Currently, it is assumed that the health risks resulting from radiation exposure are linearly proportional to dose without a threshold. However, the scientific knowledge emerging over the last decades clearly indicates that biological effects and the underpinning risk for human adverse health outcomes at doses below 50-100 mGy is uncertain. This includes radiation effects related to chronic and acute exposures, low and high doses and varied dose rates. There is also lack of clarity on the effects from different radiation qualities and how they impact different organs, tissues and induce cellular damage eventually leading to cancer and other adverse outcomes. It is widely recognised that more mechanistic research is needed to help address and reduce uncertainties at low doses. This study is investigating the biological effects of low-dose radiation; it exploits "omics" (e.g. proteomics, genomics) technology, a validated tool in biological research to generate new knowledge regarding the shape of the dose-response relationship; identifying key mechanistic pathways and threshold doses at which these pathways are activated and how they differ with radiation qualities and biological tissues. The results will feed into the related activities of developing of Adverse Outcome Pathway for ionizing radiation. A better understanding will provide a more biologically meaningful basis for reliable health risk estimation essential for a robust system of radiation protection. (PI: Vinita Chauhan)

Cost effectiveness analyses of interventions to reduce residential radon exposure in Canada

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. The inhalation of radon poses a risk to human health and long-term exposure to radon is the second leading cause of lung cancer, after smoking. This work estimates the incremental cost effectiveness ratios for the 2012 populations in Canada, each province/territory, and 17 census metropolitan areas, for practical radon mitigation scenarios to reduce residential radon exposures. Sixteen intervention scenarios compare radon mitigation implemented at differing rates in new and existing housing relative to preventive measures installed at construction, using three different radon mitigation thresholds. A period life-table analysis, a secondary data analysis, was conducted using data derived from two recent Canadian radon surveys, along with Canadian mortality and quality of life data. Analyses adopted a lifetime horizon and a discount rate of 1.5%. Results of the work to date indicate that reducing radon ingress in new construction is cost effective across Canada, and expanding the intervention to also include the mitigating of high radon levels in existing housing is cost effective where regional radon levels are high. This information on the cost per unit health benefit estimated to result from an intervention will be used to prioritize strategies for reducing the burden of radon-induced lung cancer in Canada. (PI: Janet Gaskin; Jeff Whyte (NRC); Doug Coyle, Nicholas Birkett, Daniel Krewksi (University of Ottawa))

Development of a reference dosimeter for separating the neutron contribution from the other cosmic ray components

The Radiation Protection Bureau (RPB) has a long-standing commitment to protect and promote the health of Canadians from ionizing radiation exposure in daily living and working environments. For almost two decades, RPB has been operating a Fixed Point Surveillance (FPS) network for monitoring radiation exposure and the associated health risks arising from man-made sources and naturally occurring radiation materials. The network is comprised of more than seventy 3”x3” sodium iodide (NaI) gamma spectroscopic dosimeters distributed across Canada and the recorded energy spectrum below 3MeV has been used for radiation identification and dose estimations. The FPS network’s potential as a cosmic dose monitoring system has recently been explored by using the recorded count rate above 3MeV. The observed counts at various FPS locations were found to correlate well with the theoretical cosmic doses in which the geographical and solar cycle effects were included. The result suggested that the FPS network can be used to monitor not only terrestrial radiation but also cosmic radiation if well calibrated. To become a cosmic ray dose monitoring system, the FPS network has to be experimentally calibrated by a reference dosimeter. For this purpose, Tissue Equivalent Proportional Counter (TEPC) is proposed as a reference dosimeter to calibrate the recorded FPS cosmic ray count rate to H*(10) dose rate. TEPC has been widely used for cosmic ray dose estimation at high altitude (e.g at commercial aviation level or international space station) and is capable of separating the neutron contribution from the other cosmic ray components. As a reference dosimeter, the TEPC instrument itself has to be calibrated; conducted in various exposure scenarios (gamma, neutron, mixed field, high energy neutron field). The calibrated TEPC instrument will then be used to perform side-by-side measurement with our FPS detectors to calibrate the count rates. It has participated in a boat survey, comparing/calibrating multiple types of detectors. (PI: Weihua Zhang)

Development of an adverse outcome pathway (AOP) relevant to uranium induced kidney toxicity

Uranium is a naturally occurring radioactive element as well as a heavy metal. Biological and health effects of uranium have been attributed to both its radiological and chemical toxicity. While the majority of the published studies indicate uranium toxicity is primarily due to chemical damage to the kidney,

other *in vitro* and *in vivo* experiments show genotoxic effects that could be attributed to both chemical and radiological toxicity. Due to potential occupational exposure in the uranium-based nuclear fuel cycle, environmental exposure from mining and other industrial activities and chronic exposure through drinking water, especially in communities served by underground well water, adverse health effects of uranium is a concern to risk assessors and regulators in both radiological and chemical communities. The objective of this project is to define an adverse outcome pathway (AOP) relevant to uranium-induced kidney toxicity for submission to the Organization for Economic Co-operation and Development (OECD) Extended Advisory Group on Molecular Screening and Toxicogenomics (EAGMST). (PI: Baki Sadi)

Domestic radon exposure and childhood leukemia: a population-based study in Canada

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Long-term exposure to radon gas is recognized as an important cause of lung cancer. This study examines the possibility, first raised using a data set collected in the 1970s, or a possible link between average radon concentrations in the home and the incidence of childhood leukemia and lymphoma in Canada. Following the launch of the National Radon Program in 2007, Health Canada completed a long-term radon survey in 33 census metropolitan areas (CMAs), which covers about 70% of the Canadian population. Data obtained was examined alongside leukemia and lymphoma incidence rates among children (0 - 14 years of age) in the past decade (2006-2015), exploring linkages between city-level average radon concentrations and leukemia and lymphoma incidence rates in 33 major Canadian cities. Analyses were conducted for 6 subtypes of leukemia and lymphoma. Estimated exposures of red bone marrow to domestic radon were low and no associations were found between radon exposure at home and an increased risk for developing leukemia among children under 15 years of age living in the CMAs. These result add to the body of evidence indicating no significant correlation between radon exposure and leukemia. Article published in *Radiation Environment and Medicine* (March 2021) (PI: Jing Chen; Lin Xie)

Emergency dosimetry

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities of a nuclear emergency. Nuclear and radiological emergencies are relatively rare but, when they occur, emergency workers, first responders and the general public may receive significant external and internal exposures from a range of radionuclides. Radiological assessment and protective actions need to be implemented promptly to mitigate the impact on human health. A methodology for the quantitative description of exposures is among the essential elements of emergency management systems. The current dosimetry system recommended by the International Commission on Radiological Protection (ICRP) focuses on situations where doses and associated radiological risks are low and the primary objectives are to optimize protection against stochastic health effects and to demonstrate compliance with regulatory requirements; such system needs to be expanded to address the requirements for emergency situations. The goal of this research study is to develop reference methodologies and datasets that would expand the current ICRP dosimetry system for performing radiological assessments in emergency exposure situations. An expanded dosimetry system will consider both stochastic effects and harmful tissue reactions, situation-specific conditions, such as contamination of wounds, thyroid blocking, decorporation treatment, individual- or group-specific characteristics (e.g. iodine-deficient diet in the affected region). Standard estimates of effective dose will be complemented by more detailed individualised assessments of absorbed doses/absorbed dose rates in organ and tissues of individuals of various ages. (PI: Chunsheng Li; ICRP Task Group 112).

Estimating the geospatial requirements for protective actions in the vicinity of Canadian nuclear generating stations

Health Canada is the lead department responsible for administration of the Federal Nuclear Emergency Plan (FNEP). Under the FNEP, Health Canada has specific responsibilities related to assessing the radiological impacts of a nuclear emergency in Canada or abroad and recommending the use of protective actions to reduce radiation exposures. Current international guidance related to preparedness planning for protective actions is based on an understanding of the impact of nuclear emergencies at Light Water Reactor (LWR) technology nuclear generating stations rather than the CANada Deuterium Uranium (CANDU) technology used at nuclear generating stations in Canada. This research will examine the potential environmental contamination and radiation doses resulting from a hypothetical severe CANDU reactor accident and will take into consideration the unique meteorological conditions encountered at each of the four nuclear generating station locations in Canada. The study will analyse daily atmospheric dispersion modeling runs completed using the Accident Reporting and Guidance Operations System (ARGOS) in combination with Environment and Climate Change Canada's long-range atmospheric dispersion model, Modèle Lagrangien de Dispersion de Particules (MLDP). MLDP is the only atmospheric dispersion model available in Canada that utilises a full 3-D representation of the atmosphere based on the Global or Regional Deterministic Prediction System and is operationally used for modeling the transport, dispersion and deposition of various types of pollutants (e.g. radioactive materials, volcanic ash, chemicals, etc.). To date, two years of modelling runs have been completed. The results will be analysed in the framework of the dosimetric guidance values recommended in Health Canada's 2018 publication 'Generic Criteria and Operational Intervention Levels for Nuclear Emergency Preparedness and Response' and will provide insight on the geospatial extent of the need for protective actions to reduce radiation exposures due to a nuclear emergency in Canada. Analysis of the first year model results is currently underway. (PI: Lauren Bergman)

Exploring the adverse outcome pathway in radiation risk assessment

Toxicological assessments carried out by Health Canada support the Department's mandate for ensuring health and safety of Canadians in that they contribute to the overall characterization of risk of a substance. The Organisation for Economic Co-operation and Development (OECD), operating under the Extended Advisory Group for Molecular Screening and Toxicogenomics (EAGMST), has been developing the Adverse Outcome Pathway (AOP) approach to consolidate evidence for chemical toxicity spanning multiple levels of biological organization. The knowledge transcribed in AOPs, provides a structured framework to transparently organize data, examine the weight of evidence and identify causal relationships between stressors and adverse effects of regulatory relevance. The AOP framework has undergone substantial maturation in the field of hazard characterization of chemicals over the last decade, and most recently gained attention from the radiation research community as a means to advance the mechanistic understanding of human and ecological health effects from exposure to ionizing radiation at low dose and low dose-rates. To fully exploit the value of such approaches for facilitating risk assessment and radiation protection, solicitation of experiences and active cooperation between research communities is needed. As a result, the Radiation and Chemical joint AOP topical group was formed in December 2020 on initiative from the OECD Nuclear Energy Agency Committee on Radiation Protection and Public Health High Level Group on Low Dose Research. The purpose of the joint AOP topical group, chaired by Health Canada, is to advance the use of AOPs in radiation research and foster broader implementation of AOPs into hazard and risk assessment. With global representation, it serves as a forum to discuss, identify and collaboratively develop joint initiatives that support research and possibly regulatory sciences. The topical group will specifically engage, promote, implement and assess the feasibility of using the AOP framework to a) organize and evaluate mechanistic knowledge

relevant to protection of human and environmental health, b) identify data gaps and research needs pertinent to expanding the knowledge domain for low dose/dose rate radiation effects, and (c) demonstrate utility to support risk assessment by developing radiation-relevant case studies (PI: Vinita Chauhan).

Exposure characterization – Cone beam computed tomography x-ray

Health Canada has a mandate to assess and manage health risks from devices that emit radiation. Cone beam computed tomography (CBCT) is a diagnostic X-ray imaging modality, used in dental and medical radiography, that produces 3-dimensional (3D) images of the volume of interest, which is similar to conventional computed tomography (CT). However, CBCT devices acquire X-ray images with a single, sometimes partial, rotation of a wide X-ray beam around the patient, as opposed to conventional CT devices which typically use numerous axial or helical rotations of a narrow X-ray fan-beam around the patient. In order to measure the radiation output of conventional CT devices, there are a number of different metrics that can be used. But the different methods used to generate/produce an image by CBCT devices can significantly impact the applicability and accuracy of the various metrics used to assess radiation output. This research study will investigate various CT radiation output metrics as applied to CBCT devices, including metrics proposed by industry/radiation protection organisations specifically for CBCT, to determine their ability/capacity to accurately measure the radiation output of the devices. Furthermore, the level of scattered radiation received by a patient with and without a lead apron will also be evaluated. As exposures to X-rays carries a risk of biological damage, which decreases as the level of exposure is reduced, this research will allow for more effective evaluation of the risks to patients from CBCT devices, including in comparison to other modalities of medical X-ray imaging. The results will also help to better inform regulatory and guidance initiatives for the devices. (PI: Sarah Cuddy-Walsh)

Fixed point surveillance network

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities in the event of a nuclear emergency. The Radiation Surveillance Division (RSD) operates a network of 80 Fixed Point Surveillance (FPS) spectroscopic Sodium Iodide (NaI) detectors measuring, in real-time, airborne radiation. The detectors are distributed across the country to provide population representative radiation risk assessments with enhanced monitoring around Canadian nuclear power plants in support of emergency management and response. Data collected by the FPS network is used to assess radiation dose levels, which are subsequently made available to Canadians through the Government of Canada public website. The networks can also be used to assist decision-making during a nuclear emergency to ensure the health and safety of Canadians. Real-time FPS monitoring data is automatically transmitted to the International Atomic Energy Agency's (IAEA) International Radiation Monitoring Information System (IRMIS) to help fulfil Canada's obligations under the Convention on Early Notification of a Nuclear Accident. The data is also posted automatically on the European Radiation Data Exchange Platform (EURDEP) for public consumption alongside data from over 5500 monitoring stations in 39 countries. The amount of data automatically transferred to these systems on an annual basis represents approximately 2.5 million data points. (PI: Kurt Ungar)

Forensic Radionuclide Event Analysis and Reconstruction (FREAR)

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities in the event of a nuclear emergency. The Radiation Protection Bureau (RPB) receives and analyzes data from hundreds of radiation sensors within

Canada and around the world. When unattributed releases of radioactive material are detected, for example Ru-106 nuclear tests and nuclear accidents (Fukushima), decision-makers require a forensic capability to characterize, locate and assess the nature of radionuclides for an effective incident response. The FREAR project is unique in that it makes use of monitoring sites that detect and do not detect the release to characterize the source to inform response actions and better protect the public. The FREAR project seeks to use all available information to create a Bayesian (statistical) characterization of the source. The output of the FREAR algorithm provides decision makers with the best assessment to better protect the health of Canadians. (PI: Ian Hoffman)

Handheld laser device usage and injuries: Results from the Canadian Community Health Survey (CCHS)

Health Canada has a mandate that includes assessing and managing risks from radiation emitting devices. In 2014, Health Canada used the Canadian Community Health Survey (CCHS) to collect prevalence estimates of laser device usage and injuries in Canada. The survey found that 1.1% of Canadians reported an injury from a laser device. The majority of injuries were to the eye, with injuries also occurring in the skin, and often were the result of laser exposure from someone else's use of the device. Cosmetic treatments employing lasers were the most common cause of injuries. In 2019, Health Canada conducted a 5-year follow-up study using the CCHS, focusing on the prevalence of injuries from handheld laser devices in the previous 12 months, excluding cosmetic laser exposure. Factors such as the frequency and type of injury sustained, as well as whether the injury was the result of personal use or someone else's use was collected and analysed. The 2019 survey found that 12.4% Canadians reported using or being exposed to a handheld laser in the previous year. Laser pointers represented the majority of handheld lasers used in Canada. Youth between the ages of 12 to 17 made up almost a quarter of all users of these devices. Higher handheld laser device usage was found among those with university education and those within the higher income categories. Overall, very few Canadians reported discomfort or injury involving a handheld laser device in the past 12 months. A quarter of users indicated that they had intentionally directed the laser beam at their eyes or skin or those of someone else. Most respondents obtained their handheld lasers by some undisclosed means or purchased it from a retail store or online. Handheld lasers pose a potential hazard to the public, particularly to children, who are unaware of the risks. This information was gathered to support efforts to monitor and address an emerging health concern regarding handheld laser devices. (PI: Sami Qutob)

Health Canada's Total Diet Study

Ingestion of excessive amounts of contaminants, including radioactive elements, through the food supply can be detrimental for the health of Canadians. Every year, the Radiation Surveillance Division (RSD) participates in Health Canada's Total Diet Study program. The program analyzes a wide range of food products present in a typical Canadian diet, to estimate levels of exposure that Canadians accumulate through the food supply. The RSD is responsible for analyzing the samples for radioactive elements and ensuring that the levels found in foods remain safely within acceptable national and international guidelines. The results of Health Canada's Total Diet Study help ensure food available to Canadians remains safely within acceptable national and international guidelines. (PI: JF Mercier; Robert Dabeka)

Identification of biomarkers of radon gas exposure

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Radon gas is a well-characterized human carcinogen. Studies have provided evidence of an association between residential radon and lung cancer

risk, however, an understanding of the mechanistic basis of this relationship remains limited. Radon gas enters homes from different sources including: surrounding soil and rocks, and water supplies, where it can diffuse and accumulate to levels where it can pose a health risk. This study will examine how radon gas can affect blood and whether indicators of exposure, known as biomarkers, can be identified. The work will be conducted in partnership with members of the Canadian Partnership for Tomorrow Project (CPTP), a program that contains a repository of bio-banked biological samples. Geographic mapping will be leveraged to help identify participants living in high and low radon risk zones. Blood samples will be taken from participants and then analyzed to identify associations between radon gas exposure and the presence of specific biomarkers. The outcomes of this work will provide an understanding of the types of bio-molecules that are released into the blood when individuals are living in high radon areas and the types of technologies that are sensitive to the detection of chronic-level exposures. New knowledge in this area will help direct future research at Health Canada and will inform current national/international standards. (PI: Vinita Chauhan; Michel Gauthier)

Indoor tanning equipment usage and injuries: Results from the Canadian Community Health Survey (CCHS)

Health Canada has a mandate that includes assessing and managing risks from radiation emitting devices. The early onset of skin cancer has been associated with tanning equipment use, where increased use is correlated with increased risk. In 2014, Health Canada used the Canadian Community Health Survey (CCHS) to collect prevalence estimates of indoor tanning and associated injuries (to the eyes and skin). The survey found that 4.5% of Canadians used indoor UV tanning equipment in the past 12 months and usage was more prevalent among young females (aged 18-34). The majority of users indicated they used tanning equipment to develop a base tan. The current results from the 2019 CCHS represent a 5-year follow-up from the 2014 survey. As before, the rapid response component of the 2019 CCHS collected data on the use of tanning equipment in the previous 12 months, including reasons for use, frequency/duration of use, precautions taken, and adverse reactions or injuries providing a more robust estimate of the extent tanning equipment usage and injuries. The 2019 survey found that 3.0% of Canadians reported that they had used indoor tanning equipment in the past year, representing a 33% significant decline from usage prevalence in 2014. The majority of users were female and females aged 18-34 were significantly more prevalent users compared to females aged 45 or older. The prevalence of indoor tanning was higher among people without a university degree, however there were no differences in prevalence by household income or region. Most users indicated they used indoor tanning equipment within a tanning salon and the most common reason for usage continued to be for the development of a base tan. Over one third of all users reported undergoing more than 10 sessions in the past year. The information generated by this research will strengthen our knowledge base on trends in usage and user behaviour which is valuable for targeting communications to the public and developing evidence-based risk management decisions. (PI: Sami Qutob)

Justification and methodology for the characterization of baseline noise

Health Canada's mandate includes the assessment and management of health risks from sound emitting devices, as well as a legal obligation to provide advice on environmental noise under the Impact Assessment Act. Outdoors, background noise sources can interfere with or prevent valid measurements. Measurement methods are needed to quantify the noise from these sources. When acoustical measurements are conducted outdoors, dominant intruding background noise sources include: low to mid frequency environmental noise from distant anthropomorphic sources; high frequency noise from nearby insects and birds; and low frequency noise from wind acting directly on the microphone. The purpose of this project is to quantify these sources. Measurements are made throughout the year in local

suburban and rural outdoor environments, as well as at a residential location near the ocean. Local high frequency noise from birds and insects is filtered out of the measurement following an American National Standards Institute (ANSI) standard for environmental noise measurement. This standard is used because the air absorbs most of the high frequency noise after it travels a few hundred meters. Its use allows the anthropomorphic, and the insect or bird noise to be separated. All measurements use an oversized 0.75 m diameter spherical microphone windscreen to obtain measurements uncontaminated by wind noise. Comparison with simultaneous measurements using commonly used windscreens allows quantification of the wind noise levels in typical measurements. This research approach is novel because measurements are being made in realistic environments as opposed to a wind tunnel. (PI: Stephen Keith)

Longitudinal analyses of nuclear energy workers in the National Dose Registry (CANDU Owners Group's low dose Strategic Research and Development program)

Health Canada has a mandate to protect the population from risks due to radiation. Radiation is a recognized carcinogen; however, there are many uncertainties about the nature of the dose-response relationship at lower levels. Radiation can also influence the risk of other adverse health outcomes. This study will make use of the updated record linkage of workers in the Canadian National Dose Registry to national mortality and cancer incidence data in order to characterize associations between low levels of radiation exposure and different causes of death, and low levels of exposure and different types of cancer incidence. Modelling efforts will evaluate the impact of exposure latencies and differential exposure-response relationships by age and sex, and life table methods will be used to estimate the impacts of ionizing radiation on life expectancy. Results will add to the body of evidence that underpins national and international recommendations for radation risk assessment and risk management. (PI: Paul Villeneuve (Carleton University); Lydia Zablotska (University of California, San Francisco); Rachel Lane (Canadian Nuclear Safety Commission); Minh Do (Carleton University and the Ontario Occupational Cancer Research Center); Susana Abraham Cottagirl (Carleton University); Tim Prendergast (HC)).

Measuring psychosocial impacts from protective actions in nuclear emergencies

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities of a nuclear emergency. Lessons from past nuclear emergencies indicate that psychosocial impacts like Post Traumatic Stress Disorder, depression, suicide rates and anxiety in impacted populations may outweigh radiological health impacts; and should be considered when developing emergency response plans. Internationally, there are no tools to compare psychosocial and mental health impacts to radiological impacts. Nuclear emergency response plans and protective actions are based on radiation detriment (measured in Sieverts). A corresponding unit of psychosocial detriment is required to consider psychosocial impacts in emergency response plans. The first phase of the study will develop the psychosocial unit of detriment for nuclear emergency planning and response. Statistical analysis of mental health survey data on Canadian population to measure the psychosocial impact of protective actions in emergencies will also be conducted. Key factors for psychosocial effects include evacuations, extended displacements, risk perception and socioeconomic changes. By applying a weighting factor to psychosocial impact from other emergencies, a unit of detriment that can be compared to the Sievert is proposed. A Difference-in-Difference (DiD) statistical model is applied to quantify psychosocial impacts between the disaster impacted and control populations. Repeating DiD analysis on data from other countries, will help validate quantification of psychosocial impacts measured in Canada with other countries. Finally, a decision-making tool will be developed to incorporate radiological and non-radiological psychosocial health consequences when implementing protective actions following a nuclear emergency. This tool is applicable in all phases of nuclear emergency preparedness and response. In mitigation, the tool will communicate importance of

psychosocial impacts in emergencies to educate planners, responders and public on risks associated with impacts. In preparedness, it will help develop protection strategies so that plans consider the psychosocial impacts and mechanisms to balance these against radiological impacts. During response, decision makers will be able to consider psychosocial impacts of implementing protective actions for radiation exposures. In recovery, it will account for resources needed to address and mitigate psychosocial impacts following the emergency. (PI: Tristan Barr)

Measuring workload with paired detectors

Health Canada has a mandate to protect the population from risks due to radiation. Linear accelerators (LINACs) are commonly used to treat patients with cancer by targeting tumours with beams of high-energy radiation. For the health and safety of workers it is important to measure the LINAC's annual workload for each available photon energy, which determines the radiation dose outside the bunker. As Canada's leading dosimetry provider, NDSD has partnered with radiotherapy experts to explore a technique to measure the workload using paired detectors. The signals from the two detectors can give sufficient information to separate the signal contributions from 6 and 18 MV photon fields and combined with a calibration factor to yield the number of monitor units (a measure of accelerator output) delivered for each energy. Initial experiments used a pairing of a CR-39 NTD neutron dosimeter, capable of discriminating between the two fields, with a TLD-100 thermoluminescent dosimeter responsive to both fields. While the CR-39 NTD signals were too saturated to be of use under this experiment's exposure conditions, the TLD-100 proved to be excellent for determining workloads when it was exposed to a single energy, suggesting that the TLD-100 could be an excellent detector choice if paired with a suitable second detector. Experiments currently underway are investigating the pairing of the TLD-100 with an optically-stimulated luminescence (OSL) dosimeter, which does not saturate at high doses. If successful, this research could lead to a much more efficient way for LINAC operators to calculate workload, thereby making it easier to manage their radiation safety programs. (PI: Robert Corns (Eastern Carolina University, USA); Charles Schroeder (CancerCare Manitoba); Gurpreet Sandhu (BC Cancer); Keith Henderson; Elizabeth Inrig; Ian McKay)

Medical countermeasures for lung deposition

Health Canada has a mandate to protect the population from risks due to radiation. During a radiological or nuclear emergency, first responders and the public may be internally contaminated by radionuclides via inhalation. This study aims to evaluate the effectiveness and/or applicability of specific measures to counter a large deposition of these contaminants. There are two types of contaminants being studied in this research project: (1) Inhaled insoluble radioactive materials that remain in the lungs for a prolonged time period and are not removed easily. This component investigates the application of approved drugs or their combination for effective removal of inhaled insoluble materials from the lungs, using an animal model; and (2) Inhaled soluble radioactive materials that are currently treated using decorporation agents, such as DTPA-Zn. For these, the treatment efficacy is compromised due to the rapid clearance of the drug from the body. This component investigates the application of nanoparticles to slow down the clearance of the drug so to improve the removal efficacy, using an animal model. Results of this project will support the preparedness and response to radiological and nuclear emergencies, in both guideline development and medical countermeasures preparedness. (PI: Chunsheng Li; Canadian Nuclear Laboratories)

Modelling temperature elevation in the skin from millimeter wave radiofrequency fields

The growth of devices emitting radiofrequencies (RF) and emerging wireless broadband technology in the millimeter wave spectrum over the last few years has raised public concerns about possible

associations between RF energy and adverse health outcomes. The Department's mandate regarding human exposure to RF electromagnetic energy from wireless devices includes carrying out research into possible health effects, monitoring the scientific literature related to such effects on an ongoing basis, and developing RF exposure guidelines, commonly referred to as Safety Code 6. Safety Code 6 sets recommended limits for safe human exposure to electromagnetic fields (EMF). The objective of this study is to model the potential increase in temperature in human skin from exposure to millimetre wave radiofrequency (RF) fields. Since millimeter wave RF fields are absorbed almost entirely within the uppermost layers of the skin and subcutaneous fat, numerical models are being developed to predict the rate of and/or steady-state increase in skin surface temperature taking into account both intensity and beam-diameter. The analytical model developed in this study can be used to assess frequency-dependent power density thresholds that would result in a defined tissue temperature increase. Alternatively this model can be used to estimate a maximum tissue temperature resulting from RF emitting devices based upon the radiation characteristics of the device. The results of this research are intended to provide Health Canada, other levels of government and the broader scientific community with models that can be used to analyse thermal health effect limits for human exposure to millimeter wave. (PI: Greg Gajda; Mykola Zhuk)

Monitoring of radioactivity in caribou and beluga in response to the Fukushima accident (Northern Contaminants Program)

Health Canada has a mandate to protect the population from risks due to radiation. Following the 2011 accident at the Fukushima Daiichi nuclear power station in Japan, concerns in northern communities were expressed regarding the safety of caribou and beluga whales as food sources. Historically, studies following the Chernobyl accident in 1986 had shown that radioactivity in some northern Canadian caribou increased, although the animals were still considered safe to eat. Using samples provided through the Northern Contaminants Program, radionuclides are being measured in samples of caribou, beluga, and beluga prey species collected before the Fukushima accident, shortly afterwards, and several years later, after the radioactive contamination had crossed the Pacific Ocean. The results of the comparison of some of the samples before the accident and shortly afterwards have been published. To date, no increase has been observed in any of the species and levels are expected to remain well below established guidelines for radioactivity in food. (PI: Trevor Stocki)

National Radon Program behavioural study

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. The National Radon Program (NRP) has an extensive outreach program to motivate Canadians to take action to protect themselves from radon-induced lung cancer. In January 2020, the NRP initiated a behaviour intervention trial to assess the whether a behaviourally-informed intervention – specifically, a postcard with straightforward messaging – led to a significant incremental increase in awareness and in test kit purchases. Separate treatment and control groups were drawn from areas where there was little grassroots radon activity, which was assumed to correspond to limited radon awareness in the community, and where there was a high level of activity, corresponding to higher pre-existing radon awareness levels. All communities in the trial had previously been identified as having an elevated risk of high residential radon levels (based on the Cross Canada Radon Survey and other data). Influence was assessed by comparing website traffic and test kit purchases between groups who received the postcard and those who did not. Anecdotal evidence was also collected. Findings indicate that the behaviourally informed postcard increased awareness of radon and, further, increased awareness more within high grassroots communities compared to low grassroots communities. The study also found that receiving the postcard increased the likelihood that people

would purchase a radon test kit, and that this increase was higher in communities with more pre-existing grassroots activity compared to those with less. While the study showed an increase in test kit purchases among those who received the postcard, absolute numbers were still quite small, indicating that behaviourally-informed postcards on their own are not an effective solution to the challenge of increasing Canadian radon testing and mitigation rates. This early study shows promise for using behavioural science to assess and improve the effectiveness of radon action campaigns. Results are available at https://takeactiononradon.ca/wp-content/uploads/NRP-Behavioural-Study-Final-Report-ENG-2020.pdf (PI: Jane Howe (Deloitte Canada); Kelley Bush, Katelyn Penstone)

New methodology for the analysis of radio-strontium in milk

Safeguarding the well-being of Canadians with respect to environmental radioactivity is underpinned by the nation-wide monitoring and measurement activities of the Radiation Surveillance Division (RSD). Of the sample types used to assess direct radiological impact to Canadians, commercial milk products are important considering that: 1) many radionuclides of concern are efficiently incorporated into milk from the surrounding environment 2) they are pooled-samples that represent large geographical areas, and 3) the consumption of milk is very common. For these reasons, the radio-analysis of milk is an important component of comprehensive environmental surveillance programs around the world. From a health-impact perspective, the most relevant radionuclide associated with milk is strontium-90 in consideration of its abundance, nature of decay, and long radiological and biological persistence (i.e. half-life). Unfortunately, owing mostly to the complex nature of milk, it is also one of the most demanding radionuclides to measure precisely and unequivocally in a reasonable timeframe. For this reason, current methodology employed in the RSD is reserved for ad hoc capacity and, even then, has proven to fall well-short of sample throughput demands encountered in an emergency context. To address this gap, new methodology has been developed to dramatically reduce sample analysis time, effort, and complexity with a concomitant bolstering of data integrity and confidence. This achievement has been rooted in several innovations that are being stitched together to form a rigorously characterized and demonstrably robust analysis methodology. (PI: Dr. Michael Cooke)

Personal listening devices (PLDs) and impairment to hearing

Health Canada conducts research to assess the potential health risks from noise as part of its mandate to protect the health and safety of Canadians. This includes noise risks from PLDs. It is well known that prolonged exposure to loud noise can cause noise induced hearing loss. Previously, Health Canada has assessed the typical volume setting on PLDs (e.g. MP3 players) used by students and correlated these findings to their self-reported and measured hearing status. These pilot studies have served as the rationale to conduct larger investigations. For the first time, national data was collected on hearing health among Canadians aged 3-79 as part of the Canadian Health Measures Survey (CHMS) (Cycles 3 and 4). This data included objectively measured hearing acuity in addition to self-reported exposures to loud workplace and leisure noise, and has led to publications on the prevalence of occupation-related hearing loss among Canadians. In 2019, Health Canada published a report on the prevalence of loud leisure noise exposure among Canadians, aged 6 to 79. Noise exposure from cumulative and specific sources of loud leisure noise activities, including PLDs, were estimated based on a common occupational limit (i.e. equivalent to or greater than 85 dBA (A-weighted decibels) for 40 hours or more per week). Health Canada will be undertaking a subsequent analysis to evaluate the impact of loud PLD usage and other loud leisure noise exposures on the hearing health of Canadians, aged 6 to 29. Collectively, these study findings will be used by Health Canada to estimate (characterize) the prevalence of noise-induced hearing loss among Canadians, including children/adolescents and young adults, from prolonged

exposure to noisy devices (e.g. PLDs) capable of hazardously high volume levels. It will also help to inform policy makers, educators and health care professionals. (PI: Katya Feder)

Radioactivity monitoring and assessment in the Canadian Arctic: participation in an international research project of the Arctic Monitoring and Assessment Programme (AMAP) 2023

Access to reliable and up-to-date information is essential for the development of science-based decision-making regarding ongoing changes in the Arctic and their global implications. Related AMAP summary reports have therefore been developed specifically for policy-makers, summarizing the main findings of the assessment. Since 2019, an international team of experts (including Health Canada) has been conducting an assessment of Arctic radioactivity issues. The information contained in this study will be fully referenced, and is based on peer-reviewed and published research and monitoring results since 2014. The updated radioactivity assessment will include new radioactivity data, effects of radon on human health, and data on radionuclides dumped or transferred into the Arctic. It will also introduce Health Canada research on the impact of climate change on the transportation of natural radionuclides in the Arctic. These studies will improve Health Canada's ability to estimate the increased Pb-210 and Po-210 activity level in the Arctic region due to northern contaminants, and to model atmospheric radionuclide transportation that is crucial to assess radiation dose to humans. (PI: Weihua Zhang).

Radon research - understanding radon risk in occupational and residential settings

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Long-term exposure to radon gas is recognized as an important cause of lung cancer. Radon is a naturally occurring radioactive gas and can accumulate in enclosed spaces that have contact with the ground, including mines, caves, other workplaces, and homes. It is important to consider exposure from all sources in order to properly assess risk and to prioritize areas where intervention will be most effective. Recent work in this area has explored whether excluding lifetime residential exposure from epidemiological studies of radon risk based on miners (i.e., including only occupational exposure) could impact the quality of the exposure characterization and, therefore, the resulting exposure risk-relationship (published in Radiation Environmental Biophysics, October 2020). In a second study, Canadian labour statistics, time statistics and more than 7600 long-term radon measurements from workplaces were used to calculate hypothetical radon exposures for 20 job categories (based on North American Industry Classification System). Results were compared with residential radon exposure based on more than 22 000 long-term radon tests conducted in Canadian homes. Due to the relatively high radon concentration in homes compared to many workplaces as well as the fact that Canadians spend more time indoors at home than they do at work, it was calculated that exposure at home contributes to 90% of workers' total radon exposure, on average (Journal of Radiological Protection, March 2021). Health Canada's National Radon Program and partners use this work to strengthen guidance, regulation, and policy and reduce the burden of radon-induced disease on Canadians. (PI: Jing Chen)

Review of equilibrium factors for dose assessment

Health Canada is committed to informing Canadians about the health risk of radon as part of the mandate to ensure the health and safety of Canadians. Exposure to indoor radon is the leading cause of lung cancer among non-smokers, and the second-leading cause among smokers. Radon enters a home as radon gas and quickly decays through a series of short-lived radioisotopes. Breathing in the radon gas actually contributes relatively little to the radiation dose to the lung. It is the inhalation of the short-lived radon decay products that delivers most of the dose that, ultimately, can lead to lung cancer. The same

radon gas concentrations can have different decay product concentrations under different environmental conditions, which are accounted for in dose assessment using an equilibrium factor. Equilibrium factors are often estimated; however, in this study, published measurements from more than 20 countries are reviewed, encompassing indoor and outdoor residential, public, and occupational environments. In the indoor residential environment, equilibrium factor values are shown to be significantly higher in poorly ventilated houses and in homes with smokers. In some occupational environments (mines, caves, and thermal spas), there was a range of equilibrium factors, suggesting that location, environment, and operation-specific values are more appropriate than an average for assessing exposure for these workers. This information is valuable for identifying populations at higher risk from radon exposure and for targeting radon reduction programs, including the National Radon Program. Article published in *Health Physics,* September 2020. (PI: Jing Chen; Naomi Harley)

Self-reported exposure to occupational noise and cardiovascular disease in Canada: Results from the Canadian Health Measures Survey

Health Canada has a mandate that includes the assessment of radiation health hazards and the provision of radiation safety advice to other federal programs and departments. Self-reported occupational noise exposure has been associated with impaired hearing, but its relationship with extra-auditory affects remains uncertain. This research assessed the association between self-reported occupational noise exposure and cardiovascular outcomes. Participants (n=6318, ~50% male) from the Canadian Health Measures Survey (2012-2015) aged 20-79 years were randomly recruited across Canada. An in-person household interview included basic demographics, perceived stress, diagnosed health conditions and self-reported exposure to a noisy work environment. Direct physiological assessment in a mobile examination centre permitted the determination of biomarkers/risk factors related to cardiovascular function. Logistic or linear regression models explored the association between self-reported occupational noise exposure and several cardiovascular endpoints after adjusting for confounding variables. After adjustments, there was no evidence for an association between occupational noise and any of the evaluated endpoints, which included but were not limited to blood pressure, heart rate, blood glucose, insulin, lipids, diagnosed hypertension, medication for hypertension, myocardial infarction, stroke, or heart disease. There was no evidence that self-reported occupational noise exposure was associated with evaluated cardiovascular-related biomarkers, or cardiovascular diseases among Canadians aged 20-79 years. This study, and others like it, provides an important contribution to an evidence base that could inform policy related to occupational noise exposure. (PI: David Michaud)

Survey of Cs-137 in bird species harvested across Canada

Health Canada has a mandate to protect the population from risks due to radiation. A historic data set containing unpublished measurements of Cs-137 radioactivity in 238 pooled samples of pectoral muscle from 1892 birds representing 37 species, was analyzed in order to determine if birds were contaminated due to global weapons fallout and/or the Chernobyl accident; to understand baseline cesium levels in birds across the country; and, to ensure the birds were safe to eat. Current work is leveraging this data set to improve capabilities to assess the impacts of release of radionuclides on country food chains. Samples were obtained from 173 locations across Canada (including locations in the Arctic); mostly in the fall hunting seasons between 1989 and 1995. Each of these composite samples was then measured by gamma spectrometry. Various methods of correlating measurements with environmental Cs-137 levels and species' habits were explored in order to determine environmental radiological transfer factors for six different foraging groups. All of the Cs-137 measurements in the samples were very low; therefore, there was no evidence of a human health risk. This work was published in *the Journal of*

Environmental Radioactivity (December 2020). Work will continue using data from samples that were obtained within the boundary for the Arctic Monitoring and Assessment Programme (AMAP) and results will be submitted as part of the 2023 AMAP report (see "Radioactivity monitoring and assessment in the Canadian Arctic" later in this report). (PI: Trevor Stocki; Birgit Braune [ECCC])

Systematic review on the strength of evidence for an association between noise exposure and changes in biological risk factors for stress-mediated illnesses.

Health Canada conducts research to assess the potential health risks from noise as part of its mandate to protect the health and safety of Canadians. Noise can lead to adverse health effects through an increase in stress reactions that may increase the risk of developing stress-mediated health effects, such as cardiovascular disease (when sustained at high levels of noise). Exposure to loud noise can cause an increase in stress reactions that can include (but are not limited to) changes in cortisol, adrenaline, epinephrine, heart rate, and blood pressure. These changes may occur independently of, or be (statistically) associated with, annoyance. The purpose of the systematic review (funded by the Safe Environment Directorate's Impact Assessment Fund (IAF)) was to evaluate the strength of evidence between noise exposure and changes in the biological parameters known to contribute to the development of stress-mediated adverse health effects in humans. That noise is capable of acting as a stressor is insufficient, by itself, to fully inform the Department's advice on noise because advice cannot aim to eliminate noise-induced stress/annoyance reactions altogether. Dose-response analyses examined the effect of a 10 dB increase in noise exposure. Risk of bias (RoB) of individual studies was assessed using the Risk of Bias of Nonrandomized Studies - of Exposures. The certainty of the body of evidence for each outcome was based on a GRADE approach. A total of 151 primary studies reporting on blood pressure, heart rate, vascular resistance, cardiac output, waist circumference, cortisol, adrenaline, noradrenaline, glucose, cholesterol, hypertension, pre-eclampsia, gestational diabetes and gestational hypertension in humans were identified. Evidence of increased noise exposure on short- and long-term biomarkers of stress was very low. Based on the systematic review, there is very low certainty evidence to support statements linking noise exposure to stress-mediated illnesses at the population level. (PI: David Michaud)

The Canadian Radiological Monitoring Network (CRMN)

The Canadian Radiological Monitoring Network (CRMN) comprises 26 sampling stations distributed across Canada that routinely send environmental samples to the Radiation Surveillance Division (RSD). These samples are analyzed for radionuclides that may adversely impact the health and well-being of Canadians as part of the mandate to ensure the health and safety of Canadians. Sample matrices include airborne particulates collected by filters, precipitation (rain or snow), drinking water, and milk. The detection techniques employed to identify and quantify radionuclides of interest are gamma spectrometry, alpha spectrometry, gas proportional counting, liquid scintillation counting, and inductively-coupled mass spectrometry. The CRMN additionally operates 12 sampling stations, predominantly concentrated about the Gentilly and Pt. Lepreau nuclear power generating stations, to collect water-vapour samples for assessment of tritium content, which is used as a metric to assess reactor leakage. Continuous and comprehensive monitoring provides a current and accurate determination of background radioactivity in Canada, and enables early detection and rapid response in the event of a national or international incident with radiological consequence. (PI: JF Mercier)

The Comprehensive Nuclear Test-Ban Treaty radionuclide stations and radionuclide laboratory monitoring

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities of a nuclear emergency. The Comprehensive Nuclear Test-Ban Treaty (CTBT) was adopted by the United Nations General Assembly in 1996 and serves as an effective nuclear non-proliferation and disarmament measure. The treaty has a comprehensive verification regime to ensure that no nuclear explosion goes undetected. The verification regime consists of the International Monitoring System (IMS) and International Data Centre (IDC), a consultation and clarification process, on-site inspections and confidence building measures and a Canadian National Data Centre (NDC) managed by Natural Resources Canada (NRCan). The IMS consists of stations and laboratories located throughout the world which use one of four technologies to collect data: 1) Seismic monitoring, 2) Infrasound monitoring, 3) Hydroacoustic monitoring, and 4) Radionuclide monitoring. As part of the IMS, the Radiation Surveillance Division (RSD) manages four radionuclide stations and one radionuclide laboratory. The RSD also maintains a platform for the automated and interactive analysis of airborne radionuclide measurements on behalf of the Canadian NDC including all such data from the IMS and from the Canadian Radioligical Monitoring Network (CRMN). Along with partners at Environment and Climate Change Canada, the Radiation Surveillance Division further supports the NDC in assessment of treaty relevant events events as well as other significant atmospheric releases of radionuclides. The activity results in a dataset from the analysis of over 30,000 samples a year. This year was highlighted by the submission CTBT radioisotope laboratory documentation as a major milestone in the addition of Noble Gas analysis to its capabilities certified by the CTBTO. Certification is to be completed in early 2022 pending a site visit by CTBTO authorities. (PI: Kurt Ungar)

Transcriptional benchmark dose modeling in a mouse skin model in response to UV radiation from a commercial sunbed

Health Canada has a mandate that includes assessing and managing risks from radiation emitting devices. In 2016, the European Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) concluded that there is strong evidence that ultraviolet radiation (UVR) from tanning equipment usage is carcinogenic and the risk of developing cancer increases with both frequency and the age of the user. SCHEER also concluded that there is no safe limit for exposure to UVR from tanning equipment as there is no defined threshold for the development of adverse long-term health associated with exposure. This is due to the stochastic nature of cancer induction and the dose levels required for the production of a tan. There is also no established threshold level of UVR-irradiance or UVR-dose for long-term stochastic effects, such as cancer, from currently available data. More sensitive mechanistic studies and advanced analysis tools may provide more insight into the estimations of UVR exposure thresholds and possible adverse outcomes through transOMIC pathway analysis. A recent review of the scientific literature suggests that the application of Bench Mark Dose (BMD) modelling of transcriptional data offers significant advantages over traditional genomic bioinformatics approaches. In 2019, Health Canada conducted a study to use BMD modelling of transcriptomic responses in mouse skin using a broad-range of UVR doses emitted from a UV cosmetic tanning lamp. This work is the first of its kind to employ BMD modelling of transcriptomic response data in a live mouse model exposed to a biologically-relevant dose range of UVR emissions approximating a spectra of a typical UVR cosmetic tanning bed. This data will provide a point-of-departure assessment of molecular responses to UVR exposure to determine biologically-relevant thresholds of UVR responses that may preclude the occurrence of longer term pathophysiological consequences. (PI: Sami Qutob)

Validating emergency surveillance activities in a known quantity of radioactive material

As the lead department of the Federal Nuclear Emergency Plan, Health Canada has the mandate for coordinating the preparedness and response activities of a nuclear emergency. Health Canada's Radiation Protection Bureau maintains a field team for assurance-monitoring activities in the event of a nuclear emergency. The field team is prepared to conduct dose rate surveys, soil sampling, in-situ gamma spectrometry in the field, and to implement contamination control procedures following radiological dispersion events. These capacities were tested when the field team deployed and monitored in a field with a known amount of evenly distributed radioactive material (La-140). Two types of dose rate surveys were conducted, one using the average of a 30 second measurement at several location and the second using a backpack system to take point measurements while walking through the grid. Radiation dose rates measured by the instruments were 30% lower than expected implying the need for a correction factor which should include the shielding effect by the operator. The soil sampling procedure proved to be effective for collecting samples quickly however should be improved to ensure a consistency of collected volumes. An accurate estimate of the distributed activity was found using in situ gamma spectroscopy measurements and applying a Monte-Carlo simulated correction factor. The measurement analysis of samples with the mobile nuclear laboratory was quick with results from 10 samples produced within 4 hours of collection. Finally, the contamination control procedures proved to be effective for both personnel and for samples, resulting in no undesirable (>2 times background) contamination outside of the controlled access zone. By testing procedures in an evenly dispersed known quantity of radioactive material, several methods were improved thereby ensuring the preparedness of the Radiation Protection Bureau's Field Response Team. (PI: Rory McCutcheon-Wickham)

Wind Turbine Noise and Health Study: Sleep Analysis

The Wind Turbine Noise and Health Study (WTNHS) (2012-2014) was conducted by Health Canada, in collaboration with Statistics Canada and other external experts, in order to better understand the effects of wind turbine noise (WTN) on human health and well-being. Measured endpoints included an automated blood pressure/heart rate assessment, hair cortisol concentrations and sleep actigraphy. In addition, self-reported data were collected during a face-to-face computer-assisted interview at participants' homes. While this study was completed and the preliminary results were announced in the fall of 2014, due to the volume of data collected, the publication of detailed results in peer reviewed scientific journals occurred throughout 2015-2019. A total of 14 journal articles have been published to date and additional analyses are ongoing. The current work from the WTNHS relates to a more detailed analysis of sleep actigraphy where, in the first analysis, sleep will be evaluated in 10-min time intervals that are time-synchronized to wind turbine operations; and, the second analysis will focus on determining the WTN sound pressure level that is associated with a 3% prevalence of self-reported high sleep disturbance, which is the sleep disturbance level on which the WHO currently bases its noise guidance. The results of this analysis will provide the most comprehensive assessment of self-reported sleep disturbance to date, and contribute to a global evidence base on which future decisions by Health Canada, other levels of government, and the broader scientific community, may be informed. The scientific results from these studies on WTN continue to inform legal proceedings related to wind turbine installations in Canada and around the world. (PI: David Michaud)

Water Quality

Designing cost-effective drinking water surveys in the 21-st century: Optimizing target analytes, site selection, sampling and analytical methods

Sampling, shipping and analysis are the most common causes of high cost for drinking water surveys. Drinking water is an active medium; therefore, specific sampling protocols are essential for some water contaminants and require well-trained personnel to obtain consistent results. Shipping is usually costly as significant volumes may be required to analyse trace levels of contaminants and different analytical methods are applied to determine various types of water contaminants, resulting in a variety of sample collection and processing requirements and sometimes various analytical laboratories. Over the years, Health Canada has conducted multiple targeted surveys and two national surveys on drinking water to generate data used for the development of Guidelines for Canadian Drinking Water Quality. The results have also been used to conduct human health risk assessments. The main objective of this project is to determine cost effective ways to design and perform future drinking water surveys. Specific areas for optimization include the selection of the sampling sites, classes of contaminants, sample volume, on-site sample concentration techniques, as well as analytical methods. The in-house expertise developed at Health Canada will be used to aggregate the knowledge generated over the years in drinking water sampling and analysis, and new emerging analytical tools explored to reduce the analytical methods-to-contaminants ratio. The ultimate goal is to reduce the cost of future surveys while improving data quantity/quality as required to fulfil Health Canada's mandate to protect and improve the health of Canadians. (PI: Anca-Maria Tugulea)

Transformation of microplastics by drinking water oxidants and its effects on sorption and leaching of emerging chemicals of potential health concern

Microplastics have been found to sorb (adsorb or absorb) organic pollutants and metals, some of which may be of concern to human health. Under certain environmental conditions and during drinking water treatment, microplastics may also undergo changes in their physical characteristics and chemical composition that may affect their sorption and leaching behaviour to these chemicals. It is unclear whether exposure to chemicals from microplastics represent a significant source of exposure compared to total exposure from other sources and more research is needed before a human health risk assessment on microplastics is possible. The aim of this research is to develop protocols for assessing how microplastics are transformed when subjected to oxidation and weathering conditions representative of oxidant and UV exposures in drinking water treatment plants, and how their capacity for sorption/leaching of selected target hydrophobic organic chemicals and a metal ion are influenced. This study enhances our understanding of the effect of weathering of microplastics from a UV-ozone advanced oxidation process on their sorption and desorption behavior. The data will have the potential to feed into longer-term studies of hydrophobic organic chemical interactions, with a wider variety of weathered plastics (fibers, fragments, pigmented particles) from other possible sources of human exposure. (PI: Subhasis Ghoshal [McGill University]; contact: Tamara Desroches (HC))