HEALTH CANADA

COMPILATION OF
RESEARCH ABSTRACTS

2021–2022

Health Canada Santé Canada

Canada

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. Health Canada is committed to improving the lives of all of Canada's people and to making this country's population among the healthiest in the world as measured by longevity, lifestyle and effective use of the public health care system.

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Également disponible en français sous le titre :
Santé Canada : Recueil de résumés de recherche 2021–2022

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Publication date: July 2023

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Cat.: H126-6E-PDF
ISBN: 2563-9900
Pub.: 230043

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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 2021–2022. 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

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
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 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

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. In 2021–2022, these data were linked to data on emergency room visits and population-based cohorts to support epidemiological analyses. Study results were published in 2021 with an additional publication anticipated for 2022. (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 cancers was published 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 attributable to short-term exposure to outdoor air pollution, 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, recognizing other changes in the Canadian demographic profile, air quality profile, and medical care system. The AHTI measures day-to-day changes in both non-accidental all-cause deaths (e.g., due to heart, circulatory and respiratory conditions) and exposures to two major air pollutants (ground-level ozone (ozone) and fine particulate matter ($PM_{2.5}$)). 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 regional differences. In order to obtain more reliable and less biased estimates of public health risks, mortality data for recent years (2013–2015) and for more cities (about 80 census divisions) have been added to the national AHTI analysis. Furthermore, daily hospitalizations have been analyzed, which amounts to approximately 10x the daily mortality, allowing researchers to obtain more information on specific causes of hospitalization. Currently, subpopulation groups are under study by age (non-senior vs. senior) and biological sex, as these subgroups are expected to be more vulnerable to air pollution. For regional AHTI, three geographical regions (Eastern, Central, and Western) are also under investigation. This project has found different trends by health outcome, pollutant, region, and sex: for example, decreasing trends in the national mortality AHTI for both ozone and $PM_{2.5}$, but an increasing trend in the national hospitalization AHTI for ozone. The project findings will update the AHTI web report in 2022 and inform future studies on subpopulations by age/sex/region vulnerable to outdoor air pollution. (PI: Hwashin Shin)

Air Quality Monitoring in the City of Hamilton with Specific Focus on Marginalized and Vulnerable Population Areas by Using Low Cost Air Monitoring Technology—NEW!

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 for vulnerable populations, is a priority for Health Canada. The Regulatory Operations and Enforcement Branch, Environmental Health Program in Ontario has funded research under a Memorandum of Agreement with the City of Hamilton involving partners from Environment Hamilton and the University of Toronto Department of Geography, Geomatics and Environment to monitor and measure levels of air pollution in Hamilton and engage the community over the course of the project. In winter and spring 2022, air quality monitors were deployed across the City of Hamilton in neighbourhoods where marginalized and vulnerable populations were predominant. Benzene (C_6H_6), nitrogen dioxide (NO_2), oxides of nitrogen (NO_X), nitric oxide (NO) (available as NO_X–NO_2), ground-level ozone (O_3), and sulphur dioxide (SO_2) were selected as the main air pollutants of concern for monitoring. The locations will be sampled seasonally over the course of two years (2021–2023) and a series of public workshops will be held to engage the community on the project. Air, socio-demographic and economic data will be combined to better understand the air quality in vulnerable neighbourhoods and can generate interventions for reduced pollution exposure and improved future health outcomes. This project is expected to raise awareness on the importance of air quality on health among the vulnerable populations living within the City of Hamilton. (PI: Mainul Husain, Phoebe Tung & The City of Hamilton)

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 journal publication outlining the results is expected to be published in 2022. (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 mortality risks associated with three major air pollutants (ground-level ozone (ozone), nitrogen dioxide (NO_2) and fine particulate matter ($PM_{2.5}$)) individually. To improve and update the current AQHI, this project has set four goals for model improvement, health outcome, temporal and spatial extensions. First, we improved the current model to account for the correlations among the three specified air pollutants, which would reduce under- or over-estimates for their combined adverse effects on health. Second, we add health outcomes with extension beyond mortality to hospitalization. Third, we update the study period from a 10-year period (1991–2000) to a more recent 15-year period (2001–2015). Fourth, we extend the study areas to additional urban locations and rural areas, covering at least 80% of the Canadian population. These updates can provide new information on short-term exposure in rural areas and during days of local extreme events such as wildfires and winter wood smoke which are related to $PM_{2.5}$ concentrations. The impact of those extremely high exposure days on local residents could be different from that of uneventful days. This project already has achieved three of the four goals, with the fourth goal remaining due to lack of data availability, which will be completed as air pollution data for the rural areas become available. The study findings on mortality AQHI and hospitalization AQHI will improve daily communications with Canadians and protect Canadians from avoidable health risks by providing updated 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 outlining the study findings was published in 2022. (PI: Éric Lavigne)

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 2023. (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-making and health messaging in addressing impacts of air pollution. A scientific manuscript focusing on the interrelationships between urban environmental factors and maternal outcomes was published in 2022. Results of impacts of forest fires on adverse birth outcomes across Canada were presented 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 was published in 2021. A second publication is expected to be published in 2022. (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 $PM_{2.5}$ were developed for a single test year, and then expanded to cover the period from 2000–2020. 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. (PI: Markey Johnson)

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

Industrial emissions contribute to local and regional air pollutant concentrations. In Quebec, marked 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 Institut National de Sante Publique du Quebec (INSPQ) and the University of Toronto to conduct a study on the associations between changes over time in exposure to ambient fine particulate matter ($PM_{2.5}$), 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 was created to study asthma incidence. The POLAIR3D chemical transport model was 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) were estimated. The associations between industrial emission-related concentrations of ambient pollutants and childhood asthma onset were studied using fixed-effects regression models adjusting for age, sex, and median annual household

income. In sensitivity analyses, environmental tobacco smoke and regional fine particulate matter and nitrogen dioxide were adjusted in models. Specific industrial sectors petroleum refineries, metal smelters and pulp and paper mills were studied separately. Preliminary results demonstrate significant associations between industrial emission-related air pollution and childhood asthma onset, in all three studied sectors. In 2022, analyses of potential health benefits of industrial emission reductions will be carried out. 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 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 was published in 2021 and a second is anticipated to be submitted for publication in 2022. (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 added 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 utilizes 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. This expansion of 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 culminated in the development of a user-friendly planning support tool that is freely available to policy makers, air zone managers, researchers, public health practitioners, and other stakeholders across Canada. The SMARTPLANS platform was developed for 5 cities across Canada: London, Halifax, Vancouver, Ottawa, and Calgary and final workshops for end users were delivered in 2022. (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). All saliva 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. Analysis of health measure data has yielded unclear results thus far and additional analysis and interpretation will be required to disentangle whether the health effects of air pollution differ between individuals with or without these gene variants. 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 manuscript on the spatio-temporal variations of aeroallergens in the city of Toronto was 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 15 years after the original study, and to examine their associations with air pollution. 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. Oxidative potential of particulate matter also increased the risk of asthma, but not allergic rhinitis or eczema. Other built environment variables (proximity to roads, greenness, pollen counts) were not associated asthma,

allergic rhinitis or eczema. Exposure to air pollution was not associated with medication nor laboratory test utilizations in this study population. 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)

National and local ecological analysis of long term $PM_{2.5}$, NO_2, greenness and COVID-19—NEW!

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to air pollutants in the environment. Many studies have shown that air pollution exposure is associated with a wide range of adverse health effects, including increased risk of respiratory infection. It is unknown whether air pollution exposure increases the risk of novel coronavirus (COVID-19) infection. This study examined whether the incidence of COVID-19 infection is related to air pollution levels among 111 Canadian health regions, as well as 140 Toronto neighbourhoods, adjusting for other factors such as race, income, weather, population density and time since the peak number of cases. The national analysis found that there was a positive association between COVID-19 incidence and long-term exposure to fine particulate matter. The association was larger in magnitude and stronger in health regions with higher rates of COVID-19, and in those health regions where estimated exposure to fine particulate matter is expected to be more accurate. The Toronto analysis found that there was a positive association between COVID-19 incidence and long-term exposure to reactive oxygen species in fine particulate matter. The association was larger in magnitude in neighbourhoods with a higher proportion of Black residents. The results require further examination using studies based on individual-level rather than area-level data. (PI: Dave Stieb)

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: Keith Van Ryswyk)

NO_2 land use regression surface modeling—NEW!

Health Canada conducts research on air pollution to support risk assessment and policy development under the Air Quality Program. Nitrogen dioxide (NO_2) is a known urban air pollutant. To assess long-term exposure of the Canadian population to NO_2 and its health risks, estimates of NO_2 levels at the national scale are required. Previously, annual estimates of NO_2 levels across Canada were developed using land use regression (LUR) models. In the fiscal year 2021–2022, new NO_2 estimates were developed for the period up to 2019, using the upgraded LUR modelling approach with updated annual National Air Pollution Surveillance (NAPS) monitoring data and newly available 2020 census block point file for Canada. Additional LUR model improvements are still necessary to estimate NO_2 for 2020 and beyond. This includes changes associated with COVID-19 travel restrictions and stay at home policies in 2020 that substantially changed NO_2 concentrations. In addition, the new satellite based TROPOspheric Monitoring Instrument (TROPOMI) should be integrated within the LUR framework to enhance prediction. In Fiscal Year 2022–2023, these two issues will be explored when updating the 2020 Canadian LUR model. (PI: Ling Liu, Pierre Raymond)

Quebec Air Pollution Exposure and Epidemiology study (QAPEE)

Urban air pollutants such as nitrogen dioxide (NO_2), black carbon (BC), fine particulate matter ($PM_{2.5}$), 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 $PM_{2.5}$ 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 $PM_{2.5}$ 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 and a manuscript is anticipated to be submitted for publication in 2022. (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. Study results were published 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. A paper linking air pollution to carotid plaque burden based on land use regression modelling in London, Ontario was published in 2020. The Halifax land use regression modelling for metals was published in 2021. Future analyses will link LUR metals to adverse health outcomes in Calgary and Halifax. (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 cardiopulmonary 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, nighttime tunnel vacuuming and changes in subway trains, for their potential to reduce fine particulate matter ($PM_{2.5}$). 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. Study results were published in 2021, with a second paper planned for 2022. (PI: Keith Van Ryswyk)

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)

The Air Quality Benefits Assessment Tool (AQBAT)

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, wildfire smoke, climate change, diesel exhaust and biodiesel. Ongoing updating of data, parameters and methodology is required to ensure that assessments of regulatory initiatives reflect the most current. Version 3 of AQBAT was released in 2019. An R-based version which can be run locally by the user or as an online application is under development. (PI: Dave Stieb)

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

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 influence 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. (PI: Sabit Cakmak, Bob Dales)

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 has been shown to be linked to heart disease, hypertension, diabetes and depression. Sleep disordered breathing (OSA), 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 (a vulnerable subpopulation) through maternal exposure during pre-pregnancy and pregnancy, with a focus on Autism Spectrum Disorder (ASD) in young children. Evaluation of the impact of maternal exposure is essential, since it is the period of critical neurodevelopment. ASD is a complex developmental disorder, characterized by difficulties in social communication and interaction. Identifying potential links between exposure during pregnancy and ASD may suggest ways to reduce the occurrence of ASD and thereby the societal, family and health care costs. 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, this project conducted an epidemiological research study to estimate the associations between exposure to air pollution (negative effects) and/or green space and walkability (positive effects), and ASD in children born between April 1, 2012 and March 31, 2020. This project has found that ASD is associated with NO_2 and $PM_{2.5}$, but not

with ozone. Study findings will help to understand potential causation or prevention of the occurrence of ASD in children and thus reduce societal and family related health care and costs. However, this study is limited to Ontario and thus a national study is warranted to confirm the Ontario study results. This project will be extended to other provinces, postnatal exposure, and to another neurological outcomes (attention deficit hyperactivity disorder, ADHD) to further examine neurological effects of outdoor air pollution on children. (PI: Hwashin Shin)

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

The COVID-19 pandemic is one of the greatest health challenges in our time. At the time of study initiation, it had 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 were assessed in a human diesel exhaust chamber study to extend laboratory findings to humans. Knowledge gained was 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. Study results were published in 2022. Current analyses (2021–2022) are being conducted to examine adverse neonatal outcomes associated with air pollution in MIREC. Future analyses will examine air pollution and preterm birth. (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 (NO_2), sulphur dioxide (SO_2), and respirable particles in multiple size fractions (UFP, $PM_{2.5}$, $PM_{2.5–10}$) 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 has been completed and preliminary study results have been communicated to stakeholders. Analysis is ongoing and a manuscript is expected in 2023. (PI: Angelos T. Anastasopolos)

CANNABIS

Acute and residual effects of smoked cannabis on mood and cognitive performance of young adults—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. The purpose of this study was to examine acute and residual mood and cognitive performance in individuals who consume or use cannabis following smoked cannabis. Participants were randomized to receive active or placebo cannabis, and mood and cognitive performance were assessed before and 1, 24, and 48 hours after smoking cannabis ad libitum. In young, regular cannabis users, smoking cannabis ad libitum (in other words to their desired high) was found to have significant effects on mood, some of which persisted 24 hours later, yet minimal effects on cognition, and no evidence of residual cognitive impairment. Results of this study will inform risk communications and development of educational resources for consumers and health professionals. *Pharmacology, Biochemistry and Behavior* (2020) (PI: Bruna Brands)

Acute and residual effects of smoked cannabis: impact on driving speed and lateral control, heart rate, and self-reported drug effects—NEW!

As more jurisdictions move toward legalization of cannabis, regulators are likely to be increasingly concerned with the road safety impact of these changes and how any negative effects can be attenuated or avoided. Although driving under the influence of cannabis is increasingly common among young adults, little is known about residual effects on driver behavior. This study examined acute and residual effects of smoked cannabis on simulated driving performance of individuals who consume or use cannabis. Cannabis was observed to cause decreased speed, increased heart rate, and increases in subjective drug effect and drug high. There was no evidence of residual effects on these measures over the two days following cannabis administration. Results of this study will inform risk communications and development of educational resources for consumers and health professionals. *Drug and Alcohol Dependence* (2019) (PI: Bruna Brands)

Annual report of adverse reactions associated with cannabis products reported to Health Canada January 1, 2020–December 31, 2020—NEW!

Health Canada's (HC) Vigilance Framework for Cannabis Products allows for detection, collection, monitoring, and assessment of adverse reactions (ARs) to support a variety of regulatory activities. Adverse reactions are submitted to HC by consumers and healthcare professionals on a voluntary basis and by licence holders on a mandatory basis for serious ARs. Reports are received and coded in the Canada Vigilance Database and monitoring, detection, prioritization, evaluation and risk management of cannabis ARs is conducted. In the 2020 Canadian Cannabis Survey, 27% of respondents reported past 12-month cannabis use with safe supply and quality reported as the most important factors when sourcing cannabis. This project is a summary of AR cases associated with legal cannabis products

reported to HC during the second year of legalization, reflective of the first full period in which new classes of cannabis products became legally available for sale. A descriptive analysis of cases involving legal cannabis products received from January 1, 2020–December 31, 2020 was conducted. A total of 159 cases involving legal cannabis products were reported to HC in 2020. More than half of these cases were among females (57%) and frequently involved cannabis use for self-reported medical purposes (77%) and orally consumed cannabis extracts (79%). The most frequently reported medical events were hallucination (n = 54), dizziness (n = 13) and nausea (n = 12). Of the cases assessed, most were assigned a causality of 'Possible' (n = 95) meaning the product may have contributed to the AR but the contribution of other factors could not be ruled out. These data will inform risk communications and development of educational resources for consumers and health professionals. HC will continue to monitor cannabis ARs to help inform evidence-based information on health and safety risks with cannabis, and public-facing summary reports are expected to be published annually. (PI: Stephanie Jack, Sieara Plebon-Huff)

Canadian Cannabis Survey (CCS)—NEW!

Health Canada has been collecting data to better understand how Canadians view and use cannabis. These data will be used to evaluate the impact of the *Cannabis Act*, which was brought into force on October 17, 2018, and to support development of policy and program initiatives, including public education and awareness activities. The Canadian Cannabis Survey (CCS) was first conducted in 2017. It examined, in more depth, patterns of use, such as the quantities of cannabis consumed and the use of cannabis for medical purposes; the cannabis market, such as sources of cannabis and pricing; and issues of public safety, such as impaired driving. Additional content has been added or changed over the years to monitor emerging issues of relevance to cannabis such as the impacts on cannabis of the Coronavirus disease 2019 (COVID 19). Data collection for CCS 2022 was conducted between April and June 2022 and the results were released in December 2022. The 2022 cycle of the survey included new content as well. All respondents were asked questions regarding exposure to cannabis advertisement/promotions and accidental consumption of cannabis by any people or pets in the home and the resulting outcome(s). Those who use cannabis were asked new questions relating to whether their use changed over the past 12 months due to the ongoing COVID-19 pandemic and whether they feel they have reasonable access to cannabis through a legal supplier. In addition, they continue to be asked about the frequency, quantity, routes of administration, forms of cannabis used, relative levels of THC and CBD, and driving after cannabis use. Furthermore, those who use cannabis are asked about harms and benefits of their cannabis use and whether they use cannabis for medical purposes. Content review is currently under way for the 2023 cycle of the survey with data collection anticipated to begin in April 2023. Results of this study will inform risk communications and development of educational resources for consumers and health professionals. (PI: Matthew Dann)

Cannabis, impaired driving and road safety: An overview of key questions and issues—NEW!

As more jurisdictions move toward legalization of cannabis, regulators are likely to be increasingly concerned with the road safety impact of these changes and how any negative effects can be attenuated or avoided. While in the past there has been controversy over whether cannabis use and driving under the influence of cannabis (DUIC) presented road safety risks, more recent research provides converging evidence that DUIC can increase collision risk and may be an important contributor to deaths and injuries resulting from collisions. Young adults appear most likely to engage in DUIC. Acute effects of cannabis on driving-related behaviors may include an increase in weaving, and a reduction in speed. Effects on reaction time have also been reported. This seems true regardless of the route of administration although more research is needed. At present, all studies of the effects of oral cannabis on driving consisted of synthetic THC (dronabinol) and no studies of cannabis edibles have been published. Evidence also exists to identify levels of cannabis in the blood at which impairment is observed and which thus may be proposed as per se levels for legal initiatives to deter DUIC. Currently, little is known about the types of collisions most likely to involve cannabis, or if cannabis affects injury severity. More research is needed to understand sex differences in the effects of cannabis. Other questions include the comparative pharmacology of different modes of administration of THC, different doses of THC and the extent to which regular or frequent uses may develop and display tolerance to the impairing effects of cannabis on driving behavior. As well, more investigation of the potential impairing effects of cannabis on people who use cannabis for medical purposes is warranted. Important questions remain as to the duration of the effects of cannabis on driving and the time course of safe use of cannabis. *Frontiers in Psychiatry* (2021) (PI: Bruna Brands)

Characterization of cannabis nanoemulsions and uptake analysis survey using zebrafish—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. New technologies such as nanoemulsions, especially in the context of orally ingested cannabis products, may decrease the amount of time it takes to feel the effects or increase uptake in the body and are available on the legal cannabis market. Additionally, the term “nano” is used to market products, along with information that they may produce effects more quickly. However, no data to verify either claim is provided. This research aims to verify if these formulations actually correspond to nanoformulated products, and how their absorption rates may differ from non-nanoformulated cannabinoids. Ten cannabis products marketed as nanoemulsions were purchased from the legal retail market and characterized using dynamic light scattering. Of these, three did not appear to be nanoemulsions. Of the remaining seven products that appeared to be nanoemulsions, four contained the small-sized, evenly dispersed nanoparticles expected in a nanoformulation, while the other three were not evenly dispersed. Following this characterization, the absorption, distribution, metabolism and excretion (ADME) of these products were further studied using a model zebrafish assay. Generally, differences were seen in cannabinoid uptake levels across different products that may be linked to their nanoemulsion formulation. Differences were also observed in cannabinoid metabolite levels measured across different products, but it is

unclear whether the nanoemulsion characteristics or other factors were responsible. This preliminary work demonstrates that the ADME zebrafish assay is suitable for testing cannabis nanoemulsions and will support future work in this area. (PI: Lee Ellis, National Research Council; Hanan Abramovici)

Deterring driving under the influence of cannabis: Knowledge and beliefs of drivers in a remedial program—NEW!

As provincial and territorial governments across Canada adjust to the federal legalization of cannabis for non-medical use, strategies to deter driving under the influence of cannabis (DUIC) are increasingly attracting attention. Development and evaluation of legal and other measures designed to deter DUIC would benefit from improved understanding of knowledge and beliefs that underpin individuals' engagement in and avoidance of DUIC. In 2017, 20 interviews were conducted with clients of a remedial program for officially processed (i.e., convicted or suspended) impaired drivers. Eligible study participants reported having driven a motor vehicle within an hour of using cannabis in the past year. We observed vague awareness of the content of drug-impaired–driving laws; perceived low likelihood of getting caught by police for DUIC, with some beliefs that enforcement would increase after legalization; and a range of opinions on four key deterrent strategies (i.e., roadside spot-check programs, legal limits for tetrahydrocannabinol, zero tolerance for novice drivers, and remedial programs). Many participants raised concerns about the accuracy of roadside testing procedures and fairness to drivers. These findings provide new support for elements of legislation and programming that might effectively deter DUIC. *Canadian Journal of Criminology and Criminal Justice* (2019) (PI: Bruna Brands)

Effects of cannabis consumed for medical purposes on simulated driving: A pilot study—NEW!

As more jurisdictions move toward legalization of cannabis for medical purposes, regulators are likely to be increasingly concerned with the road safety impact of these changes and how any negative effects can be attenuated or avoided. Although cannabis for medical purposes has been available to Canadians since 2001, there is little research on the effects of cannabis on driving in individuals who use cannabis medically. This pilot study sought to determine the effects of cannabis used for medical purposes on simulated driving. After smoking cannabis, overall mean speed was reduced. No effects of cannabis for medical purposes were found on straightaway mean speed or straightaway lateral control for either condition (standard or cognitive load) or on brake latency. After smoking cannabis in the lab, changes in speed and lateral control were negatively correlated with the amount of cannabis smoked per day. Prior to smoking cannabis in the lab, under baseline conditions, speed and lateral control under cognitive load were also correlated with the amount of cannabis used per day. Cannabis used for medical purposes increased subjective reports and blood levels of THC and metabolites. Thus, even with repeated daily use, cannabis consumption among those who use cannabis for medical purposes may alter driving behavior. This has implications for road safety and use of cannabis among those who use cannabis for medical purposes. These findings provide support for elements of legislation and programming that might effectively deter DUIC. *Journal of Concurrent Disorders* (2020) (PI: Bruna Brands)

Expanded analysis of metal contaminants in cannabis extract vaping products—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. Measuring cannabis contaminants such as heavy metals is important as heavy metal toxicity can be significant via inhalation (e.g., smoking, vaping). Legal cannabis is routinely tested for heavy metals such as cadmium, arsenic, lead and mercury as these are of highest concern from a health risk perspective. Cannabis grown by licence holders typically tests within established inhalation quality limits for these metals. However, prior work in a collaborative research project between Health Canada and the National Research Council in FY 2020-2021 compared the quality of legal and illegal cannabis vaping products and showed that in both cases other metals that are commonly used in the metal alloys of vaping devices were present. These are not widely tested for in legal cannabis, and included cobalt, copper, chromium, nickel and vanadium. Results suggested that metal particulates from the vaping devices were contaminating the samples, but it was not possible to confirm if that was the sole source of the metals contamination. High variability was also often seen between metal measurements of the same sample, so it was difficult to confidently state to what extent the samples were contaminated with metals. Building on this preliminary work, this current project achieved improvements to sampling techniques that decreased the previously observed variability in measurement. It also looked at metal contamination in a wide variety of dried cannabis samples to establish if dried cannabis used to make vaping extracts contributes to metal contamination. This research will help support policy and regulatory work, public education and awareness as well as compliance and enforcement activities. It may also support the drafting of standards or additional guidance on the testing of dried cannabis, cannabis vaping products and accessories such as vaping devices. Publication expected in 2023. (PI: Zuzana Gajdosechova, National Research Council; Hanan Abramovici)

Exploring perceptions among people who drive after cannabis use: Collision risk, comparative optimism, and normative influence—NEW!

As more jurisdictions move toward legalization of cannabis, regulators are likely to be increasingly concerned with the road safety impact of these changes and how any negative effects can be attenuated or avoided. While the perceived risks of driving under the influence of cannabis (DUIC) have been a focus of recent drug-driving research, relevant concepts from the social cognition literature have rarely been applied to inform understanding of DUIC. This study aims to expand knowledge of perceived collision risk and social influences associated with DUIC and driving after other substance use. Interviews were conducted with 20 participants of a remedial program for impaired drivers. Many participants identified DUIC as less risky than driving under the influence of alcohol or other drugs. Mixed perceptions regarding the danger of DUIC were expressed, with some participants denying increased collision risk except among novice cannabis consumers. Comparative optimism bias was also expressed by participants who perceived themselves as less likely than others to be involved in a collision when DUIC. In view of normative influence, friends were generally seen as more accepting of DUIC than family, and there were indications that the opinions of others who use cannabis were regarded as more credible than the opinions of those who do not use the drug. Comparative optimism bias and normative influence may contribute to perceived risks associated with DUIC and may, therefore, be useful concepts to employ to increase the effectiveness of public health and road safety initiatives. *Drug and Alcohol Review* (2019) (PI: Bruna Brands)

Fungal contamination monitoring in legal cannabis products: optimization of detection and quantification method for mycotoxins in cannabis inflorescence and edible oil using UHPLC-MS-MS by the HC ROEB Cannabis Laboratory—NEW!

Health Canada's mission to maintain and improve Canadian's health requires rigorous testing of cannabis legal products. Health Canada's Cannabis Laboratory has already established a method for detecting mycotoxins, a type of fungal contaminant, in cannabis inflorescence. Since 2018, when cannabis for non-medical purposes was legalized, other cannabis products have been made available for Canadians. Additionally, other mycotoxins have been targeted as potential contaminant of increasing concern. In order to ensure product safety for Canadian consumers, the existing mycotoxin detection method was revisited to increase the number of testable cannabis product type and detectable mycotoxins, while decreasing costs associated with reagent use and human-made manipulations. Health Canada's Cannabis Laboratory has worked for the past 2 years on an optimization of detection and quantification method for mycotoxins in cannabis inflorescence and ingestible oils. Parameters such as extraction solvent composition, solvent to biomass ratio, injection volume and mass spectrometry parameters have been fine-tuned for detections of *Aspergillus*-produced aflatoxins (G1, G2, B1 and B2) and ochratoxin A, as well as *Fusarium*-produced deoxynivalenol (DON). Data on method accuracy, precision and repeatability were generated. Mycotoxin analysis outlook in global cannabis production were also considered. (PI: André Robichaud)

Influence of cannabinoid receptor 1 (CNR1) genetic variants on the subjective effects of smoked cannabis—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. Mounting evidence suggests that genetics play an important role in determining psychoactive drug effects and genetic variation may contribute to individual differences in risk of developing cannabis-related problems. The cannabinoid type-1 receptor is the primary receptor that mediates most of the psychoactive effects of cannabis, and it is encoded by the CNR1 gene. We tested the hypothesis that specific polymorphic regions in the CNR1 gene (i.e., regions where the gene varies between individuals) would influence the subjective effects of smoked cannabis using data from 52 participants from a human laboratory study. Both CNR1 polymorphisms we tested (rs1049353 and rs2023239) showed a significant association with self-reported subjective cannabis effects after smoking a cannabis cigarette. Our findings demonstrate that genetic variation in the CNR1 gene contributes to differences in self-reported acute cannabis intoxication under laboratory conditions. Results of this study will inform risk communications and development of educational resources for professionals. *International Journal of Molecular Sciences* (2021) (PI: Bruna Brands)

Influence of personality on acute smoked cannabis effects on simulated driving—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. A recent study of the impact of smoked cannabis on simulated driver behavior demonstrated a reduction in mean speed after smoked cannabis. Previous research identified an association between personality and individual differences and acute drug effects. The present study examined the impact of personality on the reduction in mean speed after smoking cannabis under single- and dual-task driving conditions originally reported by Brands et al. (2019). Sixty-one participants randomly assigned to receive THC or placebo (no THC) completed a battery of self-report questionnaires measuring various personality constructs and subsequently operated a driving simulator before, and 30 min after, smoking a 12.5% Δ^9-tetrahydrocannabinol (THC) cigarette. After adjusting for the influence of sex, blood THC concentration, and pre-drug mean speed, impulsivity was a significant predictor of change in speed under both single- and dual- task driving conditions after cannabis. Higher trait impulsivity was significantly associated with greater reductions in driving speed after cannabis use, which may reflect greater sensitivity to drug effects and a stronger compensatory response. Further multidisciplinary study, including neurochemical, genetic, and psychological components, would be beneficial in helping to better understand how impulsivity and other personality or individual differences may impact the effects of cannabis on driver behavior and performance. These results will help to inform educational initiatives for safer driving. *Experimental and Clinical Psychopharmacology* (2021) (PI: Bruna Brands)

Inter-year comparison of adverse reactions associated with legal cannabis products reported to Health Canada, October 17, 2018 to December 31, 2019 and January 1, 2020 to December 31, 2020—NEW!

Since the implementation of the *Cannabis Act* in 2018, a number of events may have potentially impacted cannabis use and behaviours, as well as the number and type of cannabis adverse reactions (ARs) reported. Potential trends in reported ARs can be assessed using Health Canada's (HC) Vigilance Framework for Cannabis Products, which allows for detection, collection, monitoring, assessment, and risk management of cannabis ARs in near time and over time as aggregate data. This project aims to present a comparison of AR cases associated with legal cannabis products collected under this Framework during the first and second year of cannabis legalization. Adverse reaction cases are submitted to HC by consumers and healthcare professionals on a voluntary basis and by licence holders on a mandatory basis for serious ARs. Reports are received and coded in the Canada Vigilance Database by Health Canada's Marketed Health Products Directorate and are prioritized and evaluated by the Controlled Substances and Cannabis Branch's Office of Cannabis Science and Surveillance. Direct comparison of descriptive results for domestic cases involving legal cannabis products received by HC from October 17, 2018 to December 31, 2019 and January 1, 2020 to December 31, 2020 was conducted to identify any trends. The total number of reports received by HC increased across the reporting periods, from 151 to 161, with the number of serious cases increasing by 61%. Females were more frequently involved in cases than males. Cases in 2020 were evenly distributed between individuals <65 and ≥65 years (38% each), a shift from the previous period. Oral cannabis extracts were the most frequently reported class of products despite the availability of new classes in the second year

of legalization. Some findings in the AR data have changed while others remained consistent between the 2 years. Findings are preliminary and further years of data are required to observe and assess any long-term trends. HC will continue to monitor, analyse, and report on ARs with cannabis. (PI: Stephanie Jack, Sieara Plebon-Huff)

Investigation of degradation by-products from cannabis vaping liquid ingredients via thermal desorption—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. Cannabis vaping is gaining popularity, but little is known about the by-products formed during vaporization of cannabis vaping liquids. This research aims to provide a better understanding of potential exposure and health risks from cannabis vaping. Thermal desorption coupled to a gas chromatography/mass spectrometer (TD-GC/MS) was used to develop a vaping surrogate method to help characterize and identify degradation by-products produced during vaporization of cannabis vaping liquid ingredients. A number of ingredients commonly found in cannabis vapes were chosen for the study including ten terpenes (monoterpenes: terpinolene, α-pinene, β-pinene, myrcene and limonene; sesquiterpenes: α-humulene, β-caryophyllene; diterpene: phytol; triterpenes: squalane and squalene), as well as four commercially available terpene vaping flavour blends. Other substances that have been reported in certain types of vaping products were also tested including propylene glycol, benzyl alcohol, triactin, triethyl citrate and vitamin E acetate. A number of different oxidative and degradation by-products were detected from the tested ingredients. No obvious by-products were observed for squalane, squalene, triethyl citrate, triacetin, propylene glycol and vitamin E acetate. However, many by-products were found for benzyl alcohol, phytol and the five monoterpenes. This study provides initial information and demonstrates that in the typical vaping temperature range, oxidative by-products may be present in vaping aerosols. The toxicity of inhaling some of these products is not clear yet, and this TD-GC/MS method does not perfectly mimic consumption of a cannabis vaping product. This preliminary data will help support work towards risk assessment, risk management, regulatory policy development and public education and awareness for cannabis vaping products. Publication completed in 2022. DOI: 10.1038/s41598-022-14236-4 (PI: Jiping Zhu, Hanan Abramovici)

In vitro pharmacological testing of synthetic cannabinoids at the CB_1 and CB_2 receptors—NEW!

The Office of Drug Policy and Science (ODPS) of the Controlled Substances Directorate is responsible for providing substance status to stakeholders and making recommendations on substance scheduling under the CDSA. Synthetic cannabinoids are a diverse group of substances that can activate the cannabinoid receptor system throughout the human body. These substances have a different pharmacological profiles than phytocannabinoids found in cannabis plants, and are known to be multiple times more potent than the main psychoactive phytocannabinoid Δ^9-tetrahydrocannabinol (THC). “Synthetic cannabinoid receptor type 1 agonists, their salts, derivatives, isomers, and salts of derivatives and isomers” are currently controlled under Schedule II, Item 2 to the *Controlled Drugs and Substances Act* (CDSA). Novel synthetic cannabinoids emerge rapidly and there is an absence of information on their pharmacological properties, which is key for regulatory science decision-making

for these substances. In order to evaluate and regulate such novel synthetic cannabinoids, this project determines *in vitro* pharmacological characteristics for novel synthetic cannabinoids without published pharmacological information and which have been encountered by Canadian law enforcement partners and international monitoring programs. The affinity and efficacy of putative synthetic cannabinoids at cannabinoid receptor type 1 (CB_1) and type 2 (CB_2) are measured using *in vitro* assays. The results will inform ODPS regulatory science activities. Furthermore, the study examined the relationship between chemical structure and CB_1/CB_2 pharmacological activity will be considered for future decisions on the regulation of the synthetic cannabinoids class to ensure the safety and well-being of Canadians. (PI: Zhiyun Jin)

"Just a habit": Driving under the influence of cannabis as ordinary, convenient, and controllable experiences according to drivers in a remedial program—NEW!

As numerous jurisdictions worldwide are liberalizing cannabis laws, there is increasing need to understand the social contexts and individual perceptions involved in driving under the influence of cannabis (DUIC). Twenty one-to-one interviews were conducted with adult participants recruited from a remedial program for drivers convicted of or suspended for impaired driving. Study eligibility included having driven a motor vehicle within an hour of using cannabis in the last year. Many participants described DUIC as part of ordinary or routine experiences. Despite availability of other transportation options, DUIC was often preferred due to convenience and cost-effectiveness. While most recalled feeling some effects of cannabis use or feeling high while driving, many reported that they did not feel a need to compensate for impairment. Study findings—particularly that of DUIC as a regularly occurring behavior—highlight important challenges for designing effective education and prevention initiatives. *Journal of Drug Issues* (2019) (PI: Bruna Brands)

Mu Opioid receptor gene variant modulates increased subjective responses to smoked cannabis—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. The mu-opioid receptor underlies the rewarding properties of many psychoactive drugs and is an important target in the treatment of addictions. Multiple lines of evidence have demonstrated interactions between the opioid and cannabinoid systems in the body. The present study tested the hypothesis that specific polymorphic regions in the mu-opioid receptor gene (OPRM1) (i.e., regions where the gene varies between individuals) would influence the subjective effects of smoked cannabis using data from 52 participants from a human laboratory study. One OPRM1 polymorphism (rs510769) significantly impacted subjective cannabis effects, and also impacted blood concentrations of delta-9-tetrahydrocannabinol (THC), the primary psychoactive component of cannabis, after smoking a cannabis cigarette. Our findings demonstrate that genetic variation in the mu-opioid receptor gene (OPRM1) contributes to differences in self-reported acute cannabis intoxication under laboratory conditions. The findings of this study will add to the knowledge of the role played by cannabis in the field of epigenetics. *American Journal of Translational Research* (2022) (PI: Bruna Brands)

Sex differences in the acute effects of smoked cannabis: evidence from a human laboratory study of young adults—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. To support this objective, a better understanding of the risks associated with cannabis products is critical. Animal studies have found robust sex differences in the pharmacokinetics and pharmacodynamics of Δ9-tetrahydrocannabinol (THC). However, the human evidence remains equivocal, despite findings that women may experience more severe consequences of cannabis use than men. The objective of this study was to examine sex differences in THC pharmacokinetics and in acute subjective, physiological, and cognitive effects of smoked cannabis in a sample of regular cannabis consumers (use 1–4 days per week) aged 19–25 years. Females smoked less of the cannabis cigarette than males and had a lower peak concentration of THC and 11-Nor-carboxy-THC (THC-COOH) than males. Blood THC concentrations remained lower in females even when adjusting for differences in estimated dose of THC inhaled. There was very little evidence of sex differences in visual analog scale (VAS) ratings of subjective drug effects, mood, heart rate, blood pressure, or cognitive effects of cannabis. Females experienced the same acute effects of smoked cannabis as males at a lower observed dose, highlighting the need for more research on sex differences in the pharmacology of THC, especially when administered by routes in which titrating to the desired effect is more difficult (e.g., cannabis edibles). *Psychopharmacology* (2020) (PI: Bruna Brands)

Toxicity testing of cannabis vaping product emissions using zebrafish—NEW!

The objective of the *Cannabis Act* is to protect public health and safety. As cannabis vaping is a popular method of consumption, a better understanding of the health and safety risks of cannabis vaping is needed. In addition to studying the ingredients used in cannabis vaping products, it is important to consider the aerosol generated during vaping, as this is what consumers are ultimately exposed to. This research aims to better understand the toxicity of cannabis vaping aerosols using zebrafish as a model. Seven cannabis vaping products purchased from the legal retail market were vaped in the laboratory and the aerosol captured on filter pads. After extraction from the filter pads, samples were characterized by 1H NMR or mass spectrometry and compared to the starting cannabis vaping liquids. Generally, while differences were observed between products, the 1H NMR spectra and cannabinoid data were very similar for a cannabis vaping liquid and the respective filter extract of its aerosols, while the terpene levels in the filter extracts were significantly lower than the starting vaping liquids. When tested in zebrafish using the General and Behavioral Toxicity (GBT) and Fish Embryo Acute Toxicity (FET) assays, all of the filter extracts had very similar toxicity levels, despite differences in the composition of the extracts. It is unclear why the toxicity levels observed were much higher than expected for the aerosols containing THC and CBD based on previous experiments with pure cannabinoids. This preliminary work will inform future work in this area, to help support risk assessment, risk management, regulatory policy development and public education and awareness for cannabis vaping products. (PI: Lee Ellis, National Research Council; Hanan Abramovici)

Use of cannabidiol for the treatment of anxiety: a short synthesis of preclinical and clinical evidence—NEW!

Anxiety disorders have the highest lifetime prevalence of any mental illness worldwide, leading to high societal costs and economic burden. Current pharmacotherapies for anxiety disorders are associated with adverse effects and a relatively low effectiveness rate. Cannabidiol (CBD) is a constituent of the Cannabis plant, which has potential therapeutic properties for various indications. After the recent legalization of cannabis, CBD has drawn increased attention as a potential treatment, as the majority of existing data suggest it is safe, well tolerated, has few adverse effects, and demonstrates no potential for abuse or dependence in humans. Pre-clinical research using animal models of innate fear and anxiety-like behaviors have found anxiolytic, antistress, anticompulsive, and panicolytic-like effects of CBD. Preliminary evidence from human trials using both healthy volunteers and individuals with social anxiety disorder, suggests that CBD may have anxiety reducing effects. Although these findings are promising, future research is warranted to determine the efficacy of CBD in other anxiety disorders, establish appropriate doses, and determine its long-term efficacy. The majority of pre-clinical and clinical research has been conducted using males only. Among individuals with anxiety disorders, the prevalence rates, symptomatology, and treatment response differ between males and females. Thus, future research should focus on this area due to the lack of research in females and the knowledge gap on sex and gender differences in the effectiveness of CBD as a potential treatment for anxiety. *Cannabis and Cannabinoid Research* (2020) (PI: Bruna Brands)

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 evaluation of 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)

A retrospective analysis of health administrative data to measure the health impacts of climate change—Extreme Heat—NEW!

The Climate Change and Innovation Bureau builds knowledge on the health impacts of climate change. Public health surveillance and monitoring is limited by the availability of high quality, reliable data, and information sources. In an effort to enhance the evidence base, the present study aims to describe the burden of temperature-related morbidity and mortality in Canada, for the years 1980 to 2021 with analyses based upon currently available national level administrative data sets. The data sets used will include the Discharge Abstract Database, data from the National Ambulatory Care Reporting System and the Canadian Vital Statistics—Death Database. The analysis will attempt to highlight any trends over time in the data as they relate to heat-related illnesses and deaths. Comparison between age and gender groups will be conducted as well as comparison between the provinces and territories where data are available. The resulting report will identify the strengths and the limitations of these data and make recommendations for ways to improve the quality and the timeliness of reported data. The results of these analyzes will provide baseline estimates for ongoing work and are to be completed by August 2022. (PI: Victor Gallant, Jessica Sutinen)

An expert assessment on play space designs and thermal environments in a Canadian context—NEW!

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Playgrounds are a central hub for child play. Thus, any concerns that may impact children's play at playgrounds, such as unsafe temperatures or conditions, may hinder children's health and well-being. Extreme outdoor temperatures can increase risks in children of sunstroke, burns from playground surfaces, and exposure to harmful ultraviolet (UV) radiation from the sun. Despite the health risks from extreme heat to children, existing playground design standards around the world, including in Canada, make little to no mention of how to design playgrounds for thermal comfort across seasons, particularly in summer. To help fill this gap in the Canadian context, several organizations collaborated to develop guidance for thermally comfortable playgrounds in Canada. As part of this project, an online survey was administered to 55 experts with diverse professional backgrounds, largely from Canada and the United States, to determine how thermal comfort is viewed in playground design and safety. Survey results showed agreement among the topical experts that thermal comfort receives low or no priority in playground design. Furthermore, nearly half of respondents stated that thermal comfort should be prioritized like, or considered alongside, other safety factors in relevant playground safety guidelines and playground standards. The results of this survey not only helped inform the publication in 2019 of a Thermal Comfort annex to the CSA Group's Children's playgrounds and equipment standard (CAN/CSA Z614) but could also help inform future research and practice globally to ensure current and future playability at playgrounds under all weather conditions. Publication expected later in 2022. (PI: Gregory Richardson)

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:

- Tools for assessing climate change vulnerability of healthcare facilities;
- Targeted guidance for prioritization of available health adaptation options, and indicators for measuring overall health system resilience; and
- 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)

Development and implementation of a Heat Alert and Response System in rural British Columbia—NEW!

One of the mandates of the Climate Change and Innovation Bureau is to protect the health of Canadians from extreme heat. From 2018–2020, CCIB supported BC's Interior Health Authority to develop and implement a Heat Alert and Response System in the rural village of Ashcroft, within the interior region. Ashcroft is one of the "hot spots" within BC, with historically high temperatures, and a high proportion of the population over 60 years of age (a demographic that is particularly vulnerable to heat). The objective of this project was to support the development and implementation of a Heat Alert and Response System (HARS) in a small, rural community. The health authority facilitated collaboration among provincial and local governments, community organizations, and First Nations partners to assess community assets, draft a plan for extreme heat, and prepare for a community-supported response during heat events. Stakeholders expressed the importance of utilizing existing partnerships and community resources, such as physical and procedural infrastructure, in which to embed the HARS. It was imperative that the plan be simple, concise, and considerate of the community's unique context. Educational materials and a tailored method of dissemination were important for collective and individual risk mitigation. A community-driven approach that utilized existing assets allowed for integration of HARS within municipal response plans and established infrastructure. The result is a sustainable public health intervention that has the potential to mitigate the negative health effects of extreme heat. Knowledge acquired through this initiative is informing similar HARS planning processes in other rural BC communities, and across Canada. Published on March 18, 2022. (PI: Rachel Siblock, in partnership with BC's Interior Health Authority)

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. Final report being prepared for June 30, 2022. (PI: Victor Gallant, Kerri Warner)

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 2022

The Climate Change and Innovation Bureau (CCIB) at Health Canada led the development of the national climate change and health assessment released in February 2022, entitled *Health of Canadians in a Changing Climate: Advancing our Knowledge for Action*. The report is part of a series of report through the Government of Canada Climate Change Impacts and Adaptation Knowledge Assessment process led by Natural Resources Canada, and it assesses the latest research and informs Canadians on how climate change is affecting their health and health system.. The *Health of Canadians in a Changing Climate: Advancing our Knowledge for Action* report builds on national assessments conducted in 2008 and 2014. The final report includes separate chapters that examine climate change impacts on mental health, infectious diseases, food safety and security, water safety and security, natural hazards, air pollution, health inequities, special challenges faced by Indigenous Peoples and adaptation and resiliency of health systems. 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 final report:

- Examines climate change impacts on the health of Canadians;
- Explores climate change impacts to the health system; and,
- Investigates measures to effectively adapt to a changing climate and reduce future climate change. (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 funded 10 health authorities across 5 provinces and territories until March 2023. 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)

Impact of Ontario's Harmonized Heat Warning and Information System (HWIS) on emergency department visits for heat-related illness in Ontario, Canada: A population-based time series analysis—NEW!

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Ontario's Harmonized Heat Warning and Information System (HWIS) brings harmonized, regional heat warnings and standard heat-health messaging to provincial public health units prior to periods of extreme heat. This study explored whether the implementation of the harmonized HWIS in May 2016 was associated with a reduction in emergency department (ED) visits for heat-related illness in urban locations across Ontario, Canada. Researchers conducted a population-based interrupted time-series analysis from April 30–September 30, 2012–2018 using administrative health and outdoor temperature data, to examine if ED rates changed following implementation of the harmonized HWIS. Researchers also examined if effects differed in heat-vulnerable groups (those aged 65 years and older or under the age of 18 years, those with comorbidities, those with a recent history of homelessness), and by heat warning region. Over the study period, heat alerts became more frequent in urban areas. ED rates were particularly high in those with a recent history of homelessness. Although ED rates appeared to decline following implementation of HWIS in some subpopulations, the change was not statistically significant. Efforts to continually improve HWIS processes are important given our changing Canadian climate. This study provides an evaluation of the current protective ability of the HWIS system, and a starting point for improvement and enhancement of the system to further protect the residents of Ontario. Publication is expected in the summer of 2022. (PI: Rebecca Stranberg)

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 differences 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)

Reimagining spaces where children play: developing guidance for thermally comfortable playgrounds in Canada

The Climate Change and Innovation Bureau is committed to protecting the health of Canadians from extreme heat, especially vulnerable populations. 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. However, existing playground standards focus on equipment and surfacing to reduce acute injuries, with no mention of potential negative health consequences related to heat illness, sun exposure, and other thermal extremes. 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 playground equipment and surfacing standard. A group of multidisciplinary experts developed technical guidance for improving thermal comfort at playgrounds, including a six-page thermal comfort annex adopted within a national playground and equipment standard. The annex has been used by Canadian schools in a competition to design and implement green playgrounds. Both the technical report and the thermal comfort annex provide increased awareness and needed guidance for managing environmental conditions at playgrounds. Thermally safe and comfortable play spaces will help ensure that Canada's playgrounds are designed to minimize environmental health risks for children. Publication June 15, 2021. (PI: Gregory Richardson)

Public perceptions of the health impacts of climate change in Canada 2022

Health Canada identified the need for Public Opinion Research (POR) to understand the current views of Canadians on climate change, including the risks and impacts they believe are associated with their health, and how best to adapt and be more resilient in the future. Health Canada launched a POR in 2008 and 2017, the findings from these PORs were used to set baseline levels to which findings from the 2022 POR were compared. The objectives of the 2022 POR were to understand:

- The level of awareness of climate change and its health risks and impacts;
- Actions taken to adapt/be more resilient to the health risks or impacts of climate change;
- Trusted sources of media used and other means and opportunities for education and awareness raising; and
- The public's views on role(s) of government and non-government organizations.

The 2022 POR was conducted between February 10 and March 13, 2022 via a dual-mode method. There were responses from 1,905 Canadians (telephone: 1,520 and online: 385) aged 18 years and older. Findings indicate that 85% of Canadians are increasingly convinced that climate change is definitely happening; this belief has steadily increased over time (from 69% in 2008 and 79% in 2017). Canadians who believe that climate change is happening (definitely or probably) express widespread concern about it (79% are at least somewhat worried about climate change). The final report will be published online on the Library and Archives Canada website by December 2022. (PI: Lubna Salman)

The impacts of the 2021 western heat dome: a systematic review of media articles, reports and communications—NEW!

The deadliest weather event in Canadian history struck Canada from June 25th to July 7th, 2021. The western provinces recorded more than 103 all-time heat records, including Canada's highest temperature ever measured (49.6°C; June 29th 2021, Lytton, British Columbia). The BC Center for Disease Control (BC CDC) has released values indicating 740 excess deaths related to the Western Heat Dome. A cursory scan of media articles shows the Western Heat Dome caused impacts to Canadian economy, infrastructure, environment, health, and social well-being, however, to date there has been no systematic review conducted to assess impacts stemming from the occurrence. To fill this gap, this study series will conduct a systematic analysis of media articles and grey literature within the bounds of Canada. The results of this work will support numerous interests. They will illustrate the impacts of extreme heat events (EHEs) in Canada to people, the economy and environment, and will help BC and other parts of Canada prepare and build resilience to extreme heat. They will provide Health Canada and partners with important baseline information and lessons learned while supporting a better understanding of the economic, infrastructure, environmental, health, and social well-being impact of EHEs. They will support the Government of Canada's National Risk Profile, which is a strategic national disaster risk and capability assessment based on scientific evidence and stakeholder input, as well as the Emergency Management Strategy for Canada which includes a goal to improve the understanding of disaster risks in all sectors of society. Finally, these findings could be used by all levels of Government in Canada to inform proactive health interventions and better prepare for future EHEs. Publication expected in fall 2022. (PI: Emily Tetzlaff, Melissa Gorman)

Understanding mortality during the 2021 heat dome event in British Columbia—NEW!

Health Canada is working to protect Canadians from the health risks of extreme heat events (EHEs). To this end, Health Canada is working with Provinces and Territories to develop partnerships with varied stakeholders across the country to successfully implement and enhance Heat Alert and Response Systems (HARS). The British Columbia Centre for Disease Control (BCCDC) has expressed interest to Health Canada in understanding the mortality in BC during the 2021 western heat dome event. The BCCDC intends to use a data platform originally intended for COVID-related analyses to link all deaths to multiple administrative datasets. The project will compare people who died during the heat dome with people who died during other periods, and people who survived the heat dome event to better understand the risk and potentially protective factors. Understanding these factors is especially important given EHEs are expected to increase in frequency, severity, and duration due to climate change, resulting in increased illness and deaths. BC will use this information to inform its provincial HARS, including messaging and public health action/response to protect populations from future EHEs. The information will also be useful for other jurisdictions across Canada. The epidemiologic investigation will add to the growing body of HARS knowledge that Health Canada can draw upon as it updates its publications and informational materials. The intent is to develop peer-reviewed manuscripts that will be shared publicly, so that stakeholders across Canada and around the world can learn from the heat dome event and ultimately advance their respective evidence-based heat responses. The project will directly contribute to the Climate Change and Innovation Bureau's mandate to support Canadian

communities implement and/or enhance heat alert and response systems and understand local vulnerabilities to EHEs. Draft manuscript expected in August 2022. (PI: Melissa Gorman in partnership with the BCCDC)

WHO guidance on conducting climate change and health vulnerability and adaptation assessments—NEW!

The Climate Change and Innovation Bureau has a long-term target of ensuring that Canadians are resilient to the health effects of climate change. Understanding climate-related risks to health, the strengths and weaknesses of the health system and specific programmes to manage climate change impacts is of critical importance to plan modifications needed to increase the resilience of health systems. Vulnerability and adaptation (V&A) assessments are a tool that allows countries to evaluate which populations and specific geographies are most vulnerable to different kinds of health effects from climate change; to identify weaknesses in the systems that should protect them; and to specify interventions to respond. The aim of this report is to provide basic and flexible guidance on conducting national or subnational assessments of current and future vulnerability to the health risks of climate change, and of policies and programmes that could increase resilience, taking into account the multiple determinants of climate-sensitive health outcomes. This report builds on the previous report *Protecting health from climate change: vulnerability and adaptation assessment* published in 2013, and integrates new knowledge on climate change and health. Published in October 2021. (PI: Peter Berry)

CONSUMER PRODUCT SAFETY

Acute injury or illness related to the inhalation of vaping aerosols among children and adolescents across Canada: A cross-sectional survey of Canadian paediatricians—NEW!

Vaping prevalence rates have increased among Canadian youth. Evidence suggests that vaping poses significant health risks to children and adolescents. The objectives of the study were to investigate epidemiological characteristics of acute injury/illness cases due to the inhalation of vaping aerosols among children and adolescents across Canada and to explore factors contributing to severe cases. Data from the 2019 Canadian Paediatric Surveillance Program cross-sectional survey on vaping-related injury/illness were used. Analyses focused on injury/illness cases (n = 71) among children and adolescents aged 0 to 17 years who presented to participating paediatricians for a harm related to the inhalation of vaping aerosols. The inhalation of vaping aerosols among children and adolescents may contribute to acute injury/illness. Clear associations between study variables and severe cases could not be established due to a small sample size. Additional research is needed to determine predictors and preventable risk factors of severe vaping-related injuries. Published on August 23, 2021: https://doi.org/10.1093/pch/pxab062. (PI: Dr. Minh T Do, Lina Ghandour).

Assessment of virulence of opportunistic human pathogens in microbial mixtures—NEW!

The New Substances Assessment and Control Bureau (NSACB) Biotechnology Sections are responsible for conducting human health risk assessments of microorganisms used as products of biotechnology that could be human pathogens or have traits that could elevate their pathogenic potential. This involves a thorough analysis of the most current scientific evidence available in the literature as well as information/data provided by the notifier as prescribed by the New Substances Notification Regulations (Organisms) (NSNR(O)). Research to support regulation is important in identifying and addressing knowledge gaps for conducting these types of assessments. Emerging applications of biotechnology products that may require notification under the NSNR(O) involve products that are mixtures formulated from pure cultures. These applications include cleaning products, biofuel production, and wastewater treatment. Many of these products exist as heterogeneous microbial mixtures of several species. The work proposed in this collaborative research agreement (CRA) will provide a better understanding of the suitability and possible limitations for assessing pathogenicity of heterogeneous microbial mixtures versus virulence of each microbe separately. The findings will further our understanding of the complex interaction of microbes as they exist in mixtures intended for biotechnology applications. Furthermore, NSACB Biotechnology, in partnership with Innovations, Science and Economic Development (ISED) Canada, has commissioned a challenge to Canadian biotechnology innovators to develop predictive bioinformatics tools to understand microbial interactions and their impacts on predicting adverse effects (pathogenicity, toxicity, etc.). The research output from this CRA is expected to complement ISED's predictive analysis and provide a more comprehensive risk analysis tools. (PI: Azam Tayabali)

Compositional analysis of terpene and terpenoid containing consumer products—NEW!

The Chemicals Management Plan (CMP) is a Government of Canada initiative aimed at reducing the risks posed by chemicals to Canadians and their environment. To support risk assessment and risk management strategies for the Terpenes and Terpenoids Group under CMP, chemicals commonly found in essential oils and tinctures, the Product Safety Laboratory (PSL) performed a series of compositional analyses on products advertised as containing: cade oil, verbena officinalis, cork tree, and sandela. PSL improved on workflow strategies for qualitative analysis of oils to address instrument limitations for detection and confirmation of specific target compounds. Multiple techniques were used for detection and confirmation of compounds including gas-chromatography mass-spectrometry (GC-MS), liquid chromatography equipped with a triple quadrupole mass spectrometer (LC-MS/MS) and GC-MS/MS. Qualitative instrument parameters were developed and modified to address compound interferences and limitations to various techniques. Reference materials were acquired for some compounds of interest and quantitative analysis was performed. For other compounds, a gas chromatography—flame ionization detector (GC-FID) was used to provide semi-quantitative concentration estimates. The results from the compositional analyses and the testing expertise gained from this work will further support risk assessment and risk management strategies for terpineols. (PI: Nathalie Ritchot)

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, provides a better understanding of Canadian children's exposure to DEET and inform any future recommendations. (PI: Jennifer Gibson; Kim Irwin)

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

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. Products available to consumers 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 pressures and tendencies 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 pathogenicity test methods for assessing the hazard of microorganisms used in biotechnology

Microorganisms are 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 and sediment

Health Canada conducts 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. Surface water samples were collected monthly (May to October 2021) from six mixed-use watersheds in addition to four exploratory sites to determine the distribution and concentrations of drug substances on Health Canada's Revised In Commerce List (R-ICL). Additionally, sediment samples collected monthly in 2020 (May to October) were analyzed for a number of additional drugs. Surface water grab samples and sediment samples were analyzed by targeted LC-MS/MS methods. Sample processing for surface water was performed using online SPE in combination with an OT-2 robotic system for sample preparation. All compounds were analyzed using isotopically labelled standards (when available) with matrix matched calibration curves. Sediment samples were sequentially extracted to determine what compounds were rapidly desorbed, slowly desorbed and bound to the sediment. Collaborative work and passive sampling continues to expand and now includes the NORMAN network, provincial partners and ECCC. 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, Mark Sumarah)

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)

Migration of flame retardants from foam-containing consumer products—NEW!

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 2019–2020, in order to support risk assessment and risk management strategies for flame retardants, the Product Safety Laboratory (PSL) tested a series of polymeric foam products available to consumers 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 2019–2020, by examining the amounts 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 that migrate from the surface of the foam into simulated sweat. PSL developed and validated test methods for the migration of TEP, IPPP and melamine from foam to mimic sweat-mediated dermal exposure from lying or sitting on foam-containing products. A subset of consumer products from the 2019–2020 project were tested. A total of 27 specimens were tested for the migration of melamine, and 30 specimens were tested for the migrations of TEP and IPPP. In addition to migration, this project examined loss of flame retardant concentration over time in storage by testing the identified subset of products available to consumers 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)

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

Analysis of vaping liquids on Canadian market for chemical compounds of interest—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. Nicotine containing vaping products (VPs), or e-cigarettes, are battery powered devices that are used to create an aerosol which is inhaled by the user. Aerosol is generated from a liquid, known as vaping liquid, that is housed in a tank or cartridge and usually consists of propylene glycol, glycerol, nicotine, and various flavourings. When activated, the devices vaporize the vaping liquid by way of a heating element or coil, housed in an atomizer; this vapour then quickly condenses into an aerosol that is inhaled. VPs are used by many Canadians to obtain nicotine. Qualitative and quantitative data obtained from chemical analyses of electronic cigarette refill fluids or e-liquids focused on specific flavouring ingredients, and other chemicals of interest will be used to support Health Canada's regulatory initiatives and activities relating to vaping products. Preliminary qualitative data published in 2021 "Open Characterization of vaping liquids in Canada: chemical profiles and trends." Frontiers in Chemistry 9, Article 756716. (PI: Cariton Kubwabo, Ivana Kosarac)

An investigation into the alcohol-caused harm experienced by different drinking groups in Canada—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. This study aims to continuously characterize, by sex, the distribution of alcohol use and the distribution of alcohol-caused health harms in Canada. Alcohol per capita (APC) will be taken from official sales data and alcohol-caused health harms will be from administrative health data. APC and prevalence of alcohol use information will be used to create continuous measures of average alcohol intake across the life course. The study further defines a novel concept, the harm density function, which depicts continuously how alcohol-caused health harm is distributed amongst the population, and therefore where alcohol policies should be targeted. (PI: Dr. Tim Stockwell, Canadian Institute for Substance Use Research; Dr. Samantha Cukier (CSCB))

An outbreak of novel psychoactive substance benzodiazepines in the unregulated drug supply: Preliminary results from a community drug checking program using point-of-care and confirmatory methods—NEW!

The mandate of Health Canada's Drug Analysis Service (DAS) laboratory is to analyze suspected drug samples from law enforcement agencies and public health partners to identify whether or not they contain controlled substances under the *Controlled Drugs and Substances Act*. From mid-2018, an increase in novel psychoactive substance (NPS) benzodiazepines was noted on surveillance of drugs around Vancouver. The rise was concordant with an outbreak of atypical overdoses suspicious

for benzodiazepine adulteration of opioids. This study sought to describe the number and type of NPS benzodiazepines in a sample of a community drug checking program, and to explore accuracy of point-of-care drug checking technologies when compared to confirmatory result. Point-of-care drug checking data using fentanyl and benzodiazepine test strips as well as FTIR spectroscopy were gathered at supervised consumption sites in the Vancouver area from October 2018 to January 2020. A subsample underwent confirmatory testing in the DAS laboratory of Health Canada. Of 159 samples with both point-of-care and confirmatory results, 24 (15.1%) contained at least one NPS benzodiazepine, including etizolam (n = 18), flubromazolam (n = 3), flualprazolam (4), and flubromazepam (n = 1). Of 114 confirmatory samples expected by participants on self-report to contain opioids, 18 (15.8%) contained some NPS benzodiazepine, with 16 (14.0%) containing both an NPS benzodiazepine and an opioid, always fentanyl. False positive and negative rates were 15.5% and 37.5% for test strips, and 3.9% and 91.7% for FTIR, respectively. Combined together, false positive and negative rates of point-of-care methods were 17.8% and 29.2%. NPS benzodiazepine presents new risks compounding ongoing harms associated with the synthetic opioid epidemic. Given substantial false positive and false negative rates noted in our sample for point-of-care detection methods, needs pairing with confirmatory drug checking may aid in early detection and inform targeted harm reduction strategies and health policy approaches. (Published July 2021; **10.1016/j.drugpo.2021.103169**) (PI: Richard Laing)

An updated analysis of the extent to which Canadians exceed low-risk drinking guidelines after adjusting for under reporting—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. Research demonstrates that people greatly under-estimate (under-report) the amount of alcohol they consume when responding on surveys. Researchers know this because they compare survey responses with official alcohol sales data and see that self-report surveys usually yield estimates of between 40% and 60% of the amount of alcohol sold. Therefore, the contracted project looked to correct for that under-reporting in Canadian National surveys. The project involved the analysis of the 2019 Canadian Alcohol and Drug Survey (CADS) with additional information from the 2008–2010 Canadian Alcohol and Drug Use Monitoring Survey (CADUMS) and the official sales data provided from Statistics Canada data on age 15+ per capita alcohol consumption by beverage type. The study assessed compliance with Canada's Low-Risk Alcohol Drinking Guidelines (LRDG) in different groups (i.e., age, sex, and province) of drinkers after adjusting for under-reporting of alcohol use. Adjustments for underreporting of alcohol in Canada need to be incorporated routinely in public health monitoring in order to mitigate the widespread underestimation of risky alcohol use. (PI: Dr. Tim Stockwell, Canadian Institute for Substance Use Research; Dr. Samantha Cukier (CSCB))

Automated qualitative and quantitative analysis of complex forensic drug samples using ^{1}H NMR—NEW!

The mandate of Health Canada's Drug Analysis Service (DAS) laboratory is to analyze suspected drug samples from law enforcement agencies and public health partners to identify whether or not they contain controlled substances under the *Controlled Drugs and Substances Act*. Progress in high-resolution nuclear magnetic resonance (NMR) instrumentation has enabled fast and accurate acquisition of quantitative ^{1}H NMR (qNMR) data but analyzing complex forensic drug samples in the presence of significant peak overlap remains challenging. For example, samples containing an opioid such as fentanyl often will contain diluents such as mannitol and adulterants such as Caffeine and potent benzodiazepines. This analysis limitation has hampered the adoption of ^{1}H NMR in areas such as traditional medicine and law enforcement. The NMRquant algorithm can detect and quantitate compounds of interest within forensic mixed drug samples even when there is overlap between chemical shift regions. This algorithm is robust against variations in chemical shift resulting from temperature, concentration, and inter-analyte interactions. These desirable features were integrated into an automated workflow, enabling routine unattended proton qNMR analysis of forensic drug samples. This allows to analyze and quantitate multicomponent mixtures containing controlled substances, diluents and adulterants all in a single analysis. (Published 2022-03-05; **https://doi.org/10.1002/mrc.5265**) (PI: Richard Laing)

Canadian Alcohol and Drugs Survey (CADS)—NEW!

The Canadian Alcohol and Drugs Survey (CADS) is an ongoing, general population survey among Canadians aged 15 years and older. CADS provides Health Canada, its partners and stakeholders, as well as the Canadian public, with timely and reliable data on the prevalence of drug use and usage patterns among various age groups of Canadians (i.e., 15–19 years, 20–24 years, 25+ years) at a national level. Understanding Canadian trends in alcohol and drug use is vital to the effective development, implementation and evaluation of national and provincial strategies, policies and programs. CADS evolved from the Canadian Tobacco, Alcohol and Drugs Survey (CTADS), which was conducted biennially from 2013 to 2017, and the Canadian Alcohol and Drug Use Monitoring Survey (CADUMS), which was conducted annually from 2008 to 2012. In 2017, the decision was made to separate CTADS into two surveys: CADS, focused on alcohol and drug surveillance, and the Canadian Tobacco and Nicotine Survey (CTNS), focused on tobacco use and vaping. The CTNS is managed by the Tobacco Control Directorate. CADS provides evidence required to support regulatory and policy change and the development of programs. The most recent cycle of CADS data collection occurred in 2019 and a summary report was released in winter 2021. Because of the separation of drugs and alcohol from tobacco and vaping into separate surveys, CADS has added significantly more detail to the cannabis, alcohol, and psychoactive pharmaceuticals sections, which will yield greater estimates of drug and alcohol use behaviours than in previous cycles of CTADS/CADUMS. The next cycle of CADS data collection will begin in fall 2022. (PI: Matthew Dann, Monica Emode)

Canadian Postsecondary Education Alcohol and Drug Use Survey (CPADS)—NEW!

The Canadian Postsecondary Education Alcohol and Drug Use Survey (CPADS) is a national online survey that collects detailed information on patterns of substance use among postsecondary students in Canada, and the impacts of substance use on students' lives. Prior to the CPADS, Health Canada's substance use surveillance strategy did not specifically examine postsecondary students. Although previous studies had been conducted by groups other than Health Canada (for example, the Canadian Campus Survey; Adlaf et al, 2004), these studies were restricted to universities and did not include college students. As such, the limited available data on substance use among Canadian postsecondary students was neither current nor nationally representative. To rectify this data gap, the Office of Drug Research and Surveillance collaborated with the Postsecondary Education Partnership-Alcohol Harms (PEP-AH) network along with other partners (Universities Canada, Colleges and Institutes Canada, and the Canadian Association of College and University Student Services) to develop the CPADS. As a tool, the CPADS provides governments and non-governmental organizations with valuable information, such as substance use prevalence and other key indicators that can inform policies and programs that address substance use in postsecondary students. In its first cycle, the CPADS was pilot tested by Health Canada from April to May 2018 in four postsecondary institutions. It was then subsequently rolled out among 41 postsecondary institutions across Canada during the 2019–2020 academic year. Results of the first cycle were released in May 2021. The second cycle of the CPADS is currently underway. (PI: Anton Maslov, Jacqueline Burt)

Characterizing the subjective, observer-rated, and physiological effects of hydromorphone relative to heroin in a human laboratory study—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. This study compared the effects of several doses of the opioid agonists heroin and hydromorphone across two routes of administration in humans. The goal was to guide development of human laboratory studies of opioid effects and inform subsequent injection pharmacotherapy trials of hydromorphone-assisted treatment. Hydromorphone produced similar subjective and physiological effects as heroin but was more potent than heroin. The current findings support the use of hydromorphone as a model for heroin in human laboratory and clinical treatment studies and help identify appropriate hydromorphone dose conversion ratios to produce effects qualitatively similar to heroin. *Psychopharmacology* (2018) (PI: Bruna Brands)

Combined effect of alcohol and cannabis on simulated driving—NEW!

Alcohol and cannabis are the most commonly detected drugs in seriously and fatally injured drivers and there is a need to understand their combined effects on driving. The present study examined the effects of combinations of smoked cannabis and alcohol on simulated driving performance, subjective drug effects, cardiovascular measures, and self-reported perception of driving ability. Cannabis users (1–7 days/week) aged 19–29 years attended four drug administration sessions in which simulated driving, subjective effects, cardiovascular measures, and whole blood THC and metabolite concentrations were assessed following placebo alcohol and placebo cannabis, alcohol and placebo cannabis,

placebo alcohol and active cannabis, and alcohol and active cannabis. Combinations of alcohol and cannabis increased weaving and reaction time and tended to produce greater subjective effects compared to placebo and the single drug conditions suggesting a potential additive effect. A driving ability questionnaire showed that participants seemed unaware of their level of impairment. The fact that participants were unaware of this increased effect has important implications for driving safety. *Psychopharmacology* (2021) (PI: Bruna Brands)

Driving under the influence of prescription opioids: Self reported prevalence and association with collision risk in a large Canadian jurisdiction—NEW!

Motor vehicle collisions are an important contributor to prescription opioid use-related morbidity and mortality. The purpose of the current study was to estimate the prevalence of driving under the influence of prescription opioids (DUIPO) in Ontario, Canada, and to measure the association between this behaviour and the risk of a motor vehicle collision. Data were based on telephone interviews with 7,857 respondents who reported having driven in the past year. Data were derived from the 2011–2016 cycles of the CAMH Monitor, an ongoing cross-sectional representative survey of adults aged 18 years and older. Controlling for demographic characteristics, driving exposure, and other risk factors, self-reported DUIPO significantly increased the odds of a collision. Based on these findings, DUIPO is a notable road safety issue. Research focused on better understanding the impact of prescription opioids on driver behaviour, reducing the prevalence of DUIPO, and improving drug-impaired driving policy and interventions should be prioritized in public health strategies. *Accident; Analysis and Prevention* (2018) (PI: Bruna Brands)

Early findings from safer supply pilot projects—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. As the overdose crisis worsened during the COVID-19 pandemic, health care experts and people who use drugs called for greater access to a safer supply of prescription medications as an alternative to the toxic illegal drug supply. In 2020, the Substance Use and Addictions Program at Health Canada funded ten time-limited safer supply pilot projects in three provinces (British Columbia, Ontario, and New Brunswick). Health Canada then contracted a four-month qualitative assessment, from December 2020 to March 2021, of these projects to capture early learnings, including effective strategies for program delivery. The report was released in March 2022. Key findings included reports of improved health, well-being and quality of life, decreased overdose risk and decreased use of street drugs. A summary of the findings can be found here.

Effects of combining alcohol and cannabis on driving, breath alcohol level, blood THC, cognition, and subjective effects: A narrative review—NEW!

Alcohol and cannabis are the two most commonly found intoxicating substances in fatally injured drivers. Epidemiological studies have demonstrated that the use of alcohol or cannabis can lead to an increased risk of a motor vehicle collision. Reducing the risks associated with driving under the influence of alcohol or cannabis is achieved partly through roadside detection of breath alcohol concentrations (BrAC) or blood delta-9-tetrahydrocannabinol (THC) levels. The purpose of the present review is to compile the laboratory studies on the combined effects of alcohol and cannabis on simulated driving as well as those studies evaluating combinations of these drugs on BrAC or blood THC. Given that driving can be affected by a number of cognitive processes, the literature on the cognitive effects of combinations of alcohol and cannabis is also reviewed, along with a discussion of a potential additive effect on the subjective qualities of these drugs. In summary, it appears that alcohol and cannabis have additive effects on driving skills, cognition, and subjective effects. *Experimental and Clinical Psychopharmacology* (2022) (PI: Bruna Brands)

Exploring the use of extended release opioids at shortened dosing intervals in people with chronic pain and high risk medication or substance use—NEW!

Critical attention to rational opioid prescribing has emerged from the opioid epidemic in North America. Individuals with chronic pain are prescribed extended release opioids in an effort to maintain stable drug levels and for more convenient dosing, though evidence to support improvements in pain or function is lacking. It has been observed that extended release opioid products are used at intervals shorter than recommended by product monographs. The need for shortened intervals has been linked with potential inter-patient variability in pharmacokinetics, among other rationale. Implications of shortened dosing intervals for extended release opioids have not been systematically studied. The aim of this study was to characterize the use of extended release opioid formulations at shortened dosing intervals in a population of patients with chronic pain and high risk for opioid-related harms. Sixty-one percent of individuals using extended release opioids were using them at shortened intervals. The use of extended release opioids at shortened intervals was associated with a higher daily morphine equivalent dose, use of oxycodone extended release products, a longer duration of opioid therapy and a diagnosis of chronic neuropathic pain, with no differences in reported pain intensities, compared with use at standard intervals. Thus, the use of extended release opioids at shortened intervals is associated with an increased risk of opioid-related mortality. It is unlikely that the high proportion of extended release opioids users using at shortened intervals is the result of inter-patient differences in metabolism alone. *International Journal of Clinical Pharmacy* (2020) (PI: Bruna Brands)

Implementation of a notification system identifying new and potentially harmful psychoactive substances—NEW!

Recent Canadian data have shown a rapid increase in substance-related fatalities following the onset of the COVID-19 Pandemic. Disruptions in local drug market play a part in this ongoing crisis. Although the Drug Analysis Service's (DAS) primary mandate is to analyze drug seized by law enforcement officers, it is also committed to sharing information with partners in order to provide the latest information on potentially harmful substances currently available in Canada based on laboratory data from drug seizures. To improve communication and timeliness, DAS undertook the automation of drug notifications in four steps. Firstly, operational definitions of the terms new substance of concern were articulated, new mixture, new form (stamp, shape, colour, powdery substance or tablets) in a geographic location. Secondly, a program producing a list of daily warnings was created. Thirdly, a procedure for screening the warnings which includes considerations such as whether a drug or mixture was previously seen with a different adulterant was elaborated. Lastly, the procedure was piloted in three laboratories across the country. As a result, sharing of drug notifications is done in two streams: (1) directly to health authorities and law enforcement partners and (2) eventually on-line using interactive maps and dashboards. In conclusions, the development and full implementation of the system took place over the course of two years. It produces a more exhaustive output and is expected to reduce the burden on laboratory staff. (PI: Marie-Line Gilbert)

Individual differences in self-reported human opioid abuse potential as observed in a human laboratory study—NEW!

Opioids have high abuse potential and pose a major public health concern. Yet, a large percentage of individuals exposed to opioids do not develop problematic use. Individual differences in opioid abuse potential are not well understood. This study evaluated individual differences in response to dose following administration of heroin and hydromorphone through intravenous and subcutaneous routes, in opioid-experienced but non physically dependent participants. Visual inspection reveals a myriad response pattern across participants, with some demonstrating classic dose-effect responses and others not differentiating any active doses from placebo. Data suggest the abuse potential of opioids is significantly different between individuals but that the experience within an individual is highly consistent. Research to prospectively characterize and evaluate mechanisms underlying these differences is warranted and may provide a foundation to help identify persons at heightened risk of transitioning from opioid exposure to misuse and/or opioid use disorder. *Drug and Alcohol Dependence* (2019) (PI: Bruna Brands)

In vitro pharmacological testing of novel hallucinogens at the 5-HT_{2A} and 5-HT_{2B} receptors—NEW!

There is growing interest in the potential benefits of psychedelic compounds for the treatment of psychiatric conditions or for recreational use. This has stimulated research on the effects of hallucinogenss, their pharmacology, potential clinical uses, and harms. Many hallucinogens occur naturally (e.g.psilocybin and psilocin from fungal species) or are derivatives of natural substances (e.g.

lysergic acid diethylamide [LSD]), some of which are currently controlled under Schedule III to the *Controlled Drugs and Substances Act* (CDSA). These substances act on brain serotonin receptors 5-HT_{2A} and 5-HT_{2B}, which evidence suggests are responsible for many of the hallucinogenic effects. Numerous novel synthetic derivatives of these compounds are now available through illicit and grey markets. However, our scientific understanding of them remains quite limited. The Office of Drug Policy and Science (ODPS) of the Controlled Substances Directorate is responsible for providing substance status to stakeholders and making recommendations for scheduling under the CDSA. The primary goal of this project is to determine the affinity and efficacy of putative hallucinogenic compounds at the human 5-$HT_{2A/B}$ receptors using *in vitro* assays. Radioligand binding is used to measure test compound affinity to the receptors. For efficacy, two signaling pathways are compared: G protein activation and β-arrestin-2 recruitment. The results will inform ODPS scheduling and status determination activities, which are important regulatory and control measures for the safety and well-being of Canadians. (PI: Nemanja Mladjenovic)

In vitro pharmacological testing of novel opioids at the hMOR1 receptor—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. The synthetic and non-synthetic drug supply has become increasingly tainted with powerful opioids. Initially these drugs included fentanyl and its analogues, and more recently, novel synthetic opioids are emerging in the illegal drug supply. Their psychoactive, analgesic, and harmful physiological effects result from their activity on the mu opioid receptor (MOR). Some of these novel opioids were primarily developed as analgesics but discontinued due to severe side effect profiles. The *Controlled Drugs and Substances Act* (CDSA) limits the possession, production, and sale of harmful opioids. The Office of Drug Policy and Science (ODPS) of the Controlled Substances Directorate is responsible for providing substance status to stakeholders and making recommendations for scheduling under the CDSA. Data on effects and harms of novel synthetic opioids are quite sparse. Therefore, the primary goal of this project is to determine the efficacy of suspected opioids at the human MOR (hMOR1) using *in vitro* assays for G protein activation and β-arrestin-2 recruitment under different experimental conditions. Bioinformatic analyses using signaling profiles have been validated to predict the risks of hypoventilation, respiratory depression, and somnolence for novel opioids. The results will inform ODPS regulatory science activities and will help to rapidly identify potentially harmful substances that may emerge in the illegal drug supply. (PI: Frederic Langlois)

Method validation for the analysis of 18 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 18 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)), norfentanyl, naloxone, acetaminophen and acesulfame. The method has a method detection limit ranging from 0.2 ng/L to 16ng/L and a method quantitation limit ranging from 0.9 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. (PI: Keri Kwong)

Monitoring harms associated with substance use—NEW!

The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada. Harms associated with substance use in Canada can be monitored using hospitalization data captured through the Discharge Abstract Database (DAD), maintained by the Canadian Institute for Health Information (CIHI). CIHI DAD data are used by Health Canada in monitoring hospitalizations from opioid- and stimulant-related poisonings and reported as part of the Opioid- and Stimulant-related Harms in Canada quarterly update from the Special Advisory Committee on the Epidemic of Opioid Overdoses. DAD data will further be used to describe broader harms associated with all substances (including alcohol, cannabinoids and benzodiazepines). Results will be used to support policy and regulatory initiatives. The results of these analyses will also feed into the development of a Canadian Early Warning System through the provision of information on harms associated with substance use. (PI: Daniela Panait)

Sex differences in the acute pharmacological and subjective effects of smoked cannabis combined with alcohol in young adults—NEW!

The prevalence of co-use of alcohol and cannabis is increasing, particularly among young adults. Sex differences in the effects of alcohol alone and cannabis alone have been observed in animals and humans. However, sex differences in the acute pharmacological effects of cannabis combined with alcohol have not yet been studied. In young adults, aged 19–29 years, we aimed to examine sex differences following an intoxicating dose of alcohol (target 0.08% breath alcohol content) combined with a moderate dose of cannabis (12.5% Δ9-tetrahydrocannabinol; THC) using an ad libitum smoking procedure. 28 regular cannabis users (16 males; 12 females) received in random order: (a) placebo alcohol and placebo cannabis, (b) active alcohol and placebo cannabis, (c) placebo alcohol and active cannabis, and (d) active alcohol and active cannabis. Blood samples for THC were collected and measures of vital signs, subjective drug effects, and cognition were collected. In the alcohol–cannabis combined condition, females smoked significantly less of the cannabis cigarette compared to males, although both sexes smoked similar amounts in the other conditions. There was minimal evidence that females and males differed in THC blood concentrations, vitals, subjective effects, or cognitive measures. In conclusion, in the alcohol–cannabis combined condition, females experienced the same

acute pharmacological and subjective effects of alcohol and cannabis as males, after smoking less cannabis, which has potential implications for informing education and policy. Further research is warranted on sex differences in cannabis pharmacology, as well as the combined effects of alcohol and cannabis. *Psychology of Addictive Behaviors* (2021) (PI: Bruna Brands)

Time-series analysis of fentanyl concentration in the unregulated opioid drug supply in a Canadian setting—NEW!

North America has been contending with an unregulated street drug supply in which opioids are often adulterated with illicitly manufactured fentanyl. The unpredictability of composition may result in an increased risk of overdose due to unexpected elevated concentrations of the high-potency drug. Using data from a community-based drug-checking project, trends in fentanyl concentration of illicit opioids in the context of an overdose epidemic were evaluated. Using a quantification model for fentanyl hydrochloride, historical Fourier-transform infrared spectra from opioid drug-checking samples were analyzed to determine fentanyl concentrations. Median monthly fentanyl concentrations were plotted, and polynomial and autoregressive time-series analyses were performed to examine trends over time. A total of 3,621 fentanyl-positive samples were included in the study, spanning November 2017 to December 2019. Monthly median fentanyl concentrations ranged from 4.5% to 10.4%. Time-series analyses indicated that a third-degree polynomial model fit the data well ($R2 = 0.639$), suggesting a cyclical pattern in median concentration over time. Notably, absolute variance in fentanyl concentration decreased by an average 0.1% per month ($P < 0.001$). Future research should explore the relationship between fentanyl concentration and overdose to identify potential targeted harm-reduction interventions that can respond to changes in observed fentanyl concentration. (Published 2022-01-24; **https://doi.org/10.1093/aje/kwab129**) (PI: Richard Laing)

FOOD & NUTRITION

Method for analysis 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)

Replacing an essential toxic chemical used for analysis of amino acids in retail foods in support of the Canadian Nutrient File—NEW!

The Canadian Nutrient File (CNF) is a comprehensive food composition database for reporting amounts of nutrients in foods commonly consumed in Canada, including amino acids. Amino acids are biologically important molecules having diverse physical functions. They are necessary for vital body processes, such as building proteins, hormones and neurotransmitters. Amino acids are found in protein rich foods, including meat, fish and soybeans. ROEB's Food laboratory analyses a total of 18 amino acids from a wide variety of food samples using two distinct extraction methods with liquid chromatography tandem mass spectrometry detection (LC-MS/MS) at trace levels. Typical limit of detection levels are 3 ng/mL to 20 ng/mL, depending on the amino acid. Analyzing amino acids is-highly challenging due to their individual chemical properties. LC-MS/MS methods use perfluorooctanoic acid (PFOA) as an ion-pairing agent in the mobile phase. This type of chemical helps improve the ability to detect specific amino acids using the LC-MS/MS at low levels. However, PFOA is a Schedule 1 toxic substance as per *Canadian Environmental Protection Act* (CEPA) and has health and ecological hazards. With the objective of continuously improving the methods and making them more

environmentally sustainable, significant effort was spent to replace this chemical without compromising results. Instead of simply swapping PFOA with another similar chemical, it was necessary to develop completely new LC-MS/MS methods. As a result, this toxic chemical was replaced with more environmentally friendly chemicals without impacting the analysis of all 18 amino acids. For more details on the Canadian Nutrient file please follow this link: **https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/nutrient-data/canadian-nutrient-file-about-us.html**
(PI: Marija Cosic)

HEALTH IMPACTS OF CHEMICALS

A rapid assay of human thyroid peroxidase activity—NEW

Health Canada's mandate requires the review and assessment of potential health risks due to commercial chemical use in Canada to manage and mitigate these risks. For many chemicals in commerce, information about potential toxicity to vulnerable parts of the endocrine system is lacking. Disruption of thyroid hormone synthesis is recognized as a key mechanism by which some endocrine disrupting chemicals can cause impaired brain development and other adverse effects. The current study modified a rapid method to screen chemicals for inhibition of a critically vulnerable enzyme (thyroid peroxidase—TPO) necessary for thyroid hormone production to make this assay more relevant for human hazard characterization and less dependent on lab animal use. Activity of human TPO (hTPO)—harvested from either of two transgenic cell lines expressing high levels of the hTPO—was compared to TPO activity harvested from rat thyroid glands in its ability to identify TPO inhibiting activity among a group of chemicals with known effect. Human TPO was as effective as the rat enzyme in identifying chemicals with moderate to high potency. Chemicals shown to have weak activity on rat TPO were less effectively identified with hTPO from either cell line. These results demonstrate that hTPO from transgenic cells can be used for a rapid assay to reliably identify TPO-inhibiting chemicals. These results will be included in Health Canada's contribution to international efforts at the Organization of Economic Cooperation and Development to developing test methods to screen and test chemicals for endocrine disrupting activity. (PI: Mike Wade)

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 led 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)

An *in silico* decision workflow to screen chemicals for indicators of developmental neurotoxicity—NEW!

Developmental neurotoxicity (DNT) is one of many important toxicological endpoints to evaluate as part of the human health risk assessments under the Chemicals Management Plan. Since the developing nervous system is highly vulnerable, it is imperative to prevent exposure during critical developmental periods to chemicals with the potential for DNT To date, this has presented challenges due to the limited data that is available. Accordingly, this provides an opportunity to address an essential need using computational approaches to enhance the ability to screen and identify chemicals of potential concern. International efforts to assess chemicals for their DNT effects are ongoing. In this study, a decision workflow based on in silico methods is being proposed. Existing *in silico* models will provide information on the physicochemical properties (molecular weight, hydrogen bond acceptor/donor), partition coefficients to assess permeability (Blood brain barrier, Log Kow, placental barrier), molecular initiating events (MIEs such as AChEI, PgP, ER, TR), and adverse outcomes (zebra fish AC50, neurotoxicity). Physiologically based pharmacokinetic (PBPK) models for pregnant mothers will be explored to determine placental transfer of chemicals to the fetus. In addition to in-house modelled parameters, those generated by our international collaborator will also be incorporated. The proposed decision workflow will be used to bin chemicals as permeable DNT actives/inactives, and impermeable DNT actives/inactives. The workflow will be validated using a known set of active and inactive DNT chemicals. Post validation the DSL chemical inventory will be screened using the workflow and the results analyzed in detail. A comparative analysis of the results obtained through this decision workflow with those generated from workflows developed independently by our collaborator will be carried out to further evaluate performance and precision of the approach to accurately identify chemicals with the potential to induce DNT. (PIs: Sunil Kulkarni, Shamika Wickramasuriya, Emilio Benfenati [Mario Negri Institute, Milan, Italy])

Advanced multi-omics integration for risk evaluation of microbial-based containing products—NEW!

Microbial-based products (MBPs) are biotechnology products that contain microbial mixtures as the active ingredients; used for a variety of environmentally sustainable applications. The current *New Substances Notification Regulations (Organisms)* require each component of microbial mixtures be tested. Through the Innovative Solutions Canada Program (ISC), Health Canada sought private sector innovation to create cost-effective, robust and reliable solutions to address testing costs. As part of the Phase 1 challenge, Microbiome Insights (MI) developed a proof of concept (PoC) that partially fulfilled three objectives: (1) accurate identification and description of micro-organisms in mixtures; (2) characterization of microbial population dynamics and (3) interactions that may attenuate or augment

adverse effects (e.g., pathogenicity). Firstly, metagenomics were used to characterize the taxonomy and functional potential of four commercial MBPs, including genes involved in antimicrobial resistance and virulence. MI also built a "strain passport"—a relational database to integrate information on key genomic features for each species and related literature obtained in public repositories and patents. To examine population dynamics and interactions that may affect pathogenicity, MI measured gene expression changes in lab assembled microbial communities as a function of short-term environmental stresses and modeled gene co-expression dynamics. Building on the PoC, MI is currently developing a prototype to (i) facilitate reproducible analysis of 'omics datasets, (ii) improve genome recovery from MBPs, (iii) further understand the pathogenic relevance of interactions among micro-organisms in MBPs via metatranscriptomics, and (iv) enhance the ability of the strain passport to support in silico hazard profiling of micro-organisms. The Phase 2 goal is to validate the prototype using metabolomics, 3D organoids, and *in vivo* animal assays, which will help develop tailored new alternate methods and testing strategies with less reliance on animal testing, thereby reducing the cost of pathogenicity/toxicity testing for biotechnology small and medium enterprises. (PI: Valar Anoop)

Analysis of human biomonitoring data from the Canadian Health Measures Survey using biomonitoring guidance values—NEW!

The Canadian Health Measures Survey (CHMS) collects nationally representative biomonitoring data for several environmental chemicals. This work assessed the biomonitoring data for 42 chemicals or groups of chemicals including metals, perfluoroalkyl substances (PFAS), pesticides, plasticizers, and volatile organic compounds collected as part the CHMS in a health risk context using biomonitoring guidance values (BGV). The assessment included a number of chemicals measured in CHMS cycles 5 (2016 to 2017) and 6 (2018 to 2019) and a few chemicals measured in earlier cycles. Whereas the data for fourteen of these chemicals were assessed in a health-risk context for the first time in this study, the assessments for 28 other chemicals were updates to the earlier evaluations by St-Amand et al. (2014) and Faure et al. (2020) using more recent biomonitoring data or recently established or updated biomonitoring guidance values. Hazard quotients (HQs) were calculated as the ratio of the mean concentrations (geometric mean (GM) or arithmetic mean (AM)) and upper concentrations (95th percentile or maximum) of a chemical to a BGV. The results showed that HQs remained below one for a number of chemicals suggesting that population exposures are not exceeding the existing exposure guidance values for those chemicals. However, HQ exceedances of one were noted for other chemicals such as acrylamide, cadmium and benzene in smokers, and for inorganic arsenic, 3-phenoxybenzoic acid (3-PBA), PFAS and xylenes in the general population, and these chemicals may be prioritized for future follow-up activities including monitoring and research. Ongoing work aims to conduct a limited analysis of exceedances in racial subpopulations as well as an assessment of temporal changes in HQs across CHMS cycles using comparable data from previous analyses. (PIs: Subramanian Karthikeyan, Annie St-Amand)

Antidepressant Embryo-Larval Study (ADELS) of citalopram on embryonic and larval fathead minnows (*Pimephales promelas*)—NEW!

Selective Serotonin Reuptake Inhibitors (SSRIs) on the Revised In Commerce List (R-ICL) have been identified as priorities for environmental risk assessment. Citalopram (CIT) is one of the most commonly prescribed antidepressants/anti-anxiety drugs in Canada. Municipal wastewater effluents in southern Ontario have measured CIT concentrations up to 0.203 µg /L, while the pharmaceutical was measured in Canadian rivers ranging from 0.0032–0.206 µg/L. There is little information in the literature on how CIT affects the development, growth and behavior of larval fish, therefore, the objective of the current study was to assess the effects of CIT on the development, growth and behavior of larval fathead minnows. A 21-day embryo larval exposure was performed exposing fathead minnow embryos post hatch to environmentally relevant concentrations (0.02 and 0.2 µg/L), and higher (2, 10 and 20 µg/L). A slight increase in larval weight at the lowest CIT concentration was observed, while a decrease in larval length was observed in the highest CIT concentration. Additionally, a decreasing trend in embryonic movement was observed with increasing CIT concentration with an increase in embryonic movement only at the highest concentration which could be explained by potential neurodegeneration. These data will be used directly in the environmental assessments of SSRIs on the R-ICL and will be used to explore the use of cumulative risk assessment under the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Dianne Hughes, Jean Grundy, Erin Ussery)

Assessing environmental fate of SSRIs in environments that receive municipal wastewater effluent—NEW!

Selective Serotonin Reuptake Inhibitors (SSRIs) on the Revised In Commerce List (R-ICL) have been identified as priorities for environmental risk assessment. SSRIs are widely prescribed to treat depression and anxiety disorders in humans and have been reported in municipal wastewaters and receiving environments both in Canada and globally. Six SSRIs, including Norfluoxetine, Paroxetine, Sertraline, Citalopram, Venlafaxine, and Fluoxetine were examined in this study. Samples of the final effluent from 11 wastewater treatment plants (WWTP) from across Ontario were obtained for analysis. Based on the presence of targeted biota (small-bodied fish and freshwater mussels), riverine habitats were sampled immediately upstream and downstream of each of two WWTPs in southern Ontario, as well as from upstream and downstream reference sites. Greenside darters (*Etheostoma blennioides*) were collected to assess the concentration of targeted SSRIs. Fish tissues were also dissected for health assessment endpoints (e.g., condition factor, gonadosomatic index) and indicators of contaminant exposure including oxidative stress. At each wild fish collection site, the abundance, species richness, and population size structure of the resident freshwater mussel population was assessed. Tissues were preserved for SSRI and oxidative stress analysis. Surface water and sediment samples were also collected from each of the six wild biota study sites. These data will be used directly in the environmental assessments of SSRIs on the R-ICL and will be used to explore the use of cumulative risk assessment under the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Dianne Hughes, Jane Pappas, Patty Gillis)

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 sets standards for industry worldwide to identify toxic chemicals. The "Syrian Hamster Embryo Cell Transformation Assay" (SHE-CTA) was proposed to detect chemicals inducing cancer by damaging DNA as well as through other harder-to-detect mechanisms. The SHE-CTA exposes normal cells in culture to chemicals, with the intention of accurately identifying their ability to induce cancer. The U.S. Environmental Protection Agency had been considering the SHE-CTA in chemical testing strategies, in part because human cells are more similar to Syrian hamster embryo cells to those from rat or mice, which are used in other CTAs. HC research involved developing the SHE-CTA in the laboratory to: (1) gain expertise in conducting this assay by using it to test priority chemicals, (2) investigate mechanisms of cell transformation upon exposure to different types of carcinogens, and (3) identify molecular markers of cancer development, that could lead to assay improvements. Based on project results, HC identified concerns related to the reproducibility of the data generated by the proposed SHE-CTA. Nevertheless, HC was able to successfully establish the chronology of DNA changes in response to chemical exposures, starting with normal cells up to the time they become potential cancer cells. Furthermore, the study identified early DNA changes associated with critical steps in cancer development that were reproducible in samples analyzed by different laboratories. The measurements of these early DNA changes can now be tested to improve the SHE-CTA, as well as to test their applicability in a more relevant CTA using human cells. Finally, the *in vitro* data from this project will assist HC in the development of new chemical testing strategies, in strengthening predictions of chemicals that can increase the risk of developing cancers, and in providing alternatives to reduce dependence on 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

Health Canada is committed to the reduction of animal use in toxicity testing and to the development of alternative high-throughput in vitro New Approach Methods (NAMs). 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) originating from rat pup brains are a popular *in vitro* model used to study neurodevelopment and neurotoxicity. CGCs are easy to grow and can exhibit neuron differentiation and maturation processes observed *in vivo*. The use of genes associated with CGC neurodevelopment in order to monitor neuronal differentiation and maturation and screen chemicals for potential developmental neurotoxicity was described in the literature. However, Health Canada was not able to replicate these findings, as gene expression measurement protocols were often poorly designed or described, quality controls were infrequently reported and CGCs themselves presented significant batch-to-batch variability. Nevertheless, Health Canada was able to overcome these impediments to develop a robust and

reliable *in vitro* DNT protocol based on commercially-sourced CGCs and reagents and an optimized subset of neurodevelopmental biomarker genes presenting reproducible expression patterns across multiple laboratories. Preliminary results suggest that known developmental neurotoxicants can perturb the expression of the optimized subset of biomarker genes involved in neuronal differentiation and maturation processes. The complete and transparent description of this new Health Canada *in vitro* DNT assay using well-characterised CGCs and neurodevelopmental biomarker genes will facilitate future investigations and inter-laboratory comparisons. Further, development and validation of this CGC-based assay may contribute to the OECD-led effort towards the development of a battery of *in vitro* DNT assays to support the screening and prioritization of potential developmental neurotoxicants. (PI: Guillaume Pelletier)

Case study and workshop for guiding the selection of appropriate exposure models for risk assessment using the EAS-E Suite platform—NEW!

Chemical fate and exposure data are necessary parts of the risk assessments conducted by the New Substances Assessment and Control Bureau (NSACB). Unfortunately, high quality monitoring and biomonitoring data for new chemicals are limited, as such, the application of models is routinely used to characterize the exposure. The primary objective of this research was to compare and evaluate various models and tools that Health Canada can use to inform decision-making for chemical risk assessment. A dataset of chemicals was selected to conduct the model comparisons. The model comparisons considered several endpoints including calculations for chemical emission rates; mode-of-entry to the environment; chemical removal efficiency in wastewater treatment plants; relative fate and distribution of chemicals in air, water, soil, and sediment; predicted environmental concentrations; bioaccumulation; and exposures to humans and ecological receptors. The model evaluations clearly show that dilution models cannot capture exposure to all environmental biota and consideration of chemical ionization can more accurately inform chemical fate, distribution, and bioaccumulation. This report demonstrates that "higher tiered" models can easily be applied and improve risk assessment. The Exposure And Safety Estimation (EAS-E) Suite platform developed by ARC Arnot Research and Consulting (ARC) includes chemical information databases, quantitative structure activity relationships (QSARs) for predicting chemical information, and some relevant tools and models to support chemical hazard, exposure, and risk estimation. EAS-E Suite quantifies the relationships between chemical production volumes, partitioning properties, degradation rates, fate and transport in natural and manufactured environments (i.e., indoors), human and ecological exposures, and the potential for adverse effects at a screening-level. EAS-E Suite contains chemical information required to use many environmental fate and exposure models, as well as bioaccumulation and physiologically based toxicokinetic (PBTK) models. Through the course of this project, revisions were made to modules in EAS-E Suite to improve the usability and clarity of the outputs to meet NSACB's needs when evaluating new substances. In addition, two, four-hour training courses were held showing the utility of the models and tools in EAS-E Suite to provide more realistic simulations in comparison to others already in use or proposed for use for risk assessment. (PI: Mark Lewis)

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

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 (TiO_2), copper oxide (CuO), and nanocellulose. This project also investigated the potential toxicological effects of TiO_2 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. (PI: 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)

Characterizing variability in hair to blood mercury ratio in the general Canadian population—NEW!

The Canadian Health Measures Survey (CHMS) collects nationally representative biomonitoring data for several environmental chemicals, including mercury, a potent neurotoxicant. Exposure to mercury in humans is usually examined by measuring biomarkers in hair or blood. It is often necessary to convert between the levels of the two biomarkers, for example, the mercury in hair to equivalent levels in blood, to calculate exposure estimates needed in risk assessment. A default hair:blood ratio of 250:1 as recommended by the World Health Organization is commonly applied for this conversion, although the actual ratio may vary within and between populations. The purpose of this work was to better characterize the hair:blood total mercury (THg) ratio in the general Canadian adult population using data from the CHMS, Cycle 5 (2016–2017). The work showed that the hair:blood THg ratio was greater than 250 in most CHMS participants, and there was considerable variability among the ratios. When the Canadian population was stratified by factors such as age, sex, socioeconomic status, and diet, the average ratios for different subpopulations ranged from 181 to 382. Dietary variables, and in particular, the consumption of fish and seafood appeared to be highly influencing the THg hair:blood ratio. In addition to fully characterizing the variability in hair:blood THg ratios, this work also assessed potential implications of the variations in the ratios for any re-evaluation of the existing dietary guidance value (pTDI). (PIs: Kavita Singh, Subramanian Karthikeyan, Annie St-Amand)

Chemical exposures of municipal firefighters: Analysis of available data on human biomonitoring and occupational environments—NEW!

Compared to the general population, professional firefighters (FFs) experience elevated risks of chronic diseases such as cancer and respiratory illnesses. In response to concerns regarding the carcinogenic hazards posed by FRs (flame retardants) and surfactants (e.g., per- and polyfluoroalkyl substances or PFAS), HC (Health Canada) and ECCC (Environment and Climate Change Canada) have implemented an Action Plan aimed to help protect firefighters from harmful chemicals. The Action Plan includes a project that is collecting, summarizing and analysing publicly available data pertaining to FF exposures to chemicals such as FRs, PFAS, PAHs (polycyclic aromatic hydrocarbons), VOCs (volatile organic compounds) and PCDDs (polychlorinated dibenzodioxins). The project includes comparing published FF biomonitoring data (i.e., levels of chemicals and/or their metabolites in blood or urine) to available data from the general population from national and international biomonitoring surveys (e.g., Canadian Health Measures Survey, U.S. National Health and Nutrition Examination Survey). Additionally, to improve understanding regarding routes and sources of chemical exposure, the review collected published data pertaining to the presence and concentrations of the aforementioned substances in fire hall dust, air at the fire suppression scene, air in the fire hall and/or truck cabs, and on PPE (Personal Protective

Equipment). The analyses conducted to date indicate that, in some cases, FFs have higher levels of certain substances in their blood or urine than the general population (e.g., certain PAHs, PFAS, and organophosphate FR substances). With respect to contamination of the occupational environment, the analysis reveals that, for example, dust samples collected in fire stations had higher values of brominated and organophosphate FRs than residential dust. This work will help identify chemicals for future biomonitoring studies and guideline work to improve interpretation of FF biomonitoring levels; it may provide insight into operating procedures that could mitigate FF exposures. (PI: Paul White, Rocio Aranda-Rodriguez, Leona MacKinnon, Elyse Bernard, Peter Mochungong, Virginie Bergeron, Catherine Campbell)

Chronic toxicity of Selective Serotonin Reuptake Inhibitors to *Daphnia magna*—NEW!

Selective Serotonin Reuptake Inhibitors (SSRIs) on the Revised In Commerce List (R-ICL) have been identified as priorities for environmental risk assessment. SSRIs are psychoactive drugs regularly used to treat various degrees of clinical depression in populations worldwide. A significant proportion of these drugs are released through excretion finding their way to the sewer water treatment systems. Previous studies revealed that individual SSRIs are found in municipal wastewater effluents at relatively low levels, however given the common mode of action, they could become harmful when these compounds are present at the same time in effluents. This study examined the chronic toxicity to daphnids (*Daphnia magna*) of a mixture of five SSRIs found in municipal wastewaters at environmentally realistic concentrations: Citalopram (Celexa), Fluoxetine (Prozac), Flovoxamine (Luvox), Paroxetine (Paxil) and Sertraline (Zoloft). The results revealed that the mixture had no deleterious effect on survival after 21 days (no mortality) and no change in behavior (mobility). However, the number of neonates followed a U-shaped concentration-response curve. These results are consistent with the observation that serotonin stimulation increased the production and release of neonates from the parent. Therefore, environmental mixtures of SSRIs could influence the number of offspring in daphnids. These data will be used directly in the environmental assessments of SSRIs on the R-ICL and will be used to explore the use of cumulative risk assessment under the *Canadian Environmental Protection Act, 1999* (CEPA). (PI: Dianne Hughes, Jean Grundy, François Gagné)

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

In the context of major projects subject to federal impact assessments, Health Canada provides advice regarding the human health risk assessment (HHRA) of contaminants found in country foods, including mercury (Hg). Health Canada's current HHRA framework assumes that all of the Hg in country foods is present as methylmercury (MeHg), the neurotoxic form that is readily absorbed. However, 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. 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 was created using Microsoft

Excel 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 subject-matter experts in the field. A critical review of the literature was carried out to document existing data on concentrations of Hg species reported/measured in the country food items identified. The dataset provided could be used to generate more accurate estimates of MeHg concentrations in country foods, and thereby more accurate risk assessments, even if only THg levels are available. It could also allow risk assessors 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)

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 regulators are in urgent need of new tests to meet legislated mandates. 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 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 genomic methods in human cells in culture for hazard identification and risk assessment of environmental chemicals (that damage DNA). This project harnesses the Adverse Outcome Pathways (AOP) knowledgebase 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: 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 can occur 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 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. 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 offspring. In addition, a new sequencing approach is being evaluated that 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. Initial data is showing that this new methodology compares well with the current gold standard method for assessing mutations in vivo. 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 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 consensus-based screening approach to assess endocrine disrupting activity of chemicals using (Quantitative) Structure Activity Relationship ([Q]SAR) approaches

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. 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 endocrine disruption-potential to a series of estrogen and androgen receptors using *in silico* models.–Models under evaluation include Oasis TIMES, VEGA, CASE Ultratox, CERAPP, CoMPARA and CASEUltra as well as random forest based in-house models. These models are not only assessed for their own performance, but also as a combination of them into what are known as consensus models. To begin, the predictions of *in silico* models are combined using a variety of methods to arrive at a single value. These results can be compared against a validation dataset to determine ideal combination of models to give the highest predictive performance. The information acquired from the analysis and integration of the *in silico* consensus models will support the early development of a proposed tiered approach to screen chemicals for potential endocrine disrupting activity. (PI: Sunil Kulkarni, Sean Collins)

Development of an Integrated Analysis Tool for Genotoxicity Assessment (IATGA)

The international community, including the Government of Canada, is increasingly committed to reducing the use of animals in scientific research and regulatory testing. Consequently, numerous groups worldwide are developing and deploying NAMs (New Approach Methodologies) for effective animal-free (geno)toxicity assessment. The Genetic Toxicology laboratory group in the EHSRB (Environmental Health Science and Research Bureau) is currently developing a multiplexed, high(er) throughput, animal-free platform for genetic toxicity assessment, i.e., the GeneTox21 platform. The platform is comprised of six complementary assays; they collectively encompass more than 20 endpoints that assess induction of mutations, chromosomal abnormalities, DNA strand breaks, and increased responses of several genomic and proteomic genetic damage reporters. Since platforms like GeneTox21 generate large amounts of dose-response data, regulatory interpretation of test results can be complex and cumbersome. Consequently, the research team is developing an informatics tool known as IATGA. The tool includes a user-friendly dashboard that provides access to tools for effective visualization, analysis and interpretation of complex multiplexed data sets. Progress to date (i.e., v8.6.7) has implemented a qualitative assessment review module, a dose-response analysis module based on the BMD (Benchmark Dose) approach, and a GeneToxPi module for integrated compound scoring and MOA (mode of action) analysis. The BMD module permits custom dose-response analyses with plot visualization and custom potency rankings. Recent progress has refined quantitative assessment capability and implemented GeneToxPi capability. Upcoming activities will further refine the GeneToxPi module, develop and implement an IVIVE (in vitro-to-in vivo extrapolation) module, incorporate additional endpoint evaluation rules, add enhanced visualization tools, and port the entire system to a more scalable programming environment. Once completed, the tool will be deployed for effective and efficient genotoxicity screening of data-poor chemicals. IATGA will permit comprehensive qualitative evaluations, as well as detailed quantitative enquiry for integrated potency ranking and MOA determination. (PI: Paul White)

Development of machine learning algorithms for the predictions of functional uses of substances for screening and prioritization—NEW!

Over the last years there has been a parallel interest in developing *in silico* methods to support higher throughput exposure estimation for screening and chemical assessment. By utilising emerging data and techniques, large numbers of substances can rapidly be screening and triaged for further work as relevant. Significant progress has been made on advancing the novel testing and assessment strategies on the hazard side of the risk assessment equation, with many quantitative (or qualitative) structure-activity relationships ([Q]SAR) models being developed for a number of toxicological endpoints. To date there has been less emphasis on new approach methods for exposure assessment. This can be primarily due to the underlying idea that the structure of a substance may be heavily related to the hazard, while this view does not appear to be as commonly held relating what a substance may be used for. This provides an opportunity to explore the area of exposure models to aid risk assessment activities by providing predications about how a substance may be used. The potential use of a substance can be predicted using machine learning methods known as quantitative (or qualitative)

structure-use relationship ([Q]SUR) and works in the same way as (Q)SAR. For this work we will look at employing machine learning (ML) techniques to develop (Q)SUR models. A variety of models, including an in-house developed random forest (RF) will be applied to datasets with substance use or function information. Using the several types of models, multiple ML models will be developed and performance compared against an unused evaluation dataset to determine ideal models. Data on the uses of substances is already available from the US EPA, ECHA, and UL Prospector. The models and resultant predictions will be integrated into prioritization and screening efforts, providing insight on functional uses of substances that would otherwise be without this information. (PI: Sean Collins)

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 has considerably improved for 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 in human biofluids (e.g., urine and blood). As a result, non-targeted approaches have gained much attention in risk assessment of human exposure to unknown and emerging chemical contaminants. This 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 fragmentation patterns, retention time, 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 predicted retention time for identification of unknowns and semi-quantitative information of identified unknown chemicals without using standards. The project 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 will also be beneficial to broader scientific communities. Method development and validation will include metabolites of selected CMP priority chemicals, including bisphenols, plasticizers, UV stabilizers, and their alternative or replacement chemicals in human biofluids such as urine and serum. (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 and used notably in the production of polycarbonate plastics and epoxy resins. Bisphenol F (BPF) and bisphenol S (BPS) are important bisphenol A (BPA) substitutes prioritized for measurement in 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 more limited than for BPA, making it difficult to properly evaluate the potential human health impacts of BPA substitution. In this study, the toxicities of BPA, BPF and BPS were directly compared following administration to rats 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 assessed by the OECD 407 Guidelines, additional measurements of endocrine-related endpoints were also carried out. Based on published information on the *in vivo* and *in vitro* toxicities of BPA, BPF and BPS, additional hormones were measured in rat serum, while the expression of specific selected genes that may provide additional insights on bisphenol molecular mechanisms of toxicity was 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 replacement 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

Mercury (Hg) found in country foods, which are consumed more frequently by Indigenous communities, can pose health risks Health Canada's approach to estimating human exposure to Hg from consuming country foods relies on assumptions that may be overly conservative, including: all Hg is present as methylmercury (MeHg), the neurotoxic form; Hg levels remain constant during food preparation; all MeHg in country food is absorbed by humans; and, Hg interactions with selenium (Se) and arsenic (As) do not alter human exposure. This could potentially lead to unnecessary consumption advisories and causing Indigenous communities to turn to less nutritious commercial foods. To test these assumptions, concentrations of Total Hg (THg), MeHg, As,Se and metal speciation (i.e. different forms of a metal) were measured in fresh, frozen and cooked samples of grey seal liver, muscle and kidney, and of whitefish muscle and change in bioaccessbility (the proportion of a chemical that is available for absorption following digestion) of these metals in grey seal tissues were estimated following simulated digestion experiments. The study results could help refine of Health Canada's 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. (PI: Dr Barbara Hales, McGill University; Tara Barton McLaren. Collaborators: Mike Wade; Ella Atlas; Cariton Kubwabo)

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)

Health Canada assesses and manages the health risks posed by environmental chemicals. FFs (firefighters) are exposed to a variety of combustion-derived toxicants both in and around fires, and statistics have shown that they have an increased cancer risk. Previous studies have shown that FFs are exposed to combustion-derived carcinogens such as PAHs (polycyclic aromatic hydrocarbons); moreover, that the dermal surface is an important route of exposure. Skin cleaning wipes have been proposed for post-suppression removal of dermally deposited toxicants; however, the efficacy of dermal decontamination has not been effectively investigated. This work is comparatively evaluating the ability of different cleaning strategies for post-suppression removal of PAHs deposited on the dermal surface. The work, which was conducted at a FF training facility in Ottawa, assessed the level of airborne PAHs at the fire suppression scene, and the post-suppression level of PAHs on the dermal surface. Following fire suppression, FFs were assigned to one of four intervention groups; three engaged in post-suppression dermal decontamination, the fourth was a control. The results revealed that FFs were uniformly exposed to high concentrations of PAHs, and that fire suppression resulted in significant dermal contamination. Post-suppression decontamination with two commercial cleaning wipes did not remove significant amounts of dermally deposited PAHs. In contrast, soap and water removed approximately half of the PAHs on the dermal surface. None of the investigated interventions reduced the internal dose of PAHs, as measured by quantification of PAH metabolites in urine. The results suggest that dermal penetration may be occurring too quickly to employ post-suppression decontamination to reduce dermal penetration and internal dose. The results of this research will be used to develop operating procedures, and/or PPE (personal protective equipment), that may be able to minimize FFs' exposures to combustion-derived toxicants. (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 powerhouse 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)

Exploring association between maternal PBDE levels, maternal plasma markers and maternal/infant health outcomes in the MIREC study—NEW!

The Maternal-Infant Research on Environmental Chemicals (MIREC) study is a Pan-Canadian study and is one of the biomonitoring efforts of the Department. Pregnancy is a vulnerable period and exposure to environmental chemicals can be harmful to the health of this vulnerable population. Polybrominated diphenyl ethers (PBDEs) are a class of flame-retardants used in a variety of consumer products and detected in the environment. These chemicals are known to exhibit endocrine disrupting properties. Less is understood in terms of the relationship between PBDEs in pregnancy and adverse maternal/infant health outcomes. This work was designed to initially conduct a systematic review to compile findings thus far on associations between maternal PBDE levels, maternal/infant health outcomes (e.g., infant birth weight, birth length, head circumference, gestational hypertension) and maternal blood markers. Also, examination of relationships among maternal PBDE levels, blood biomarkers and maternal/infant birth outcomes will be carried out in the MIREC study cohort. Findings from this work will generate information on maternal and infant health risks associated with PBDE exposures in pregnancy, and also provide insight into potential toxicity mechanisms. (PI: Premkumari Kumarathasan)

Exploring the application of new approach methods to establish in vitro transcriptomics-based points of departure to facilitate regulatory decision-making—NEW!

The growing number and increased complexity of substances present in consumer products and introduced annually to the Canadian market presents a challenge for regulators evaluating their potential hazard and risk to human health. The increased demand is compounded by the resource and time limitations of traditional animal test methods often leading to inadequate data available for hazard and risk characterization. New approach methods implementing novel technologies using in vitro and in silico methods provide a viable non-animal and high-throughput alternative to inform prioritization and risk assessment decisions. The purpose of this project is to develop defined metrics to demonstrate the capability of in vitro gene expression (transcriptomic) data to provide robust and reproducible quantitative information for implementation in regulatory frameworks. A uniform workflow was developed to accommodate a single large set of data that was consolidated to represent a diverse chemical space (i.e., numerous substances from multiple chemical classes). The endpoints were derived from gene expression data to represent robust and reliable transcriptomic points of departure (tPODs). To provide human relevance, the process of in vitro to in vivo extrapolation (IVIVE) was incorporated into the workflow that models an administered equivalent dose to estimate a human blood concentration equivalent that corresponds to the in vitro derived effect (e.g., the tPOD). Preliminary analysis and previous work from Health Canada have demonstrated that in vitro derived endpoints are protective of human health, providing more conservative estimates in comparison to traditional methods using whole animal models. The current work increases confidence in the application of NAM-based approaches in screening exercises that identify and prioritize substances of greater potential concern for further work. Global efforts are currently underway to harmonize these workflows and approaches to increase their acceptance and use within international regulatory frameworks. (PI: Anthony Reardon, Tara Barton-Maclaren, Reza Farmahin)

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 metric has been developed to quantify multi-chemical exposures and understand how chemical burdens vary within a population by taking advantage of human biomonitoring data. Exposure Load counts the number of chemicals measured in people above a defined concentration threshold. Data from the Canadian Health Measures Survey (CHMS) cycles 3 and 4 (2012–2015) were used for this analysis, which included 1,858 participants aged 12 to 79 years and 44 blood and urine biomarkers representing 26 chemical groups. The first phase of analysis found that Canadians are concurrently exposed to many chemicals at lower concentrations, and to fewer chemicals at high concentrations while the youngest age group (aged 12–19 years) had a significantly lower Exposure Load than older individuals, smokers incurred a much higher Exposure Load than non-smokers, but males and females did not substantially differ. In the second phase of analysis that is currently under way, the association between Exposure Load and additional exposure factors such as household income and education is being investigated. Whether certain chemical classes differentially influence Exposure Load is also being examined. 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. Link: **https://doi.org/10.1016/j.ijheh.2021.113704** (PIs: Jeff Willey, Tyler Pollock, Annie St-Amand)

Fetal exposure to microplastics—NEW!

Microplastics (MP) are tiny fragments of plastic that pollute our environment from a variety of plastic items that fill our modern lives. These fragments are resistant to decomposition and there is concern that they may pose damaging consequences for humans and wildlife. The extent of human exposure and impact on health are poorly known. A recent, highly publicised study from Italy identified MP in the human placenta, suggesting that they may infiltrate the womb and where they may affect fetal health and development. This study proposes to use the same approach; examining placentas from Canadian women for the presence of MP to determine if contamination of the womb is present. Plastics are ubiquitous in our environment and, therefore, to rule out the possibility of placenta contamination during the process of childbirth, the study will compare MP contamination in placentas delivered via caesarian section versus vaginal delivery. It is hypothesized that differences in the standard of hygiene required for caesarian section (abdominal surgery) may result in differences in surface contamination of the placenta compared to passage through the vaginal canal. In addition, to better understand the potential presence of MPs within the placenta in utero, samples will be collected from below the exposed placenta surfaces, to minimize the potential of contamination from either form of birth. This study will reveal if placentas from Canadian women contain MP and suggest if these reflect fetal exposure throughout pregnancy or exposure during delivery. This distinction is critically important to interpret the nature of risk posed by this pollutant to the developing fetus. (PI: Mike Wade)

Further development of consensus-based screening approaches for toxicological activity of chemicals from (quantitative) structure activity relationship ([Q]SAR)—NEW!

The application of Machine learning (ML) models within the toxicological space continues to mature. For many years researchers have developed numerous *in silico* models which predict the activity of substances on defined toxicological effects such as endocrine activity or genotoxicity. This does create a challenge for the regulatory community however, as with so many ML models available for a particular endpoint, it may be difficult to evaluate and select the most appropriate model(s) to ensure reliable results for the chemical space of interest. A simplistic approach could be to use the single model with the best performance, however that may limit the potential of *in silico* models and available computational power. A more robust approach is to identify or develop a methodology that can combine the models into a consensus model demonstrated to outperform any single model. Such a methodology has already been developed and used in Health Canada however it was focused only on (quantitative) structure activity relationships ([Q]SAR) for endocrine activity. The next phase will expand on the toxicological endpoints which are covered by *in silico* consensus models. For example, there are several ML models which can predict genotoxicity (from ACD, AMES, and CaseUltra) to name a few, and readily available high-quality datasets from Leadscope. By selecting well defined endpoints with high-quality datasets, and numerous ML models available for evaluation we aim to evaluate the performance of consensus models across diverse toxicological endpoints as possible. Initially focus will be on genotoxicity with the vision to expand to other endpoints of relevance such as developmental and reproductive toxicity. As developed, these consensus models will be integrated into a workflow as a first tier to help screen and prioritize substances for further risk assessment activities. (PI: Sean Collins)

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* (i.e., animal free) 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 traditional approaches (e.g., manual microscopy). This project aims to establish an integrated, animal-free, 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), and a gene expression profiling assay for cellular responses to DNA damage. The performance of the higher throughput system is

being evaluated by analysis of 35 carefully chosen 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. A companion project is developing an informatics tool to facilitate analysis and interpretation of GeneTox21 results. (PI: Paul White)

Genotoxicity of nanoforms of metal oxides on the Domestic Substance List: role of material solubility—NEW!

Health Canada is responsible for assessment and management of risks associated with engineered nanomaterials. Engineered nanomaterials (NM/NMs, 1–100 nanometers in size), because of their size-associated properties, are increasingly desired for industrial applications and are readily incorporated in several commercial products. Metal and metal oxide NMs are extensively incorporated in consumer products including cosmetics and sunscreens, textiles, self-cleaning products and purification units, and make up 37% of entries on the Nanomaterial Consumer Products Inventory. Although most metal oxides are not known to cause toxicity in their micron form, in some occupational settings such as in the case of welders and people working in steel mills, workers exposed to nanoparticles of metals show symptoms of lung diseases. Thus, there is clear evidence to suggest that exposure to nanoforms of metals and metal oxides could increase the risk of human diseases. This study is applying novel high throughput COMET assay and micronuclei assay for the investigation of DNA damaging and genotoxicity potential of NM that are prioritized by the New Substances Assessment and Control Bureau (NSACB) for assessment. The proposal will specifically investigate property variants of titanium dioxide and copper oxide NM. Under Phase 3 of the Chemicals Management Plan, NSACB has been tasked with assessing the nanoscale forms of substances on the Domestic Substances List, and there is a pressing need for quality experimental data for the human health risk assessment. The information generated from this proposal will facilitate the assessment of select set of NMs for their potential to induce genotoxicity. (PI: Sabina Halappanavar)

Grounding resource development and infrastructure projects in health impact assessment and sex- and gender-based analysis Plus—NEW!

As a federal authority, Health Canada provides specialist or expert information and knowledge to support the assessment of impacts on human health from projects considered individually or cumulatively under the *Impact Assessment Act* (2019). Health Impact Assessment (HIA) and Sex- and Gender-Based Analysis PLUS (SGBAPLUS) are foundational components of federal projects undergoing impact assessment. Often, a project's HIA and SGBAPLUS take place simultaneously but independently from each other, despite similar requirements (e.g., engagement of rights holders and stakeholders, the need to consider and evaluate disproportionate impacts on sub-populations who may be identified as vulnerable). Conducting an HIA and SGBAPLUS independently from one another may create a duplication of efforts as well as gaps in understanding significant health impacts. The goal of this project is to produce a toolkit with clear steps and concrete examples to guide project proponents

in the integration of SGBAPLUS in the HIA process, including practices for collecting the right level of sex and gender disaggregated data. Developing this unique methodology will support Health Canada's delivery of its health expertise and mandate in the impact assessment process by generating a more nuanced assessment of the interplay between health impacts and sex, gender, and other dimensions of peoples' identities including age, race, Indigeneity, and (dis)ability. (PI: Dr. Faiza Waheed, Intrinsik Corp.; Tihut Asfaw; Matthew Goncalves)

Healthy Home Environmental Health Survey 2021–2022—NEW!

The Chemicals Management Plan (CMP) is a jointly managed, (Health Canada and Environment and Climate Change Canada) horizontal initiative aimed at reducing the risks posed by chemicals to Canadians and their environment. Health Canada works to increase the public's awareness of the risks associated with chemicals and pollutants, as well as proposing actions that could be taken by Canadians to reduce their exposures. In 2017, an online survey was conducted to assess Canadians' knowledge, awareness and behaviours on environmental health issues. Results of this survey helped to shape the Healthy Home campaign that was launched in 2019. The Healthy Home campaign provides science-based information to Canadians that motivates them to take action to protect themselves and their families from chemicals and pollutants in and around the home. The campaign aims to move from awareness to actual behaviour change. Additional research was conducted with Canadians in 2021–2022 to help the program measure its effectiveness under a renewed CMP. The overall objective of this research was to determine Canadians' awareness and understanding of chemicals and pollutants, as well as their actual behaviours related to these risks at home. The results of the survey will help to identify areas of concern and help to shape the Healthy Home campaign. (PI: Ann Charboneau, Steve Clarke).

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)

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)

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 developed the Health Canada Automated Workflow for Prioritization (HCAWPr). HAWPr automates the collection and weighing of evidence related to in vivo, in vitro and in silico outcomes across the 28,000 chemicals on the DSL. Moreover, exposure information is collected regarding chemical use across millions of records such MSDS. 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. 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 and exposure pathways 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. A Science Approach Document is being prepared and will be published on the CMP website in 2023. (PI: Matthew Gagné)

Interpreting biomonitoring data: i-HBM working group's guidance value dashboard—NEW!

Biomonitoring guidance values (BGVs) enable interpretation of human biomonitoring (HBM) data in health-risk context. However, until now, there has been no central, international repository for this information. This work describes a free, on-line repository for international health-based guidance values to facilitate the interpretation of HBM data. The repository, referred to as the "Human Biomonitoring Health-based Guidance Value Dashboard" [(HB)2GV] Dashboard, represents the efforts of the International Human Biomonitoring Working Group (i-HBM), affiliated with the International Society of Exposure Science (ISES). The i-HBM's mission is to promote the use of population-level HBM data to inform public health decision-making by developing harmonized resources to facilitate the interpretation of HBM data in a health-based context. National Biomonitoring Section of Health Canada as the founding member of the i-HBM working group has played an important role in the conceptual design and development of the database, and in building the collaboration around the continued maintenance, update and development of the tool for the interpretation of biomonitoring data. This new resource can assist HBM data users such as risk assessors, risk managers and biomonitoring programs with a readily available compilation of guidance values. (PIs: Annie St-Amand, Tyler Pollock).

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 was submitted. (PI: Sean Collins)

Maternal-Infant Research on Environmental Chemicals: Associations between perfluoroalkyl substances (PFAS) and lipids and liver function biomarkers—NEW!

Health Canada helps to protect the health of Canadians by assessing and managing the risks associated with exposure to environmental chemicals. Perfluoroalkyl substances (PFAS) are a class of chemicals widely used in consumer products for their water, stain, and oil repellant properties. Exposure to PFAS is ubiquitous and 99% of Canadians have detectable levels of these persistent chemicals in their blood. Evidence suggests that exposure to PFAS can negatively affect cardiovascular health and liver function in the general population. However, it is not known if exposure during pregnancy results in similar effects or if these effects are sustained into later life. This project will investigate the potential effects of exposure to PFAS on selected biomarkers of cardiovascular health and liver function in women during pregnancy and as well as 10 years later. Data and biospecimens from the original Maternal-Infant Research on Environmental Chemicals (MIREC) study as well as the most recent

follow-up study, MIREC-ENDO, will be used to obtain measures of lipids and liver function biomarkers. In addition, new PFAS will be measured in serum samples collected at follow-up and the associations between PFAS and biomarkers of cardiovascular health and liver function will be quantified. This will include analyses of individual PFAS as well as their mixtures. This project will generate new knowledge on priority chemicals and their mixtures and potential health risks in vulnerable populations of pregnant women that will support risk assessment and risk management activities. (PI: Michael Borghese)

Maternal-Infant Research on Environmental Chemicals (MIREC): Associations between prenatal perfluoroalkyl substances (PFAS) and immune markers in offspring—NEW!

Health Canada helps to protect the health of Canadians by assessing and managing the health risks associated with exposures to environmental chemicals. Perfluoroalkyl substances (PFAS) are a class of over 5000 chemicals used for their heat, oil, water, and stain repellant properties in a wide range of consumer products. These chemicals have been called 'forever chemicals' because they do not break down in the environment or in humans. Data are limited on exposure levels and health effects in Canadians, especially in vulnerable populations such as pregnant women and children. Scientific studies have demonstrated that high levels of exposure to PFAS may increase the risk of a number of health outcomes. For example, PFAS exposure may affect immune system functions and subsequently impair an individual's ability to fight off infections. During pregnancy, infections can have serious effects for the health of mothers and their children. A reduced level of antibodies may increase the risk of infection in women and their newborns. Identifying the levels of exposure to multiple PFAS during pregnancy and childhood and potential effects on the developing immune system would, therefore, address an important gap in scientific understanding and contribute to policy guidelines for these chemicals. To address this gap, nine different PFAS will be measured in blood samples collected from pregnant women and preschool-aged children (2 to 5 years) as part of studies carried out under the Maternal-Infant Research on Environmental Chemicals (MIREC) Research Platform. Antibodies to measles, mumps, rubella,and varicella at birth and during childhood will also be measured and associations between PFAS and antibody levels will be quantified. This project will generate new knowledge on priority chemicals and potential health effects in vulnerable populations of pregnant women, fetuses, infants, and young children that will support risk assessment and management activities. (PI: Jillian-Ashley Martin)

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 additional 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)

Metal oxide nanomaterial induced DNA damage—NEW!

The New Substances Assessment and Control Bureau's nanotechnology section is responsible for assessment of risks associated with engineered nanomaterials. Metal oxide nanomaterials (MONMs) are among the most highly used classes of nanomaterials worldwide, though their potential to induce DNA damage in living organisms is known. High-throughput in vitro assays have the potential to greatly expedite analysis and understanding of MONM induced toxicity while minimizing the overall use of animals. In this study, the high-throughput CometChip assay was used to assess the in vitro genotoxic potential of pristine copper oxide (CuO), zinc oxide (ZnO), and titanium dioxide (TiO_2) MONMs and microparticles (MPs), as well as five coated/surface-modified TiO_2 NPs and zinc (II) chloride ($ZnCl_2$) and copper (II) chloride ($CuCl_2$) after 2–4 hours of exposure. The CuO NPs, ZnO NPs and MPs, and $ZnCl_2$ exposures induced dose- and time-dependent increases in DNA damage at both timepoints. TiO_2 NPs surface coated with silica or silica–alumina and one pristine TiO_2 NP of rutile crystal structure also induced subtle dose-dependent DNA damage. Concentration modelling at both post-exposure timepoints highlighted the contribution of the dissolved species to the response of ZnO, and the role of the nanoparticle fraction for CuO mediated genotoxicity, showing the differential impact that particle and dissolved fractions can have on genotoxicity induced by MONMs. The results imply that solubility alone may be insufficient to explain the biological behavior of MONMs. These results will be used to inform risk assessments under the New Substances Notification Regulations for DSL-listed nanomaterials under the Canadian Environmental Protection Act, 1999 (CEPA). (PI: Sabina Halappanavar, Djordje Vladisavljevic)

MIREC ENDO: pubertal timing, endocrine and metabolic function

MIREC ENDO is the current 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 580 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. Preparation 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-is generating 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. Next steps are to expand the existing exposures scenarios based on observations from federal contaminated sites and simulate BLLs using the All Ages Lead Model. Additional considerations of bone Pb impacts from short duration/intermittent exposures will also be explored. (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 Canadian Health Measures Survey (CHMS) 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 various indicators of health status among Canadians. The physical measures component of the survey includes biomonitoring, the measurement of environmental chemicals or their metabolites in blood, urine and/or hair samples, led by Health Canada's National Biomonitoring Program. Key milestones for the national biomonitoring program during FY 2021–2022 included: 1) publication 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); 2) publication of biomonitoring fact sheets for arsenic, cadmium, lead, mercury, PFAS,

DEHP, bisphenol A (BPA) and parabens that highlight changes in Canadians' exposures to these chemicals over time, distributions across age groups, differences between males and females, and comparisons between the Canadian population and other populations in Canada and the United States; 3) publication of a key paper assessing time trends for 39 environmental chemicals measured in at least three time points between 2007 and 2017 in CHMS; 4) 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 5) Completion of analysis of the CHMS biobank samples for certain chemicals planned to be measured in CHMS cycle 7, and initiation of a second biobank project to collect an additional cycle of data for some previously measured chemicals, both to support short-term regulatory data needs while minimizing the impact of a delay in the start of the CHMS cycle 7. (PI: Annie St-Amand, Tyler Pollock)

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. The Northern Contaminants Program is led by Crown-Indigenous Relations and Northern Affairs Canada (CIRNAC), in partnership with Health Canada, Environment and Climate Change Canada, and Fisheries and Oceans Canada, along with Indigenous organizations such as Inuit Circumpolar Council (ICC), Inuit Tapiriit Kanatami (ITK), Dene Nation and Council of Yukon First Nations (CYFN). Health Canada's Population Studies Division is the co-chair of the Human Health Review Team and participates on the NCP Management Committee. In 2021–2022, seven human health project proposals were funded to address exposure to contaminants and links to country foods, understanding dietary decision-making and supporting the development of communication materials, and the integration of information on country foods, nutrition, food security and health messaging. The NCP currently provides Canada's main contribution to the contaminants component of the Arctic Monitoring Assessment Programme (AMAP) an expert group under the Arctic Council. The Human Health Assessment Group (HHAG) was established under AMAP, an expert group through which trend monitoring and assessment of implications and impacts of pollutants on the health of Arctic residents is undertaken. (PI: Cheryl Khoury)

Northern Ontario pilot of the EnviroScreen Tool: An interactive geospatial interface for key indicators of environmental, community and health status—NEW!

Measuring and monitoring the multiple interacting determinants of health that are modified by resource extraction and development activities is a challenge in the federal impact assessment of designated projects. The California Environmental Protection Agency's "EnviroScreen" methodology integrates environmental, socioeconomic, and health data to quantify cumulative effects with an eco-justice lens. Pilots of the EnviroScreen tool have already been established in Canada, including in British Columbia and the Alberta Foothills. This tool is being adapted to the Northwestern Ontario context to support anticipated objectives of the *Impact Assessment Act*, including the regional assessment for the Ring of Fire. The work will also identify likely relationships between indicators and the relative attribution of the ecological, social, economic and behavioural determinants of health-on-health outcomes in developed and non-developed regions of Northern Ontario. (PI: Christopher Buse, University of British Columbia; Aurelia Thevenot; Joel Kaushansky)

Occupational exposure of on-shift Ottawa firefighters to halogenated and organophosphate flame retardants, and per- and polyfluoroalkyl substances—NEW!

Compared to the general population, professional firefighters (FFs) experience elevated risks of chronic diseases such as cancer and respiratory illnesses. The International Association of Firefighters (IAFF) has expressed noteworthy concerns regarding the carcinogenic hazards posed by flame retardants (FRs) and surfactants (e.g., per- and polyfluoroalkyl substances or PFAS). In response to IAFF concerns, Health Canada (HC) has implemented an action plan aimed at assessing and managing the risks posed by FRs. Recent biomonitoring research conducted in Ottawa, assessed the sources and routes of FFs' exposures to combustion-derived carcinogens such as polycyclic aromatic hydrocarbons (PAHs). A logical extension of that work involves assessment of Ottawa FFs' exposures to FRs and PFAS. Although some studies have investigated FFs' exposures to some FRs and PFAS, no studies have conducted a comprehensive assessment of occupational exposures related to emergency, on-shift suppression of municipal structural fires. This work will employ passive samplers (i.e., silicone wristbands) to monitor exposures at the fire suppression scene, at multiple locations in the fire hall, and in truck cabs. Collection and analysis of fire hall dust samples will provide additional information about occupational exposure sources. Control samples will be collected at Ottawa Fire Services (OFS) office areas. Dust and passive samplers will be analysed for an extensive array of PFAS, halogenated FRs such as PBDEs (polybrominated diphenyl ethers), and organophosphate FRs. The results obtained will form the foundation for design of a follow-up biomonitoring study to assess the internal dose of FRs, i.e., levels of FRs in blood or FR metabolites in urine. The results obtained will provide valuable knowledge about on-shift FFs' exposures to FRs and PFAS, thus addressing IAFF concerns, and supporting HC's action plan. Results will be communicated to a wide range of local, national, and international stakeholders. (PI: Paul White)

Opportunities for the analysis of chemical exposures in racialized populations in Canada: An investigation based on the Canadian Health Measures Survey—NEW!

The Canadian Health Measures Survey (CHMS) 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. Sociodemographic characteristics are important determinants of chemical exposures; however, race or cultural background as a modifier of chemical exposures has not been systematically explored in the Canadian context. Using biomonitoring data from the CHMS, we are conducting a race-based analysis of chemical exposures in Canadians, with an objective of understanding the opportunities and limitations for such analysis using the CHMS data. The following chemicals subject to risk management performance measurement in Canada were selected for this analysis: lead, cadmium, BPA, DEHP and benzene. The initial assessment confirmed that the representation of various racial subgroups within the CHMS sample was consistent with the Canadian Census validating the use of the CHMS dataset for race-based assessment of chemical exposures. Analyses are currently in progress to generate chemical concentrations that are representative of each racial subgroup and to assess differences in chemical exposures as well as time trends in exposures among the different racial populations. This work directly addresses a key knowledge gap regarding chemical exposures in racialized populations in Canada, and will contribute to the refinement of sampling design and data analysis that may be required to conduct an effective assessment of different racial populations sampled within the CHMS. (PIs: Subramanian Karthikeyan, Annie St-Amand, Cheryl Khoury)

Pathways of effect analysis—Multiple land-use impacts on the social determinants of health in a Canadian context—NEW!

Human activities on the landscape leave lasting legacy impacts on human health and its determinants through multiple pathways and processes. This work uses factor analytic and structural equation modeling research methods to map out the ‘pathways of effect’ between ecological, social, economic, and behavioral conditions in the context of resource development and associated impacts on physical and mental health. The model is aligned with Health Canada’s interim social determinants of health in the health impact assessment framework. It will also quantify the strength of relationships between indicators for which data is available to “prove” the relationships between identified variables in the conceptual model, and their pathways in producing negative health effects and/or outcomes. The project will also help determine which indicators are most useful in predicting and monitoring for human health impacts of resource development activities, and where data gaps persist. This will support Health Canada’s ability to advise decision makers on potential health impacts of designated projects under the *Impact Assessment Act*. (PI: Christopher Buse, University of British Columbia, Aurelia Thevenot, Joel Kaushansky)

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)

Physiological modeling of the immune response to polyfluoroalkyl substances (PFAS)—NEW!

Health Canada have been investigating the risk of exposure of poly- and perfluoroalkyl substances (PFAS) in the Canadian population. A potential link between high PFAS body burdens and human immunosuppression was reported in the scientific literature. High PFAS levels may be correlated to heighten risk of infectious diseases, including COVID-19. While mice may be more susceptible than human to immunosuppression, the immune response is similar across each species. The only known biological difference between rodents and human is the kinetic accumulation of PFAS in the body.

This research effort will attempt to model the dose-response behavior of various PFAS in drinking water and identify potential markers of altered immune functions. A series of experiments are ongoing to generate data to model plausible effects in animals and cultured cells into human daily exposures through drinking water. Kinetic experiments will provide data to predict using computer model simulations of PFAS in the body across a wide variety of PFAS substances and emerging analogs. Experiment with mice exposed to PFAS will be used to study over time and doses any significant changes in biological and immunological responses such as organ weights and antibody levels. The animal and computer models will serve as tools for regulators and scientists to extrapolate experimental results into drinking water exposure level of concern for Canadians. (PI: Andy Nong)

Physical-chemical characterization and toxicity measurements of priority nanomaterials—NEW!

Metal oxide nanoparticles are used in a wide array of commercial applications including medicines, paints, food products and packaging, and advanced electronics. They are added for color, texture and function and as a result the interaction between humans and such particles is ubiquitous and variable, with routes of exposure spanning inhalation, ingestion and physical contact. While considerable research has explored the properties and safety of individual materials, there is often insufficient characterization data to accompany biological results to make accurate regulatory decisions. Metal oxide nanoparticles often have batch to batch variability in size, composition, purity and dispersibility. The National Research Council (NRC) has performed substantial physical and chemical characterization across a wide array of metal oxide particles exploring the effects of size, surface coating and manufacturer for different metal oxide families. The particles, suspended from powder materials in water, often lack significant nano-sized fractions. Nevertheless, these materials still can have a significant impact on cells in *in vitro* assays. This study identified trends and findings from work on manganese oxide nanoparticles to examine how different commercial manganese oxides behave and identify where potential risks from exposure may arise. (PI: David Kennedy, Djordje Vladisavljevic)

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. Based on existing literature, game-based learning has the potential 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 due their greater biological susceptibility to environmental health hazards. The Regulatory Operations and Enforcement Branch, Environmental Health Program—Ontario Region, the Transformation Office, the Canada School of Public Service, Technology Lab, EcoSchools Canada and VR Vision Inc 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 (ages 13–18). Activities have included a research report on market trends/academic literature and facilitated group discussions with high school students on game-based learning. Project Apollo investigators will present the findings of the abovementioned activities to the Solutions Fund Panel in fall 2022 and propose next steps for the project, which may include prototype development and consultations with relevant stakeholders. (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)

Rapid screening tool for disruption of endocrine stress responses linked to the developmental origins of disease—NEW!

Health Canada is responsible for the assessment and management of health risks to Canadians associated with exposure to chemicals in the environment. The hypothalamic-pituitary-adrenal (HPA) axis is essential for survival, playing a critical role in mobilizing resources to respond to stressors, combat infection, and resolve inflammatory processes. These functions are mediated primarily through the actions of glucocorticoid stress hormones, allowing an individual to cope and to survive. Dysregulation or impairment of HPA axis function is associated with numerous disease processes, including cardiovascular disease, metabolic disorders, dementia, and depression. Exposure to environmental chemicals can trigger and/or interfere with glucocorticoid signaling, impairing the capacity to respond appropriately to other stressors and increasing the risk of disease. Accordingly, assessing whether environmental exposures impact the stress response system captures a measure with cross-cutting relevance to potential health impacts in the exposed population. Assessing effects of chemicals on endocrine stress responses, however, requires an intact fully functional HPA axis and whole-body response. Until now, this has severely limited the potential for high-throughput screening. Zebrafish embryos have been put forward as a bridge between traditional high-throughput in vitro models and in vivo testing. By day 5, zebrafish embryos have a functional HPA axis and produce cortisol, the same adrenal steroid as humans, in response to stressor exposures. In collaboration with University of Ottawa researchers, Health Canada is conducting experiments to establish optimal design, define protocols for dose-selection, and test reproducibility in order to establish a model for rapid screening of stress response-disrupting chemicals. Expected outcomes include a rapid screening tool that can be applied broadly to assess chemicals for disruption of stress responses that cannot be readily assessed by traditional in vitro methods. (Co-PIs: Vance Trudeau, University of Ottawa; Carole Yauk, University of Ottawa; Errol Thomson)

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)

Screening of ToxCast chemicals through assay for human thyroid peroxidase inhibition—NEW!

Health Canada has the mandate to identify and manage risks of commercial chemicals and to replace animals in toxicity testing. Thyroid peroxidase (TPO) is an enzyme present on thyroid gland cells whose activity is essential for thyroid hormone synthesis. The OECD Test Guidelines Program (Thyroid Scoping Effort Group, OECD, 2014) identified that TPO was the most promising target to develop screening assays for thyroid disrupting chemicals. Despite considerable international effort to date in developing screening assays for TPO activity, there is still no proposal for this assay before the OECD Test Guidelines Program. A promulgated OECD Test Guideline based on this assay would provide a valuable tool to rapidly assess effect on vulnerable biology leading to endocrine disruption. Funded under the Chemicals Management Plan, this project screened 788 chemicals for inhibition of TPO activity or for potential confounding activity. Results will be compared with those obtained for the same chemicals by our US EPA collaborators using TPO from rat thyroid gland microsomes. This dataset will be used by the Newly formed Thyroid Disruption Expert Group of the OECD Test Guidelines Program for validation of rapid TPO methods. (PI: Mike Wade)

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

Health Canada conducts 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. Evidence suggests that chronic exposure to Selective Serotonin Reuptake Inhibitors (SSRIs) may affect aquatic organisms. Several SSRIs share a mechanism of action, including fluoxetine, citalopram, escitalopram, paroxetine and sertraline. The present study assessed the chronic effects of five SSRIs in two native freshwater invertebrates, the File Ramshorn snail *Planorbella pilsbryi* and the amphipod *Hyalella azteca*. Snail tests included static renewal tests of up to 13 days with egg masses collected from breeding adults, and 7-day tests with juvenile snails 24–96 hours post-hatch. Tests with snail embryos assessed viability and hatching, while tests with juvenile snails and amphipods assessed survival and growth. All LC50/EC50 values varied between 0.1 and 2.0 mg/L. Sertraline was more toxic than the other compounds. There were no significant differences between the toxicity of citalopram and escitalopram. Further research will investigate the chronic effects of a mixture of SSRIs in freshwater snails and amphipods. 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, Ève Gilroy)

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)

Testing nanomaterials with zebrafish toxicity models—NEW!

The New Substances Assessment and Control Bureau's Nanotechnology Section requested a pilot level project to use the NRC's standardized zebrafish toxicity models for testing different classes of nanomaterials. The initial phase of the study was designed to evaluate stability and solubility of different classes of nanomaterials in the test solutions used for the zebrafish studies. Eleven nanomaterials were evaluated for their properties in aqueous media used for zebrafish larvae. Five metal oxide nanoparticles, titanium dioxide coated with silica, copper oxide, aluminum oxide, nickel oxide and cerium oxide coated with PVP were determined to be the most stable in zebrafish buffer solution. These five nanomaterials were therefore selected for testing using two standard zebrafish toxicity tests. The first is based on the OECD recognized fish embryo toxicity test (FET) and represents an assessment of developmental toxicity. The second is the general and behavioural toxicity test (GBT) where larvae were exposed to the nanomaterials at a time point when all major organs and systems are developed and the larvae are free swimming. Aluminum Oxide (Al_2O_3) was the most toxic nanomaterial tested, producing lethality and phenotypic effects in both the FET and GBT assays, with concomitant behavioural defects. Copper Oxide (CuO) produced a significant hatching deficit, which may be partially responsible for the behavioural deficits seen in the FET assay. This is supported by the lack of toxicity in the GBT assay. Cerium Oxide (CeO_2) and Nickel Oxide (NiO) did not show any effect. Titanium dioxide (TiO_2) exposure also showed no effect for either of the assays other than a slight decrease in the first light-dark transition for both of the assays. These results show that the zebrafish models are suitable to test toxicity of nanomaterials and provide a platform for future studies. (PI: Lee Ellis, Djordje Vladisavljevic)

Testing the effects of Selective Serotonin Reuptake Inhibitors (SSRIs) on zebrafish (*Brachydanio rerio*)

Health Canada conducts 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. Selective Serotonin Reuptake Inhibitors (SSRIs) on the Revised In Commerce List (R-ICL) 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 could provide information on the potential consequences of long-term exposure to environmentally-relevant levels of five different SSRIs from a higher (systems) perspective. Previous studies tested the concentration-response profile of five SSRIs on zebrafish larval behaviour alone and in mixtures. The current study was to ascertain if prolonged exposure of juvenile and adult fish to concentrations of SSRIs close to those found in the environment would affect normal growth, behaviour and reproductive behaviour of fish. While no difference was observed for growth or sex ratio, SSRI exposed fish showed behaviours suggestive of a decreased level of anxiety/stress. There was a prominent effect of SSRI exposure on three measures related to breeding, suggesting that SSRI exposure reduces the reproductive rate of the fish. Overall, while there did not appear to be an obvious phenotypic effect on the fish, the SSRIs appeared to have an anxiolytic effect along with an effect on their reproduction. These data will be used directly in the

environmental assessments of SSRIs on the R-ICL and will be used to determine whether a cumulative risk assessment process for substances notified under the New Substances Notification Regulations of the *Canadian Environmental Protection Act, 1999* (CEPA) is feasible. (PI: Lee Ellis, Dianne Hughes)

The association between blood PFAS concentrations and biochemical and hematologic tests reflecting organ function in participants of the Canadian Health Measures Survey (CMP)—NEW!

Per- and Polyfluoroalkyl substances (PFAS) are human-made chemicals commonly used in many consumer and industry products such as food packaging, household products (cookware, carpets, textiles and leather), paints and fire-fighting foams. They are persistent, repel oil and water, and are resistant to heat. PFAS do not breakdown easily and may remain and accumulate for a long time. There is some evidence in the scientific literature that exposure to PFAS substances may cause adverse health effects in humans. This research will test the association between plasma PFA concentrations, and blood cell counts and blood tests of thyroid, liver and kidney function, and tests reflecting diabetes and glucose control and serum lipids. To accomplish this, data will be used from cycles 1, 2, and 5 of the Canadian Health Measures Survey (CHMS), a national survey representative of the Canadian population, which contains all the information required for our study. If significant associations are found, this would provide evidence suggesting that PFAS, at levels found in the Canadian population, may affect vital organ function, and would justify further biomonitoring studies on PFAS exposure levels in various environmental mediums (e.g., food, air, drinking water, soil) and in human tissues. This information should be of interest to those involved in regulation of PFAS. This study fits within Health Canada's mandate of reducing the negative impacts of environmental exposures on the health of Canadians through research. (PI: Sabit Cakmak, Bob Dales)

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 method for integrated screening of genotoxic chemicals—NEW!

New Approach Methods (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 animal derived toxicity data. Currently, there are substantial international efforts to develop NAM-based approaches that provide information related to regulatory endpoints. Genotoxicity assessment is a critical component of all chemical safety evaluations, and the aims of this project are to provide support for applying in vitro (outside of a living organism) genetic toxicity data, with a novel data analysis and interpretation framework, in future priority setting initiatives and quantitative risk assessments of organic chemicals. More recent higher-throughput *in vitro* genotoxicity assays (i.e., genetox NAMs), many of which also provide mechanistic information, offer a powerful approach for determining high-precision benchmark concentrations for potency ranking and risk assessment. In order to obtain human dose context from in vitro assay results, we use an approach referred to as in vitro-to-in vivo extrapolation (IVIVE). Using IVIVE, we convert a concentration that causes a genotoxic effect in exposed cells (i.e., in vitro bioactivity) to a dose expected to cause an effect in humans using high-throughput computational methods. Previous work has demonstrated that the application of IVIVE to *in vitro* bioactivity data can provide points of departure (PODs) that are protective of human health, but there has been no evaluation of how these models perform with genotoxicity NAMs. An in-depth case study is being conducted to scrutinize the utility of the genotoxicity NAM-based approach for risk assessment and regulatory decision-making. Specifically, quantitative analysis of genetox NAM results coupled with the application of IVIVE models of varying complexity will be carried out to establish human administered equivalent doses (AEDs). These NAM-derived AEDs will be compared with PODs from traditional genetox animal studies, as well as human exposure estimates. Once established, this integrated approach could be applied for routine chemical screening, prioritization, and/or risk assessment. (PI: Alexandra Long; Paul White, Marc Beal)

Toxicokinetic extrapolation for high throughput screening of pro-mutagen chemicals—NEW!

Health Canada have been studying the applications of new alternative methods for the next generation of risk assessment. High throughput toxicity testing screens and content are used to predict potential biological changes leading into harmful health effects. Kinetic data have been generated for over one hundred chemicals that help convert the concentrations leading to toxic effects in cells into daily exposure doses for the Canadian population. Due to the setup of previous experiments, assumptions were made that biological changes are caused by the parent form of the chemical. However, many environmental chemicals undergo metabolic or chemical transformation in the body before causing harmful effects. This study therefore proposes to investigate the activation of chemicals causing genetic toxic effects. The research effort includes using computer models to simulate the biological transformation of these mutagenic chemicals into an active form. Data will be collected through the US EPA's HTTK simulation package, existing published animal exposure studies and experiments generated at the Computational Toxicology Laboratory. Investigators will compare the predicted metabolic activated form of chemicals based on the various form of data collected. The present pilot study will provide a framework to help predict metabolic active mutagenic chemicals and identify potential data gaps for broader classes of chemicals that can be addressed in a larger comprehensive research study. (PI: Andy Nong)

Trends in environmental chemical concentrations in the Canadian population: Analysis of human biomonitoring data from the Canadian Health Measures Survey—NEW!

Data from the Canadian Health Measures Survey (CHMS) establish baseline environmental chemical concentrations in the general population. Two separate studies seek to evaluate temporal trends in environmental chemical exposures in the Canadian population. The first study using data from the first 5 cycles of the CHMS (2007–2017) identified 39 chemicals that were measured in blood or urine in at least three cycles and had detection rates over 50% in the Canadian population. Statistically significant linear trends were noted across cycles for 21 chemicals. A decreasing trend was observed for 19 chemicals from diverse chemical groups, including metals and trace elements, phenols and parabens, organophosphate pesticides, per- and polyfluoroalkyl substances, and plasticizers. Increasing trends were noted for two pyrethroid pesticide metabolites. No significant trends were observed for the remaining 18 chemicals that included arsenic, mercury, fluoride, acrylamide, volatile organic compounds, and polycyclic aromatic hydrocarbons. The findings were published in **https://doi.org/10.1016/j.envint.2021.106678**. The second study compared time trends in whole blood and red blood cell (RBC) concentrations of lead, cadmium, and mercury for Canada and the U.S. using data from the CHMS (2007–2017) and the U.S. National Health and Nutrition Examination Survey (NHANES) (1999–2018). For blood and RBC levels of lead and cadmium in both the U.S. and Canada, and for blood and RBC mercury in the U.S., statistically significant declining trends were noted in total population aged 3–79 as well as in most sex-age subgroups. For blood and RBC mercury in Canada, declining trends were limited to some adult sex-age subgroups only. There were no significant differences in annual percent changes for all three metals between the two countries. A manuscript describing the findings is prepared. Continued collection of national biomonitoring data is necessary to monitor trends in exposures over time, which in turn may inform risk management performance measurements (PIs: Tyler Pollock, Subramanian Karthikeyan, Annie St-Amand).

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) is 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 priority PFAS and PFAS Mixtures—NEW!

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 23 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 information on PFAS and to facilitate read-across for human health risk assessment; 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: Ella Atlas)

Use of gene expression profiling for the evaluation of potency and mode of action of bisphenols mixtures—NEW!

Canadians are exposed daily to a variety of manmade chemicals, including bisphenols. Bisphenols are chemicals used in the plastics industry and are present in many consumer products such as food packaging, plastic bottles, dental sealants, thermal paper and more. As a consequence, humans are inadvertently exposed to these chemicals. Bisphenol A (BPA) was one of the first chemicals shown to mimic the hormone estrogen and was linked to numerous adverse health effects in many studies. Due to public concern, BPA was replaced with other structurally similar bisphenols. Previously, our lab examined the potency and mode of action of 17 individual bisphenols using cells in culture and gene expression profiling. However, in reality, humans are being exposed to mixtures of these bisphenols. The experiments proposed herein build on our existing data to examine the effects of bisphenols in mixtures. This study will investigate whether the potency and gene expression profiles of bisphenols change when cells are treated with environmentally realistic combinations and concentrations of the chemicals. The project applies new approach methodologies (NAMs) to provide critical toxicity information for the risk assessment of bisphenols. (PI: Ella Atlas)

Use of New Approach Methodologies to facilitate potency ranking and evaluate 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 regulatory actions have led to increased use of alternatives as replacements, many of which are chemically similar to BPA. Bisphenols and alternatives were examined using a New Approach Method (NAMs) that integrate *in silico* and *in vitro* methods. BPA's cellular effects occur primarily through its interaction with the estrogen receptor (ER) that when active, 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 were: (1) derive a value that represents the bioactivity threshold for in vitro assays defined for general systemic toxicity and ER activation; (2) use in vitro to in vivo extrapolation (IVIVE) to convert in vitro concentrations to human relevant surrogate dose values; (3) demonstrate the capacity of NAM-based values to serve as lower-bound (i.e., protective) estimates by comparing these outcomes to available in vivo (i.e., animal) studies. Using a weight of evidence approach, the in vitro data was combined with in silico predictions to characterize the potential hazards by comparing the relative potencies of chemicals within this group and identify specific substances as potential endocrine disruptors. 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: Anthony Reardon, 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. This work has led to the publication of the toxicity profiling of 20 compounds selected by HC using two in-house zebrafish toxicity testing models, the fish embryo toxicity (FET) assay and the general and behavioral toxicity (GBT) assay. After phenotypic assessment of toxicity, we developed a transcriptomic analysis pipeline that has demonstrated that the compounds tested activate similar molecular pathways to those found in higher vertebrates along with novel toxicological pathways that have not been previously reported. In addition, by using Benchmark Dosing, we demonstrated that the transcriptomic points of departure (PODs) represent a more sensitive measure for the purposes of risk assessment than phenotypic profiling.

In addition to supporting HC's risk assessment activities, a potential important outcome of this continuing research is collaborative contributions to international NAM validation projects, including the NTP SEAZIT initiative, the OECD DNT expert group and a case study under APCRA. Through these collaborations, this research will serve to facilitate the 3Rs in chemical risk assessment as it bridges transition from traditional animal testing to NAMs and thereby further HC's collaborative commitment to the international regulatory community. (PI: Lee Ellis, Cindy Woodland)

Virulence of opportunistic *Acinetobacter baumannii* in biotechnology-related microbial mixtures—NEW!

The New Substances Assessment and Control Bureau's Biotechnology Section has encountered an increasing number of notifications associated with mixtures of micro-organisms for use in biotechnology applications. Under current regulatory requirements, each micro-organism in the mixture must be notified to regulators as individual micro-organisms (i.e., one notification per micro-organism), which is costly and laborious. Furthermore, there is considerable uncertainty in our understanding of how pathogens may express virulence in mixtures of microbes approved for use in biotechnology compared to their homogeneous cultures. The pathogen *Acinetobacter baumannii* (Ab) was used as an example to demonstrate how biotechnology microbial mixtures may mask virulence during coculture. To do this, the virulence of Ab in pure culture was compared to that of Ab added to twelve bacteria that

are non-hazardous and approved for use in biotechnology. *A. baumannii* showed an advantage for growth at higher temperatures (37ºC, 42ºC) compared to the biotechnology bacteria. The presence of biotechnology bacteria did not alter A549 lung cell cytotoxicity induced by Ab, which is consistent with the adaptation of the pathogen for growth at 37ºC. However, Ab survival was significantly reduced in the presence of biotechnology bacteria using a J774A.1 macrophage-killing assay, which suggests that Ab virulence is suppressed under these conditions. This research posits that if a biotechnology product were to contain Ab, assessing the virulence of an entire microbial biotechnology mixture may not be equivalent to that of each microbe tested separately. With follow-up studies, it will contribute towards the development of updates for regulatory guidance on microbial biotechnology product submissions, and further our understanding of the complex interaction of pathogens as they exist with other micro-organisms. (PI: Azam Tayabali, Valar Anoop)

PESTICIDES

Development of a reporting framework to support a waiver rationale for cancer studies in pesticide risk assessment—NEW!

Rodent cancer studies are required by regulators to evaluate the cancer potential of pesticides. Certain limitations of these studies have been highlighted in recent years, such as a lack of human relevance for some aspects of these studies. As a result, the Rethinking Carcinogenicity Assessment for Agrochemicals Project (ReCAAP) was initiated by experts from different sectors including academia, non-governmental organizations, industry stakeholders, and regulators such as Health Canada's Pest Management Regulatory Agency. The purpose of the ReCAAP was to develop a weight of evidence (WoE)-based reporting framework that could be used to develop waiver rationales for cancer studies, while still achieving health protective risk assessments. A reporting framework was drafted using publicly available information to structure a WoE assessment to determine the type of information needed to support a waiver rationale for the cancer study. Using this draft framework, ReCAAP evaluated 15 pesticides with chemical profiles spanning 10 tumor types and 15 chemical classes. The workgroup used an iterative approach to refine the proposed framework, incorporating regulatory feedback to identify critical information to be considered in a WoE determination of the need for rodent cancer studies. Analysis of the 15 case studies allowed for the development of the final reporting framework to support a cancer study waiver rationale. The framework includes information on use patterns, exposure scenarios, pesticidal and mammalian mode-of-action, physicochemical properties, metabolism, toxicokinetics, toxicology data including mechanistic data, and chemical read-across from similar registered pesticides. The framework provides structure to organize existing critical information that could be used by a regulatory authority to make a risk-based decision to waive cancer studies in rodents for a pesticide. The ReCAAP effort complements other ongoing collaborative initiatives aimed at improving the quality of pesticide risk assessments, and the framework provides an opportunity to globally harmonize data needs and assessments. (PI: D. Ramsingh, C. Adcock)

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

Dermal absorption (DA) is used by Health Canada's Pest Management Regulatory Agency (PMRA) as a correction factor in determining occupational and residential pesticide exposure when an effect via the oral route is used for dermal exposure risk assessment. DA reflects the amount of chemical absorbed into the body through the skin. PMRA typically selected DA values from in vivo DA studies, or 'triple pack' studies of in vivo rat, in vitro rat skin and in vitro human skin. In vitro DA studies alone were not considered sufficiently robust or validated for determining a DA value for pesticide risk assessment. To address these concerns, PMRA worked with other international regulatory agencies, industry, academia, and non-governmental organisations. This multi-year global initiative included workshops, a retrospective analysis of 30 'triple pack' DA studies, and development of a standard in vitro DA method. This DA method supplements the current test guidelines and reduces the variability of results between studies. The retrospective analysis of 'triple pack' DA data validated the results from in vitro DA studies conducted according to this standardized method. The results also demonstrated that DA from the standardized in vitro method in rats is predictive of in vivo DA in rats. Therefore, by extrapolation, in vitro methods using human tissue were considered to be predictive of in vivo human DA. As a result of this work, concerns with using in vitro DA studies alone for risk assessments of pesticides have been addressed. PMRA is now accepting in vitro DA studies for most pesticide risk assessments. In vivo and 'Triple pack' studies will also continue to be accepted by PMRA (e.g., when they are already available) and may be required in specific circumstances. (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)

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 safety 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, including validation, 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. (PI: Vincent Marleau)

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)

A summary of residential radon surveys and the influence of housing characteristics on indoor radon levels in Canada—NEW!

Radon is a known carcinogen that can accumulate inside homes and buildings and is the leading cause of lung cancers in Canada for non-smokers. As part of the mandate to ensure the health and safety of Canadians, Health Canada's National Radon Program is committed to informing Canadians about the health risk of radon and to monitoring trends in exposure. This study calculates mean radon concentrations for homes in Canada, by province, combining data collected by Health Canada and data from community surveys published in the scientific literature over the past 15 years. In addition, the study revisits data collected from the Cross-Canada Radon Survey (2012) to assess connections between housing characteristics and indoor radon levels. For example, the Cross-Canada survey data indicates that radon levels in houses with a basement are, on average, about twice as high as radon levels in houses without a basement, and houses with private wells tend to have higher radon concentrations than houses on a municipal water supply. This information is valuable for identifying populations where radon risk is elevated and for developing strategies to help Canadians manage their exposure. Article published in Health Physics, June 2021. (PI: Jing Chen)

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 biological effects of exposure to semiconductor light of different wavelengths on cultured human lens and retinal cells—NEW!

Health Canada has a mandate that includes assessing and managing risks from radiation emitting devices. This project examines the activation of a number of biochemical pathways in the eye following exposure to specific wavelengths from a semiconductor light source, similar to that of current light-emitting diode (LED) technologies. This study serves to evaluate biological effects of LED light-exposure and address knowledge gaps concerning potential oxidative threats to the eye, particularly from high-energy blue light that makes up a large component in the white-light emission from diodes. This is of importance as studies have shown that oxidative stress from blue light may result in a decrease in lens opacity that can lead to the development of cataracts which is one of the leading causes of blindness worldwide. Also, chronic and excessive exposure to light can lead to a loss of vision as the central portion of the retina called the macula deteriorates leading to macular degeneration. To address this knowledge gap, human-derived cell lines from both the lens and the retina of the eye were exposed to a relevant dose of various colors of LED light (e.g., white, blue (470 nm), green (530 nm), and red (625 nm)) and then assessed 4 hours later for changes in the expression of proteins. This research will support hazard characterization and dose response assessments needed to characterize risks from devices emitting visible light and UV radiation. (PI: Sami Qutob)

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 with follow-up surveys and further analysis including demographic data occurring in 2022. 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. Preliminary results indicate this campaign appears to have been successful in increasing the engagement of the public by 5–6 fold. Additionally, it indicates that they are younger relative to participants who were recruited in the previous year. Full data on age and gender will be available later in 2022. (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"). 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. Preliminary results indicate that these are effective radon reduction solutions under test conditions. 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)

Assessment of thoron contribution to indoor radon exposure in Canada—NEW!

Radon is a known carcinogen that can accumulate inside homes and buildings and is the leading cause of lung cancers in Canada for non-smokers. While the most prevalent source of radon is the uranium-238 decay chain, which produces the isotope radon-222 ("radon"), radon-220 ("thoron") produced from the thorium-232 decay chain can be an important contributor to total radon dose in some circumstances. Damage to lung tissue from either radon or thoron is caused by short-lived alpha-emitters that they produce. To quantify the relative contributions, a number of surveys were conducted in 34 Canadian metropolitan areas between 2007 and 2013, covering 71% of the Canadian population. This study summarizes this data, from a total of 3,534 residential homes, to provide information on thoron distribution characteristics across Canada and to assess the contribution of thoron to total indoor radon exposure. In addition, this assessment revisits the treatment of thoron measurements below the detection limit that was used to assess average thoron exposure in a previous study (Chen et al. 2015). Because thoron has a very short half-life (56 seconds), it can be difficult to measure directly: it may be present in indoor air but decay before reaching the measurement device, releasing the alpha emitters but not registering as detected. This was demonstrated in limited studies that had specifically measured thoron and thoron progeny (e.g., Chen et al. 2011). The present study reassessed estimates of thoron concentration using

only measurements where thoron was actually detected and calculated average concentrations that were significantly higher than the 2015 study. Thoron contribution to indoor radon dose varied widely, ranging from 1.3% to 32% geographically. This information is valuable for identifying populations where radon risk can be elevated and for developing strategies to help Canadians manage their exposure. Article published in Radiation Environmental Biophysics, January 2022. (PI: Jing Chen)

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)

Coincidence summing: a review of the literature and implementation of an coincidence summing algorithm—NEW!

Gamma ray spectrometry is an extremely sensitive methodology that counts gamma rays from individual radioactive atoms (radionuclides). This powerful technique is used to assess radioactivity after a nuclear accident, natural occurring radioactivity, or the contamination level in environmental samples. The efficiency of the gamma ray detector for a given radionuclide is a function of the energy of the gamma rays. Some radionuclides emit multiple gamma rays and if both of these gamma rays hit the detector at the same time, the energy deposited in the detector is the sum of the energies of the two gamma rays. This is known as coincidence summing and will affect the efficiency calibration. Coincidence summing has been extensively studied and continues to be a research topic for radioactive volume sources. The problem of coincidence summing for point sources has been solved. This project involved a literature review of coincidence summing and then application of information relevant to characterizing a detector with point sources to implement an algorithm based on that information. The algorithm was the amalgamation of concepts from three papers: the concept of using an iterative method; the radionuclide specific constants; and the study of the mathematical relationship of two efficiency types. (In one paper the authors explained the fact that coincidence summing was used to do their efficiency calibration; i.e. they didn’t see coincidence summing as a problem, but as an advantage.) An algorithm based on a literature review has been developed for coincidence summing corrections and used on measurement data. To date, the algorithm has been successfully tested on known results which don’t have coincidence summing issues as an initial validation that the algorithm works. It has also been successfully tested on spectra with known coincidence summing effects. Coincidence summing is an important parameter for calibrating and using gamma ray spectroscopy systems. Once further validated, the algorithm will be used to help characterize a detector. (PI: Trevor J. Stocki)

Canadian Perspectives on Environmental Noise Survey (CPENS)—NEW!

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. Canada’s *Impact Assessment Act* (IAA, 2019) requires that certain major resource and infrastructure development projects undergo an impact assessment before receiving federal government approval. Designed to implement actions that promote sustainable development, the impact assessment process aims to identify and mitigate project-related adverse environmental effects, including health effects from project noise. In the implementation of the *IAA*, Federal Authorities (i.e., federal departments or agencies) provide, upon request, specialist

information or knowledge with respect to a project to the Impact Assessment Agency of Canada (IAAC), review panel, or body conducting the impact assessment, to inform critical decision-making pertaining to project approval. As a Federal Authority, Health Canada has published guidance on the evaluation of noise impacts in impact assessments (Health Canada, 2017). To support Health Canada recommendations and guidance development, Health Canada conducted the Canadian Perspectives on Environmental Noise Survey (CPENS) to investigate expectations and attitudes toward environmental noise in rural and non-rural Canada. CPENS, a 26-item questionnaire, was completed online by 6647 randomly selected Indigenous and non-Indigenous Canadians, aged 18 years and older between April and May 2021. Annoyance, sleep disturbance, health status and perceived impacts of COVID-19 on health and environmental noise were assessed. A series of publications over the next two years will explore potential differences between Indigenous Peoples of Canada and non-Indigenous Canadians in their attitudes and expectations toward environmental noise. (PI: David Michaud)

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 (Nal) 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

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. 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)

Effect of sleep disturbance on biomarkers related to the development of adverse health outcomes: A systematic review of the human literature—NEW!

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. Literature suggests that unrestricted and undisturbed sleep is vital for basic human function and performance; however, it is unclear as to what amount of sleep disturbance leads to dysregulation in biomarkers, which may underscore the development of adverse health effects. This systematic review aims to identify the amount of sleep disturbance that contributes biomarker changes as a potential precursor to the development of adverse health effects. English-language comparative studies available in PubMed, Cochrane Central, EMBASE, and CINAHL databases from January 1, 1980, to July 31, 2021, were searched. The search identified 92 primary studies reporting on blood pressure, hypertension, heart rate, cardiac arrhythmia, cardiac output, waist circumference, cortisol, adrenaline, noradrenaline, immune system markers, glucose, insulin, cholesterol, and triglyceride levels. Although some meta-analyses suggested there may be an association between sleep disturbances and certain outcomes, the certainty in the evidence was very low due to concerns with risk of bias, inconsistency across exposures, populations, and imprecision in the estimates of effects. Further research is needed to explore the point at which disturbed sleep begins to increase the risk of developing adverse health outcomes to inform and tailor health interventions. (PI: David Michaud)

Effectiveness of the 2010 National Building Code requirements—NEW!

Radon gas is the leading cause of lung cancer for people who live in a non-smoking household. Building measures to facilitate the future mitigation of radon in homes feature in the 2010 National Building Code (NBC). These measures include installing a sealed radon barrier above a gravel layer and below the concrete slab. A capped pipe stub is extended through the slab into the gravel layer. If required, this allows for an easier installation of a future radon mitigation system. In 2011, Nova Scotia adopted the 2010 NBC. In October 2021, Health Canada's National Radon Laboratory (NRL) recruited approximately 330 residents in the Halifax Municipality Region (HRM) to test their homes for radon as part of a study to test the efficacy of the NBC 2010 radon measures. Homes built in the years 2001–2021—either side of the NBC 2010 adoption—were chosen for the study. As of June 2022, the results of over 300 radon tests have been collected from homes alongside information on their foundation, building and heating types. The results from this data are planned for a publication in late 2022/early 2023. The output of this work provides a direct input into Health Canada's continued involvement in the development and improvement of radon measures for new buildings and their inclusion in future versions of the NBC. (PI: Janet Gaskin, Robert Stainforth, Colin Gutcher, Ngoc Vuong)

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 higher doses, such as could occur in 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)

Environmental monitoring and external exposure to natural radiation in Canada—NEW!

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. External sources of radiation originate from cosmic rays and natural radioactive elements, principally 40K and decay products in the uranium and thorium decay series occurring in the ground. People are exposed to terrestrial radiation and cosmic rays everywhere, and at all times. To assess Canadians' external exposure to natural radiation, five years (2016–2020) of real-time environment monitoring data recorded by Health Canada's Fixed Point Surveillance (FPS) network were analysed for 36 monitoring stations across Canada. Absorbed dose rates in air from terrestrial radiation vary geographically and seasonally. Absorbed dose rate due to cosmic rays depend strongly on the elevation and vary with solar activities. The population-weighted annual outdoor ambient dose equivalent rates are 20 nSv/h for terrestrial radiation and 52 nSv/h for cosmic rays. Considering that, on average, Canadians spend 89% of their time indoors and 11% of the time outdoors, the population-weighted annual effective doses were calculated as 443 µSv (54 µSv outdoors and 389 µSv indoors), with 20.6% (91 µSv) from terrestrial radiation and 79.4% (352 µSv) from cosmic rays. Article published in Journal of Environmental Radioactivity, January 2022. (PI: Chuanlei Liu, Mike Benotto, Kurt Ungar, Jing Chen)

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 second year model results is currently underway. (PI: Lauren Bergman)

Estimation of population exposure to terrestrial gamma rays in Canada—NEW!

The Radiation Protection Bureau (RPB) has a long-standing commitment to characterize and report on exposure to naturally occurring radioactivity in Canada in order to support radiation risk assessment and risk management. Rocks and soils contain naturally occurring radionuclides and are therefore important contributors to background dose for members of the public, both in their natural state or when transformed into building materials. This study summarizes the results of ground-based gamma surveys conducted from 2007 to 2010 in populated areas across southern Canada (data was not available for the territories). It then uses this data as well as gamma measurements from airborne surveys (published separately), combined with information about seasonal variation and Canadian habits (e.g., time spent indoors), to estimate average doses from terrestrial gamma rays in the 10 provinces and for the southern portion of Canada as a whole. Doses ranged between approximately 0.1 and 0.2 millisieverts per year. Associated health impacts are expected to be negligible, especially when compared to more significant sources of radiation exposure like indoor radon. Because Canadians spend so much of their time inside, indoor exposures at home were found to contribute 69% of the total annual dose from gamma radiation even though estimated indoor dose rates were lower. This assessment is more detailed than earlier assessments using airborne and ground-based survey data but is in general agreement with them. Understanding naturally occurring sources of radiation and associated levels of exposure provides important context for determining appropriate intervention levels, in both routine and emergency situations. Article published in Journal of Environmental Radioactivity, February 2022. (PI: Jing Chen, Ken Ford (Geological Survey of Canada, retired))

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. 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)

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 biomolecules 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, Robert Stainforth, Colin Gutcher, Ngoc Vuong)

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 radiation 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))

Measurement of natural radionuclides in soil samples from Southern Ontario and assessment of potential activity concentration index in building material of local origin—NEW!

The Radiation Protection Bureau (RPB) has a long-standing commitment to characterize and report on exposure to naturally occurring radioactivity in Canada in order to support radiation risk assessment and risk management. One potential source of exposure is building materials made from rocks and soil that contain naturally occurring radioactive elements (such as uranium, thorium, and their decay products). Compliance with the basic safety standards issued by the International Atomic Energy Agency (IAEA) requires that exposure to building materials should not result in a radiation dose of more than 1 millisievert/year. The risk at this level is insignificant. To help authorities identify situations where exposures could exceed this threshold, the IAEA recommends using an Activity Concentration Index based on the concentrations of radium-226, thorium-232, and potassium-40, all of which are naturally occurring. An Activity Concentration Index of about 1 (for bulk materials) is considered acceptable and no intervention is required. This study reports the concentrations of the three key elements in soil samples collected from southern Ontario, Canada. Assuming activity concentrations in masonry materials such as brick and concrete are similar to soil in the surrounding area, the Activity Concentration Index for masonry materials of Southern Ontario origin is estimated as 0.45 (with a range of 0.14 to 1.27). These results indicate that the annual effective gamma radiation dose from exposure to masonry materials of southern Ontario origin does not exceed 1 millisievert and so, from a radiological perspective, they are safe to use. Article published in Radiation Protection Dosimetry, October 2021. (PI: Jing Chen, Weihua Zhang)

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. 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. (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)

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. (**https://journals.lww.com/health-physics/Fulltext/9900/Analysis_of_ICNIRP_2020_Basic_Restrictions_for.15.aspx**) (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

The National Radon Program (NRP) engages in behavioural research in order to assess and improve the effectiveness of outreach campaigns to the Canadian public. In 2019, the NRP worked with the Privy Council Office Impact and Innovation Unit to perform a Behaviour Intervention and Trial Project using a behaviourally-informed postcard as a means of increasing public awareness of radon and encouraging action (expressed as the purchase of a test kit). Results from this pilot suggested that the approach was promising and further investigation was warranted. In January 2020, the NRP launched a second Behaviour Intervention Project, tied to a planned awareness campaign, to evaluate the impact of a new postcard. Responses, including website visits, public inquiries, and reports from test kit providers, were tracked for a period of 8 weeks. In November 2020, the same postcard was modified based on feedback from January 2020 and effectiveness was assessed again. The study was repeated in conjunction with subsequent postcard campaigns in November 2021 and January 2022, with minor adjustments to reflect lessons learned. To date, millions of postcards have been sent to Canadian households across Canada. Results continue to show that a behaviourally informed postcard significantly increases radon awareness. In addition, industry stakeholders regularly report significant increases in test kit purchases following distribution of the postcards. Results of the 2020 study are available at **https://takeactiononradon.ca/wp-content/uploads/NRP-Behavioural-Study-Final-Report-ENG-2020.pdf** (PI: Katelyn Penstone, Kelley Bush)

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 policymakers, summarizing the main findings of the assessment. Since 2011, 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: Jan Rene Larsen, AMAP, Norway; also involved: Weihua Zhang, Trevor Stocki, Jing Chen, and Chuanlei Lu)

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. Because self-reported noise exposure has a degree of uncertainty associated with it, a separate analysis was performed on individuals with measured high frequency hearing loss, which was used as evidence of a sustained exposure to high sound pressure levels. There was no evidence in the data to support an association between noise-induced hearing impairment and any measure of cardiovascular function/disease. This research, and others like it, provides an important contribution to an evidence base that could inform policy related to occupational noise exposure. (PI: David Michaud)

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. The overall review is presented in a 3-part series of individual systematic reviews by designated topic (1. cardiovascular effects; 2. metabolic effects and 3. obstetric effects). (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 Radiological 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 2015–2021. A total of 15 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 self-reported sleep disturbance to inform future updates to the World Health Organization's Environmental Noise Guidelines. The Guidelines suggest nighttime noise limits for various sources, although in their 2018 publication no limit for wind turbines could be provided due to a lack of research. The 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)

Investigation of the levels of legacy perfluoroalkylated substances (PFAS) and their replacement chemicals in human biological and water samples—NEW!

Per- and polyfluoroalkyl substances (perfluoroalkylated substances, PFAS) are a class of synthetic fluorinated organic chemicals that have been widely used in consumer products the past 60 years because of their oil-, grease-, and water-repellent properties. PFAS are used in almost all industrial sectors, including well-known categories such as textile impregnation and electroplating. In total, more than 200 use categories and subcategories have been identified for more than 1400 individual PFAS. During the last two decades, PFAS have received increased attention from both the public and the scientific community because they are widespread and persistent in the environment and several of them bioaccumulate in wildlife and humans. Further, associations between concentrations of PFAS in human blood, and a range of health outcomes including carcinogenicity, hormonal disruption, and immunotoxicity have been observed in epidemiological and *in vivo* toxicological studies. Potential pathways of human exposure to PFAS include dietary and non-dietary ingestion, inhalation, and dermal absorption. Humans can be directly exposed to PFAS through inhalation and/or ingestion of dust and drinking water, and indirect exposure through the intake of PFAS precursors, which are biotransformed to PFAS in the bodies. Regulatory constraints, like restrictions of several perfluoroalkyl carboxylic acids and perfluoroalkane sulfonic acids, as well as voluntary phase out programs have led to a production

shift from long-chain to short-chain perfluorinated substances and other replacement chemicals (predominantly GenX, F53B and ADONA). This research effort will generate Canadian data on legacy perfluoroalkylated substances (PFAS) and their alternatives in archived and recently collected biological matrices, and in raw and finished water. The data will inform PFAS exposure and risk assessment. (PI: Cariton Kubwabo).

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

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))