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2013 Health Canada ScienceFORUM

Book of Plain Language Summaries

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Canada

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Note: In this publication, Health Canada branches and bureaus are represented by the following acronyms:

AAB: Audit and Accountability Bureau
CFOB: Chief Financial Officer Branch
CPAB: Communications and Public Affairs Branch
CSB: Corporate Services Branch
FNIHB: First Nations and Inuit Health Branch
HECSB: Healthy Environments and Consumer Safety Branch
HPFB: Health Products and Food Branch
RPB: Regions and Programs Bureau
SPB: Strategic Policy Branch

Agencies:

AHRC: Assisted Human Reproduction Canada
CIHR: Canadian Institutes of Health Research
HMIR: Hazardous Materials Information Review
PHAC: Public Health Agency of Canada
PMPRB: Patented Medicine Products Review Board
PMRA: Pest Management Regulatory Agency

Other commonly used acronyms:

BPA – Bisphenol A
CARA – Clean Air Regulatory Agenda
CDC – Centre for Disease Control
CEPA – Canadian Environmental Protection Act
CMA – Canadian Medical Association
CMP - Chemicals Management Plan
DNA - Deoxyribonucleic Acid
E. coli – *Escherichia coli*
EPA – Environmental Protection Agency (United States)
FDA – Food and Drug Administration (United States)
F/P/T – Federal/Provincial/Territorial
GDP – Gross Domestic Product
GRDI – Genomics Research and Development Initiative
MIREC – Maternal-Infant Research on Environmental Chemicals
NCR – National Capital Region
OECD – Organisation for Economic Co-operation and Development

Environmental Pollution and Epidemiology

1.01 Isolation, Expression and Characterization of a Minor Allergen from *Penicillium crustosum*

M.S. Sevinc[1], V. Kumar[1], M. Abebe[1], M. Lemieux [2], and H.M. Vijay[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Biologics and Genetic Therapies Directorate, Centre for Vaccine Evaluation, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: One of the mandates of HECSB of Health Canada is to protect the health of Canadians from environmental pollutants including mold. Excessive mold growth in homes or workplaces is often associated with respiratory illnesses including asthma and allergies due to oral/nasal exposure. It is often the protein component of mold that is responsible for mold allergies. Purified mold allergens are useful tools to screen the sera of mold-sensitive population and develop effective protective measures. Earlier, a major allergen, Pen b 26 from *Penicillium brevicompactum* was isolated. A homolog protein, designated Pen cr 26 was isolated and characterized from *Penicillium crustosum,* which is previously not known to be allergenic mold. Pen cr 26 appears to be a minor allergen and could be a naturally occurring, hypoallergenic variant of Pen b 26. Exposure to hypoallergenic variants, like Pen cr 26 might desensitize or naturally immunize the populations against the major allergens since one of the main goals of allergen-specific immunotherapy is to develop hypoallergens that induce immunity without allergenicity.

MISSION STATEMENT FOR PROJECT: Since the main mandate of the HECSB of Health Canada is to protect the health of Canadians from environmental pollutants and mold is one of the environmental pollutants, this research supports the mandate of the department to develop regulatory policies to protect the health of Canadians. This research project has been completed.

1.02 Human Health Risk Assessment of *Bacillus Cereus* ATCC 14579

M. Breton[1], V. Albert[1], A.F. Tayabali[2], D. Bulinski[3], S. ElOuakfaoui[3] and D. Ashby[1]

[1] New Substances Assessment and Control Bureau, Safe Environment Directorate, HECSB, Health Canada, Ottawa, ON
[2] Environmental Health Science and Research Bureau, Environmental and Radiation Health Science Directorate, HECSB, Health Canada, Ottawa, ON
[3] Emerging Priorities Division, Science and Risk Assessment Directorate, Environment Canada, Gatineau, PQ

PLAIN LANGUAGE SUMMARY: Cleaning products using microorganisms are increasingly available and are considered or promoted as being safe and “green”, but could they pose risks to the health of Canadians? Under the *Canadian Environmental Protection Act,* 1999, Environment Canada and Health Canada assess risks related to the microorganisms on Canada’s Domestic Substances List (DSL), which includes microorganisms with characteristics that make them suitable for use in cleaning, degreasing and odour-control products. The poster will present a case-study of the draft risk assessment of the DSL-listed *Bacillus cereus* (*B. cereus*). The assessment considered information from various sources to evaluate hazards to human health and potential exposure of the Canadian population to *B. cereus*.

Although its use in cleaning products could lead to human infections, especially in individuals with weakened immune system, no risk was identified for the DSL-listed strain of *B. cereus*, because it was not confirmed to be in cleaning products in Canada. The draft assessment highlights the importance of research within Health Canada for generating strain-specific data to support the evaluation of hazard and risk to Canadians associated with the use of microorganisms in consumer products.

MISSION STATEMENT FOR PROJECT: This case-study will improve the risk assessment process of DSL-listed *Bacillus* species and *Bacillus* species assessed under the New Substances Notification Regulations (Organisms) ensuring that such products of biotechnology are safe for Canadians.

1.03 Integrated Approaches to Testing and Assessment (IATA): Application to the Human Health Risk Assessment of Pesticides in Canada

J. Paterson[1], B. Belliveau[1], and Y. Bhuller[2]

[1] Microbial and Biochemical Evaluation Section, Health Evaluation Directorate, PMRA, Health Canada, Ottawa, ON

[2] Health Effects Division I, Health Evaluation Directorate, PMRA, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The current regulatory testing regime for pesticides is comprehensive and has served the needs of regulatory health protection; however, the tests associated with certain data requirements can be expensive, time consuming, and could require large numbers of laboratory animals. Integrated approaches to testing and assessment (IATA) combine information from laboratory animal studies and new alternative testing methods such as biochemical and cellular tests, as well as computer models. The Pest Management Regulatory Agency (PMRA) recognizes the potential role for IATA and in 2009, the Agency asked the Council of Canadian Academies (CCA) to conduct an assessment of the use of IATA in the regulatory risk assessment of pesticides. One of the key recommendations from the CCA assessment, published in 2012, was that new alternative testing methods should be combined with data from traditional tests to transition towards more focussed testing and assessments. As a follow-up to the CCA report, the PMRA has identified a range of alternative toxicity tests that correspond to existing pesticide regulatory requirements and are already accepted by international regulatory authorities.

The PMRA is currently examining how some of these tests could be incorporated into pesticide assessments in Canada and is engaged in a number of on-going activities to further the application of IATA through contributions to the development of new alternative tests and joint projects and information sharing on IATA with partner organizations.

MISSION STATEMENT FOR PROJECT: The application of integrated approaches to testing and assessment (IATA) should lessen the reliance on laboratory animal toxicity tests, ultilize data from emerging technologies, and improve the efficiency of testing and assessment while maintaining or improving the scientific defensiblity and human health protectiveness of regulatory pesticide risk assessments.

1.04 Determination of Perchlorate, Bromate, Chlorate and Chlorite in Hypochlorite Solutions and Drinking Water

R. Aranda-Rodriguez[1], Z. Jin[1], A.-M. Tugulea[1], and F. Lemieux[2]

[1] Exposure and Biomonitoring Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Water Quality Program Division, Water and Air Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Health Canada works with national and international standard-setting organizations to develop health-based standards for materials that come in contact with drinking water during treatment and distribution, for example hypochlorite solutions. Hypochlorite is frequently used as a source of chlorine to disinfect drinking water. Concentrated solutions may still contain some impurities of concern to human health, such as perchlorate, bromate, chlorate and chlorite. The goal of the project was to investigate if those impurities are found in the drinking water and if their levels are above the maximum acceptable concentrations (MAC) established by the Guidelines for Canadian Drinking Water Quality (guidelines) or the Health Canada recommended value for perchlorate, as no guideline exists.

Water samples were collected at water treatment plants, before and after treatment, as well as at the mid- point of the distribution system. Concentrated hypochlorite solutions used in the disinfection process were also collected. Sampling took place in the summer/winter of 2012 and 2013. All the samples were tested for: perchlorate, bromate, chlorate and chlorite using an established analytical method, in the Health Canada laboratory.

It was found that the targeted chlorite, chlorate and bromate were found in the treated and distributed water samples at very low levels, below the maximum acceptable concentration guideline MAC values. Although no guideline has been established for perchlorate, the levels were all found to be below 6 µg/L, the Health Canada recommended guidance value.

MISSION STATEMENT FOR PROJECT: This study stresses the importance of proper handling of hypochlorite solutions used in the water disinfection process, as some impurities can reach the distribution system.

1.05 National Estimates of Indoor air VOC Levels in Canadian Homes: Results of the National Indoor Air Survey

J. Zhu[1], and S. Cakmak[1]

[1] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa ON

PLAIN LANGUAGE SUMMARY: A Canadian national indoor air survey was conducted in 2009-2011 as part of the Canadian Health Measures Survey. Volatile Organic Compounds (VOCs) in indoor air were collected across Canada, including both urban and rural areas. Samples were analysed in a laboratory under contract to Health Canada. The study provided Canadian national estimates of 84 VOCs. Of the 84 VOCs measured in this study, 31 have already been assessed and/or managed under the Chemicals Management Plan, and many will be assessed in the coming years. Indoor air levels of some VOCs were higher in smoking homes than non-smoking homes, in both houses and apartments. When smoking homes were excluded, levels of VOCs in general were higher in houses than in apartments. Statistical analysis also showed groups of VOCs that may have common sources. The data from this study could be used to inform the human health risk exposure portion of upcoming screening assessments as part of the Chemicals Management Program. For substances that have already been assessed, the data could potentially be used to identify needs for re-assessment in the future.

MISSION STATEMENT FOR PROJECT: We are committed to generate national representative data to support regulatory work undertaking in the government.

1.06 *Pseudomonas fluorescens* ATCC 13525: Now that it has been Assessed for Human Health Risk and is on the Road to Publication, who do we Involve?

C. Rose[1], K. Yambao[1], V. Albert[1] and D. Ashby[1]

[1] New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the *Canadian Environmental Protection Act,* 1999, Health Canada (HC) is required to assess risks to the Canadian population from micro-organisms on the Domestic Substance List (DSL). *Pseudomonas fluorescens* ATCC 13525 is a bacterium on the DSL that was reported to be in use in Canada between 1984 and 1986. It has properties that make it attractive for use as an ingredient in 'greener' cleaning products which are increasingly replacing chemical-based cleaning products. In the screening assessment, HC identified human health risks that could be realized if *P. fluorescens* ATCC 13525 were an ingredient in custodial products. Medical equipment could become contaminated or susceptible to individuals exposed if these products are used in hospitals, day cares, nursing homes and blood donor clinics. HC is considering measures to address these risks. To ensure that risk management options minimally affect industry stakeholders while protecting Canadians, a stakeholder engagement plan will be developed.

MISSION STATEMENT FOR PROJECT: Effective stakeholder engagement fosters the development of legal instruments that minimally affect industry stakeholders while effectively managing risks to the health of Canadians.

1.07 Evaluating the Effectiveness of PMRA's Implementation of Virtual Elimination Policies for Contaminants Case Study: Hexachlorobenzene (HCB)

P. Sangster[1], and M. Kivi[1]

[1] Environmental Assessment Directorate, PMRA, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Toxic Substances Management Policy (TSMP) is a federal government policy under the Canadian Environmental Protection Act (CEPA) (1995) which was developed to provide direction on the management of substances that have been found to be persistent, bio-accumulative, and toxic (PBT) . Health Canada's Pest Management Regulatory Agency uses this preventative and precautionary approach to assess and manage substances in pesticides that could harm human health or the environment. This policy also calls for the virtual elimination of the most hazardous substances. The PMRA works in partnership with pesticide registrants to reduce contaminant levels, adopt the use of best available manufacturing technology, and/or minimize releases where feasible. Reduction efforts focus on contaminants where pesticides are considered a major environmental source and on specific pesticides with the highest releases. This approach has been applied to hexachlorobenzene (HCB), a PBT environmental pollutant that has contaminated water and food-chain sources globally presenting significant risks to both human health and the environment. There are various sources of this pollutant including as a contaminant in some pesticide products.

The objective of this project was to examine PMRA's progress towards reducing the total national release of HCB from agricultural pesticides. The results showed a significant reduction in releases from 2008 to 2010 (41.7 kg to 13.6 kg) which is attributed to the implementation of contaminant reduction strategies, the phase-out of certain pesticides and the market shift toward newer/cleaner chemistries. The PMRA approach to implementing and tracking reduction efforts by targeting the major contributors has proven to be effective and thus, successfully assists in diminishing releases of contaminants that could harm human health or the environment. Similar reduction measures could be applied to other substances slated for virtual elimination found as contaminants in pesticides and other consumer products.

MISSION STATEMENT FOR PROJECT: To examine the effectiveness of the PMRA's implementation of virtual elimination policies for contaminants by estimating the release of HCB over time from pest control products.

1.08 Human Health Rapid Screening of Substances under the *Canadian Environmental Protection Act* (CEPA 1999)

H. Patterson[1], P. Robinson[1], and E. Leinala[1]

[1] Existing Substances Risk Assessment Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Risk posed by a substance is a function of both its hazard and exposure potential. Without a potential source of exposure there can be no risk regardless of the toxicity of the substance in question. The rapid screening approach aims to rapidly identify those substances that may have a higher or lower potential for risk based on exposure considerations. This approach provides a relatively rapid mechanism for identifying substances with a low priority for further assessment work. It also allows the focus of resources on substances that require further, more in-depth assessment activities, helps reduce undue burden on industry by reducing the number of substances for which more detailed information gathering is required and helps focus future research on substances for which there is an identified potential for exposure. The Government of Canada was able to identify, and thereby conduct a screening assessment for over 700 substances using the rapid screening approach, and continues to identify new groups of substances for subsequent rapid screening, which will help meet commitments made under the Chemicals Management Plan.

MISSION STATEMENT FOR PROJECT: The rapid screening approach can be used as a mechanism to efficiently deal with large numbers of substances in an efficient, timely, and scientifically defensible manner, while meeting the requirements under CEPA (1999) to conduct screening assessments for substances which met the categorization criteria.

1.09 Techniques for the Radioactive Source Location Problem

I. Hoffman[1], K. Ungar[1], J. Yi [1], P. Bourgouin[2], D. Bensimon[2], A. Malo[2], and E. Yee[3]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Canadian Meteorological Centre (CMC), Environment Canada , Dorval QC
[3] Defence Research and Development Canada (DRDC), Department of National Defence, Suffield, AB

PLAIN LANGUAGE SUMMARY: Whenever there is a significant release of radioactive material into the air, it is important to determine the source location, the release times and amounts of material released. The goal of this study is to estimate all or any of these factors, when poorly known, using measurements of contaminants from environmental monitoring networks and Environment Canada models that calculate the origin of the air sampled in these networks. We used a known dominant source of harmless airborne radioactive emissions, noble gases from the Chalk River Medical isotope facility as a known test case. Air sample data and model calculations were to determine the most likely origin of the observed emissions and this was compared to the known Chalk River source. We were able to find the chalk river source region and source size. We identified impactful areas of improvement, particularly in reducing model uncertainty, but the method already shows promise to be used in Comprehensive Nuclear Test Ban treaty (CTBT) verification and emergency response operations. The CTBT is a treaty that forbids conducting nuclear explosion tests anywhere in the environment, including space that employs monitoring radioactivity contamination as a means of demonstrating compliance.

MISSION STATEMENT FOR PROJECT: To protect the health and security of Canadians by improving our Nuclear Emergency Response and CTBT verification capabilities.

1.10 Expanding the Number of Phthalates Monitored in House Dust

X. Fan[1], C. Kubwabo[1], P.E. Rasmussen[1], I. Kosarac[1], and F. Wu[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Phthalates have been used extensively as plasticizers to improve the flexibility of polymers and also have found many industrial applications. They are ubiquitous in the environment and have been detected in a variety of environmental and biological samples. Potential adverse health effects have been reported to be associated with the exposure to phthalates in the indoor environment including house dust. House dust is known to contain semi-volatile organic compounds and particle-bound organic matter and could be a major route of human exposure to indoor environmental contaminants including phthalates. We recently reported the concentrations of 17 phthalates in Canadian house dust samples (n = 126). The main goal of the current study was to measure additional phthalates (12 in total) in the above dust samples. Major phthalates, which include diisohexyl phthalate (DIHxP), di-n-heptyl phthalate (DHepP), diisooctyl phthalate (DIOP), di-n-octyl phthalate (DOP), dinonyl phthalate (DNP), and di-n-decyl phthalate (DDP), were detected with high frequency (>85%), suggesting that indoor dust may represent a potentially significant exposure pathway to phthalates. Data generated will support Health Canada's risk assessment/management activities on phthalates.

MISSION STATEMENT FOR PROJECT: Data from this study will provide Health Canada with information for risk assessment of target phthalates. Out of the 12 phthalates measured, the Existing Substances Risk Assessment Bureau (ESRAB) is particularly interested in diallyl phthalate (DAP), di-n-propyl phthalate (DPrP), isobutyl cyclohexyl phthalate (IBCHxP), butyl cyclohexyl phthalate (BCHxP), diisooctyl phthalate (DIOP), and di-n-octyl phthalate (DOP).

1.11 The Mobile Nuclear Laboratory

T.J. Stocki[1], C. Bouchard[1], J. Rollings[1], M.-O. Boudreau[1], R. McCutcheon-Wickham, and L. Bergman[1]

[1] Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON, Canada

PLAIN LANGUAGE SUMMARY: In order to respond in the event of a nuclear accident or emergency on Canadian soil, Health Canada has designed and equipped two Mobile Nuclear Labs (MNLs) which can be deployed near a radiological accident site. One of the MNLs has been outfitted with a High Purity Germanium (HPGe) detector. A HPGe detector can be used for identification as well as quantification of gamma emitting radioisotopes present in the samples. A field deployable HPGe detector in the MNL will allow for rapid identification of contaminated areas, soils, water, and other samples. A triage can be performed on the samples, in support of the local authorities. In the event of an emergency, this information will be invaluable to local authorities and decision makers.

MISSION STATEMENT FOR PROJECT: This Mobile Nuclear Lab can be deployed to help decision makers at a time of crisis.

1.12 Development and implementation of harmonised NAFTA Groundwater Modelling of Pesticide Concentations in Groundwater

G.Malis[1], I. Kennedy[1], and L. Avon[1]

[1] Environmental Assessment Directorate, PMRA, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Pest Management Regulatory Agency (PMRA) conducts a dietary assessment as part of the pesticide registration process to help ensure the health of Canadians. In 2004, the PMRA established its direction on use of modelling to estimate pesticides in drinking water. The groundwater approach differed from that used by the United States Environmental Protection Agency (EPA) occasionally resulting in different human dietary assessments which were problematic especially with pesticides used in both countries.

Groundwater resources in Canada and the United States can be similar and it was recognised that working jointly and pooling resources would reduce redundancy and produce the best possible North American groundwater modeling protocol to address differences and provide adequate protection to human health. Shared work included establishing conceptual groundwater transport and behavioural parameters, evaluation and selection of groundwater model as well as developing guidance identifying required scenario characteristics plus modelling input selection.

A NAFTA project with the goal to develop common modeling procedures was initiated at the end of 2005 with a harmonized model and process implemented on January 3, 2013. To date, results are comparable between countries and are similar to PMRA's previous approach indicating no need to revisit previous assessments.

MISSION STATEMENT FOR PROJECT: This project has strengthened communication between the PMRA and US EPA and helps address and harmonize risk assessment processes for common pesticide regulation.

1.13 Risk Management Plans as Tools to Reduce Risk from Pesticide Use

A.Beyak[1], J.W.Dubois[1], S.Goodacre[1], M.Mainguy[1], P.G.Levesque[1], T.Caunter[1], and H.Tang[1]

[1] Value Assessment and Re-evaluation Management Directorate, PMRA, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Pest Management Regulatory Agency (PMRA) Re-evaluation Program, all active ingredients in pesticides registered prior to 1995 were re-evaluated to ensure they continue to meet the current standards of science and risk assessments. Decisions were proposed or finalized for 97% of these active ingredients, resulting in 270 that were determined to be acceptable for continued registration and106 that were withdrawn by registrants. Where risks of concern to human health or the environment could not be mitigated, the PMRA initiated phase-outs for 13 active ingredients, as well as many uses of active ingredients. Phase-out of an active ingredient or use may present a number of complicating issues, which include the lack of viable alternatives to replace the phased-out uses, the loss of uses with a high value to public health or the economy, and a significant impact on a specific industrial or agricultural sector. A Risk Management Plan (RMP) is a tool that outlines the specific strategies to manage identified risks that cannot be mitigated over the long-term.

MISSION STATEMENT FOR PROJECT: When risks of concern are identified as a result of a pesticide re-evaluation, mitigation measures are implemented to reduce the potential exposure and risk. These measures may include for example additional PPEs, REIs or phase-out of uses or the pesticides. A risk management plan can be developed in more complex cases to address the issues.

1.14 Uncertainty and Variability for Population Attributable Risk Due to Residential Radon in Canada

M. Al-Arydah[1], J. Whyte[2], and J.M. Zielinski[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Radon is a naturally occurring radioactive gas released from many rocks and soils, and found at varying concentrations in indoor air in residences. Exposure to environmental radon is the largest part of population exposure to radiation in Canada.

There remains a degree of scientific uncertainty regarding how large the risk of lung cancer is in the general population due to residential exposure. In this study, we examined how different factors determine the level of this risk.

We compared estimates of the lung cancer risk using several models derived from epidemiological studies (both occupational and residential) for Canada as a whole, and for each province individually.

We found that the estimates based on miner models are in general agreement with the estimates based on residential models; hence for the purposes of regulation of residential exposure to radon, the values based on residential models should be used. The estimated baseline risk for Canada is 16% of lung cancer deaths due to residential radon exposure, in provinces with high levels of residential radon the risk can as high as 25% of lung cancer deaths. These results will help in the implementation of the Canadian Guideline for radon at homes and in formulating future revisions of the Canadian Guideline for radon in homes as well as they can help in the formulation of outreach and mitigation programs dealing with residential radon.

MISSION STATEMENT FOR PROJECT: These results will help in the implementation of the Canadian Guideline for radon at homes and in formulating future revisions of the Canadian Guideline for radon in homes.

1.15 Concordance between Animal and Human Tumours: An Analysis of 109 Agents Known to Cause Cancer in Humans

D. Krewski[1,2], B. Colins[2], P. Lajoie[2,3], Y. Gross[4], R. Baan[4], K. Straif[4], J. Rice[5], M. Bird[2], and J.M. Zielinski[1,6]

1 Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, ON
2 McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, ON
3 Department of Epidemiology, Queens University, Kingston, ON
4 IARC Monographs Program, International Agency for Research on Cancer, Lyon, France
5 School of Medicine, Georgetown University, Washington, D.C., USA
6 Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Since the establishment of the International Agency for Research on Cancer (IARC) in 1962, the Agency has evaluated a large number of agents for which there exists some evidence of an increased cancer risk to humans. IARC has developed detailed criteria to guide scientific evaluation of potentially cancer causing agents.

The evaluations involve classifying both the human and animal scientific evidence of cancer risk as sufficient, limited, or inadequate, or evidence suggesting lack of cancer risk.

In this project we evaluated the agreement between animal and human studies for the risk of cancer from 109 different agents. These agents were all classified by the IARC as being carcinogenic to humans.

We found a moderate to high degree of agreement between the animal and human studies. These results would further support the use of animal research to evaluate the risk of cancer in humans by various agents.

MISSION STATEMENT FOR PROJECT: Help to justify the use of animal cancer models in assessing human carcinogenicity of environmental agents.

1.16 Observed Health Effects in Humans Living in the Circumpolar Regions of the Arctic

J. Provost[1], P. Wang[1], S. Donaldson[1], and B. Adlard[1]

[1] Chemicals Surveillance Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Environmental contaminants such as persistent organic pollutants (POPs) and metals have been measured at elevated concentrations in the biofluid and hair of some Arctic populations. Since the 1990's, a number of epidemiological studies have been initiated to better understand the health impacts associated with human exposure to contaminants in the Arctic. The purpose of this comprehensive literature review is to provide an update on recent research conducted since the publication of a previous report (AMAP Human Health Assessment, 2009). The search criteria was limited to key human health effect themes identified in the AMAP, 2009 publication, and focused on national and international epidemiological and toxicological studies conducted in the Arctic region. A broad range of potential human health effects associated with pre-natal and post-natal exposure to POPs and metals were identified in several cohort studies. Key human health considerations such as birth outcomes, reproductive effects (e.g., sexual maturation, sex ratios), neurodevelopment, immune system function, metabolic and cardiovascular effects, genetic effects and cancer were discussed. New studies added evidence that past and present exposures to POPs and metals in the population living in the Arctic are associated with observable health effects.

Health Canada supports the health and safety of Canadians living in the North by funding research via the Northern Contaminants Program as part of the biomonitoring component of the Chemicals Management Plan, and by participating in international organisations such as the Arctic monitoring and Assessment Program. The health effects described in this poster/presentation are important for understanding the impacts contaminant exposure have on human health, in addition to helping support national and international communications and policies.

MISSION STATEMENT FOR PROJECT: This project will impact the development of a revised AMAP Human Health Assessment report.

1.17 Managing Internal Radiation Contamination Following a Radiological or Nuclear Emergency

C.Li[1], B. Hauck[1], B. Sadi[1], R. Ko[1], and K. Capello[1]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Following a radiological or nuclear emergency, a large group of first responders and the public may become internally contaminated with radionuclides. Individuals should be screened and assessed for internal contamination in a timely fashion, providing radiation dose information for necessary medical interventions to those who are contaminated, and reassuring the others who are not. This paper presents the major technical aspects for managing internal radiation contamination, with a focus on rapid screening for potential contamination and assessment of radiation dose. Projects carried out at the Radiation Protection Bureau will be introduced and results will be shared.

MISSION STATEMENT FOR PROJECT: The results of these projects will enhance Canada's capabilities in protecting the health of Canadians from radiation exposure during a radiological or nuclear emergency.

1.18 A Gamma-Gamma Coincidence/Anticoincidence Spectrometer for Low-Level Cosmogenic $^{22}Na/^{7}Be$ Activity Ratio Measurement

W. Zhang[1], P. Mekarski[1], J. Yi[1], and K. Ungar[1]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: ^{10}Be and ^{7}Be are formed in the upper atmosphere. They can be used to validate modeling of the 3-dimensional circulation of the atmosphere important, for example, in the modelling of atmospheric contaminants from the Fukushima nuclear power plant accident. Unfortunately, the measurement of ^{10}Be takes specialised equipment with per sample analysis costs in excess of $1000. ^{22}Na is also formed in the upper atmosphere as a possible isotopic tracer but at levels 1000 to 10000 fold less than Be. However, ^{22}Na and ^{7}Be can now be measured simultaneously on a simple spectroscopic system developed at the RPB which capitalizes on a relatively unique positron emission decay mode of ^{22}Na. This improved environmental spectrometer employs a novel simultaneous gamma-gamma coincidence/anticoincidence technique sufficient to measure airborne environmental ^{22}Na and ^{7}Be.

Our application is the improved understanding and modelling of atmospheric radioactive contaminants as consistent with Health Canada missions of environmental Radiation Protection and Comprehensive Nuclear Test Ban Treaty (CTBT) verification. The same atmospheric circulation processes are also an important component in differentiating the origins of anthropogenic versus natural ozone.

MISSION STATEMENT FOR PROJECT: The impact of the research is well aligned with the Department's mandate to support the CTBT verification regime and environmental radiation protection.

1.19 Full Scale Radiological Dispersal Device Experiments in Canada

R. Berg[1], E. Korpach[1], and D. Quayle[2]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Center for Security Science, Directorate S&T Public Security Defense R&D Canada, Ottawa ON

PLAIN LANGUAGE SUMMARY: Terrorist deployment of a Radiological Dispersion Device (RDD) is identified as a primary threat to security. One of the primer concerns of any federal nuclear emergency would be what are the potential health impacts to the Canadian public. Due to the lack of high precision high-confidence modelling tools, current Radiological Dispersion Device response planning is, of necessity, overly conservative. This project addresses this identified gap by characterizing the distribution of radiological material from a RDD. The objective was to gather experimental data on the dispersion and ground deposition patterns of a real radiological dispersion in the environment. To do this many radiological and nonradiological measurements were made. Radiological measurement included in-situ ground measurements, filter deposition measuring spot density and particle size, large air volume samplers, helicopter and vehicle mounted detectors, fixed point detectors. Nonradiological measurements included LIDAR remote sensing technology, high speed videography and meteorological stations. A large effort is now underway to inter-compare and inter-calibrate all of these disparate datasets.

This experiment allows comparison of data sets to better understand the amount of material transported from a radiological dispersion device. These comparisons allow more accurate ways to calibrate detection systems for use in real world radiological dispersions. All of the information learned in this experiment can be transferred to a nuclear disaster at one of the nuclear power plants to provide accurate dose measurement and the impact to the public.

MISSION STATEMENT FOR PROJECT: Accurate real time radiation plume and ground deposition measurements during an accident and the days to follow. This improves the accuracy of the impact of an accident and the health and safety of Canadians.

1.20 Emergency Department Visits: Were there Substances on Board?

D. Panait[1], and J. Snider[1]

[1] Office of Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Substance abuse (i.e., alcohol, illicit drugs and psychoactive pharmaceuticals) is an important public health problem in Canada with an economic burden of alcohol and illicit drug abuse estimated to be $22.8 billion per year. Many harms associated with substance abuse are acute in nature (i.e., injuries, overdoses and intoxication) and may not require hospitalisation. The objective of this project is to estimate the number of visits to hospital emergency departments (ED) due to harms associated with substance abuse, using 2011-12 data from the Canadian Institute for Health Information's "National Ambulatory Care Reporting System". Results indicate that among the visits with a record of one of these substances, the majority of these ED visits had alcohol, followed by illicit drugs and psychoactive pharmaceuticals reported.

Other medical problems reported during these visits included mental and behavioural disorders, and accidents (e.g., falls, motor vehicle accidents, etc…). Results from this project are from a newly explored data source and complement existing information on the potential harms associated with substance abuse, to serve the Canada's National Drugs Observatory and to be used as evidence for the National Anti-drug Strategy and in Health Canada's regulatory work.

MISSION STATEMENT FOR PROJECT: Results from this project will provide information on the potential harms associated with these substances under the routine monitoring of Canada's National Drugs Observatory and will be used as evidence to support the National Anti-Drug Strategy and in Health Canada's regulatory work.

1.21 High Risk Populations: How Can they Inform Us?

S. Racine[1], and J. Snider[1]

[1] Office of Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Since the 90's, the drug situation in Canada has evolved and the appearance of new substances has become a reality. The objective of this project is to monitor three high-risk populations: street entrenched adults; street involved youth; and recreational drug users in six cities across Canada.

Using face-to-face interviews, estimates of drug use, harms, risk behaviours, market activity and price were obtained. In addition, qualitative information about emerging drugs was collected through open ended questions asking about any other drug or trend we should pay attention to.

The results indicate that the types of drugs used vary across these populations and cities. The qualitative information indicates that while there was a lot of talk of new substances in all locations, little use was reported. These findings complement those from general population surveys by showing that some new substances may be arriving in Canada while others, that have been actively reported in the media, do not seem to have a large presence. Results from this project are an integral part of Canada's National Drug Observatory's early warning system and will be used to support the National Anti-Drug Strategy and Health Canada's regulatory work undertaken for new substances.

MISSION STATEMENT FOR PROJECT: Results from this project are an integral part of Canada's National Drug Observatory's early warning system and will be used to support the National Anti-Drug Strategy and Health Canada's regulatory work undertaken for new substances.

1.22 Canadian Decision Support System for Managing a Nuclear Emergency

D. Nsengiyumva[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Federal Nuclear Emergency Plan (FNEP) describes the framework used to coordinate the scientific aspects of the federal government response to a nuclear emergency affecting Canadians at home or abroad. Health Canada (HC) as the FNEP lead maintains an on-call FNEP duty officer, notification and activation system, prepares federal response to an RN emergency through planning, exercising, training and building response capacity, provides technical assessment support and coordinates information sharing. To fulfill this mandate, among other capabilities, a set of decision support tools have been developed. This presentation will review these tools and explain how they are used in the preparedness and response to an RN emergency. Discussion will notably include radiological atmospheric modeling, impact analysis using geographic information systems, and web based mapping for data collection, presentation and information sharing.

MISSION STATEMENT FOR PROJECT: Emergency organisations have access to a state of the art DSS for managing nuclear emergencies.

1.23 Impact of Humid Environment on Pb, Zn, Co and Se Bioaccessibilities in Indoor Dust

S. Beauchemin[1], P.E. Rasmussen[2,3], L.C.W. MacLean[2,4], M. Chénier[2] and T. MacKinnon[1]

[1] Natural Resources Canada, CANMET-MMSL, Ottawa, ON
[2] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[3] University of Ottawa, Earth Sciences Department, Ottawa, ON
[4] Current address: SRK Consulting (Canada) Inc., Saskatoon, SK

PLAIN LANGUAGE SUMMARY: This project investigates why some metals are more bioaccessible (available for biological uptake) in indoor dust than in outdoor soil, which is an information gap in residential risk assessments. Laboratory experiments were conducted to determine if metal compounds in dust undergo chemical reactions in the indoor environment that result in an overall increase in metal bioaccessibility. House dust samples were exposed to high moisture levels that may be found indoors (such as a damp carpet or a window well during winter months). The solubility of the metals in the dust samples was measured in simulated stomach acid before and after 4 months of exposure to these humid conditions. Lead and zinc showed an increase in solubility, selenium showed a decrease in solubility, and cobalt showed a variable response. Detailed X-ray analysis confirmed that lead and zinc compounds had actually transformed into more soluble compounds under humid conditions. These results help to explain the greater bioaccessibility of certain metals in house dust compared to soil, and contribute to Health Canada's ongoing development of dust guidelines and risk assessment approaches.

MISSION STATEMENT FOR PROJECT: This research was conducted in support of Health Canada's risk assessment of 4 priority moieties (Pb, Zn, Co and Se) under the Chemicals Management Plan.

1.24 A New Strategy for Detecting Releases of Single-Wall Carbon Nanotube Particles

P.E. Rasmussen[1,2], I. Jayawardene[1], H.D. Gardner[2], M. Chénier[1], C. Levesque[1], and J. Niu[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Earth Sciences Department, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Chemicals Management Plan, the Exposure and Biomonitoring Division is developing methods to identify nanoparticles in indoor air and to measure their size, number and mass. Indoor air particles are classified according to their diameter into three sizes: ultrafine or nanoparticles (<100 nanometres), fine (100 - 2,500 nanometres), and coarse (>2, 500 nanometres). Airborne particles of all sizes are known to affect respiratory function, but nanoparticles can penetrate deeper into the lungs. It is important to be able to distinguish amongst the various sources of airborne particles in order to improve air quality, but this can be a difficult challenge.

This research focused on carbon nanotubes, which tend to cluster into fine particles known as agglomerates when they are released into the air. Samples of airborne carbon nanotubes were collected for chemical analysis using a new technology called “wet electrostatic precipitation”. The results of the analysis showed that carbon nanotube agglomerates contain metal impurities which enable us to distinguish them from other carbon particles (such as diesel fumes). The methodologies arising from this research will contribute to monitoring studies which evaluate the potential for exposures to nanoparticles either in the workplace or in the context of nanotechnology-based consumer products.

MISSION STATEMENT FOR PROJECT: This research contributes to the development of Departmental approaches for assessing risks associated with human exposures to engineered nanomaterials, under the mandate of the Chemicals Management Plan Nanotechnology Initiative. It also contributes to assessments of occupational risk posed by controlled substances through the Workplace Hazardous Materials Information System (WHMIS).

1.25 Use of Public Health Intelligence for Disease Outbreaks (PHIDO) to Enhance Routine Reportable Disease Surveillance Operation in Manitoba

W. Hu[1], and P. Caetano[1]

[1] Canadian Public Health Service, Field Service Training and Response, Centre for Public Health Capacity Development, Health Security Infrastructure Branch, PHAC, Ottawa, ON
[2] Epidemiology and Surveillance Unit, Public Health, Manitoba Health, Winnipeg, MB

PLAIN LANGUAGE SUMMARY: The Epidemiology and Surveillance Unit, of Public Health Branch of Manitoba Health, is mandated to provide routine provincial surveillance of reportable communicable diseases. The biweekly provincial EpiView report provides summary of case counts of diseases with highlights of those appeared to be abnormal, but lacks of disease base count for quantitative comparison.

We adapted a tool, Public Health Intelligence for Disease Outbreaks (PHIDO), to develop disease base case count by modeling historical occurrences of the disease and identify potential outbreaks within Manitoba. The tool is simple and easy to use, and suitable for routine operation.

As a complicated statistical analytical tool, implementation of PHIDO is a multi-staged process, involving assessment of its rationale and knowledge translation among users. At the end of the process, a formal procedure to review PHIDO alerts to determine follow-up actions has been established.

PHIDO produces expected case counts, historical disease incidence patterns, and outbreak alerts of all currently reportable communicable diseases in Manitoba. Its alert information has now been incorporated into routine diseases surveillance activities.

The current provincial communicable disease surveillance system has been enhanced through the implementation of PHIDO. It provides base case count for comparison and detects outbreak alerts. PHIDO has also been used for periodical reviews of other diseases including tuberculosis and HIV outbreaks. Knowledge translation is well demonstrated through the implementation of PHIDO for Manitoba's communicable disease surveillance.

MISSION STATEMENT FOR PROJECT: To develop comprehensive disease surveillance system for Manitoba Health.

1.26 Enhancing Compliance with Post-Application Mitigation Measures for Pesticides

T. Singal[1], D. Bell[2], D. Lee[3], H. Tang[1], I. Cornish-Hogan[3], J. Salloum[2], K. Stapleton[2], and S. Fancy[3]

[1] Value Assessment and Re-evaluation Management Directorate, PMRA, Health Canada, Ottawa, ON
[2] Policy, Communications and Regulatory Affairs Directorate, PMRA, Health Canada, Ottawa, ON
[3] Compliance, Lab Services and Regional Operations Directorate, PMRA, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Pest Management Regulatory Agency (PMRA) conducts re-evaluations of pesticides to ensure they continue to be acceptable in light of new developments in science and policy.

During a re-evaluation, the relevant worker exposure scenarios for each pesticide use are assessed, and often risk mitigation measures are required to limit exposure. Until recently, training and promoting awareness of risk mitigation measures has focussed on workers who are exposed through mixing, loading and applying agricultural pesticides to crops. This poster describes recent PMRA efforts to promote awareness of mitigation measures aimed at decreasing worker exposure during post-application activities such as scouting for pests or harvesting. This initiative required collaborations within the PMRA as well as a partnership with the Federal/Provincial/Territorial Committee on Pesticides (FPT) in order to address the unique challenges outlined in the poster.

MISSION STATEMENT FOR PROJECT: Promoting awareness of mitigation measures to limit worker exposure to pesticides is important for assisting the PMRA to enhance compliance to such measures.

1.27 The Status and Trends of Environmental Chemicals in Canada

J. Provost[1], D. Haines[2], and J. Yome[1]

[1] Chemicals Surveillance Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Monitoring and surveillance (M&S) of Canadians' exposures to environmental chemicals are key elements of the Government of Canada's Chemicals Management Plan (CMP), and are essential to identify and track exposure to chemicals in the environment and associated health implications. M&S programs provide the basis for making sound and effective public health and environmental health policies and interventions, as well as measuring the efficacy of control measures.

This presentation will present data collected in blood, urine, human milk, and food to show the status and trends of a number of chemicals in Canada. In some cases, data have been collected over a number of years, allowing us to observe changes over time. In other cases, the data presented here are baseline measurements, and provide information on the current status of exposure to those chemicals.

The information to be presented has been compiled from a variety of studies the Government of Canada has undertaken, including the Canadian Health Measures Survey (CHMS), the Maternal-Infant Research on Environmental Chemicals (MIREC) study, the Canadian Total Diet Study (TDS), the First Nations Biomonitoring Initiative (FNBI), and studies funded under the Northern Contaminants Program (NCP).

MISSION STATEMENT FOR PROJECT: Considering monitoring and surveillance information from a variety of sources helps to illustrate the current status and trends for a variety of chemicals, further enhancing our understanding of the larger Canadian exposure picture. Ongoing collection and examination of this data supports various aspects of the overall CMP, potentially impacting the effectiveness evaluation of certain actions taken on chemicals.

1.28 Nano-Silver in Drinking Water and Drinking Water Sources: Stability and Influences on Disinfection By-Products Formation

A.-M. Tugulea[1], D. Bérubé[1], M. Giddings[2], F. Lemieux[3], J. Hnatiew[1], J. Priem[1], and M.-L. Avramescu[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Water Quality and Science Division, WAQB/SED/HECSB, Health Canada, Ottawa, ON
[3] Water Quality Program Division, WAQB/SED/HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Nano-silver (nAg) is increasingly present in consumer products, as well as in Point of Use Devices (POU) for drinking water. The nAg in these products is released during use, ultimately ending up in surface waters used as drinking water sources. Health Canada's aim is to investigate the stability of nAg in drinking water sources and to observe changes in the composition of disinfection by-products (DBPs) formed when nAg is present. Information about nAg stability and potential reactivity in drinking water systems is crucial in protecting the public from potential harmful effects or, alternatively, reassuring the public of the safety of our drinking water supply.

The stability of nAg in various source waters and the transformation of nAg during water disinfection by chlorination were investigated. The study results show that the nAg particles studied are stable in surface waters, but not in groundwater. They are likely to reach waste water plants and water treatment plants, but are not likely to survive the disinfection process and reach the consumer. However, it was found that nAg is relatively stable in some treated drinking waters and could reach the consumer if introduced to the drinking water after the disinfection process (e.g., by a POU). These results are used to evaluate potential human exposure to nAg through drinking water.

MISSION STATEMENT FOR PROJECT: This project will provide data to be used in the risk assessment of nano silver-containing consumer products.

Food Contaminants and Nutrition

2.01 Determination of Arsenic Speciation in Fruit Juice and Fruit Drink Products Using Ion Pair Chromatography Hyphenated to Inductively Coupled Plasma Mass Spectrometry Analysis

Z. Wang[1], L. Nadeau[2], M. Sparling[1], and D. Forsyth[1]

[1] Food Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Department of Biopharmaceutical Sciences, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Strengthening of surveillance and food monitoring has been identified as a priority by HPFB's FD to address emerging threats to food safety. Arsenic, a well-known toxicant that can be found naturally on earth, is recognized as one of the most important environmental agents in causing chronic human diseases. In recent years, arsenic in food has also attracted much attention because of elevated concentration of arsenic were detected in certain food samples (i.e. rice), which may represent a potential health hazard to the consumer. Arsenic information provided by total analysis are not reliable as toxicity of arsenic is different among species, therefore speciation analysis (a scientific area that measures different species of one element) has become essential for assessment of arsenic exposure and risk. In order to gather data on Canadian exposure to arsenic species from food and assist in the evaluation of potential related risks, there is a need to implement a routine method for determination of arsenic species that is rapid and accurate. Hence, the current study reported a rapid analytical technique for determination of arsenic species in fruit juice and fruit drink products. The method was optimized and validated for the determination of arsenic speciation in fruit juice and fruit drink products.

This research will provide Health Canada with scientific evidence to update appropriate regulation and guidelines that better protect the Canadians from arsenic-induced adverse effects.

MISSION STATEMENT OF THE PROJECT: The project meets all the HPFB and FD's priorities of strength emergency response capacity/capability, strengthen surveillance and food monitoring, enhance the management of risks for foods derived from new technologies, through development of analytical method and provides the Canadian surveillance data on toxic trace elements in retail food needed. The new technique developed in this project will lead to substantially improved understanding of arsenic exposure (arsenic speciation) through food. This research will provide Health Canada with scientific evidence to update appropriate regulation and guidelines that better protect the Canadians from arsenic-induced adverse effects.

2.02 Halophilic *Vibrio* Species Isolated from Canadian Molluscan Seafood: Human Health and Regulatory Implications

S.K. Banerjee[1], L. Bakouche[1], and J.M. Farber[1]

[1] Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Halophilic (salt-requiring) bacteria belonging to the *Vibrio* species are abundant in estuaries around the world, including some which are pathogenic to humans. Seafood, particularly filter-feeding molluscan shellfish, concentrate marine bacteria which may survive inside the human body after ingestion, and cause morbidity and mortality in weakened individuals. Consumers, particularly those who are immune-compromised, such as the elderly and/or those with pre-existing illness, should be aware of the potential risk when consuming raw or undercooked molluscan shellfish. A combination of virulence and drug resistance in the same bacterial strain could enhance the potential hazard and risk associated with the contaminated molluscs, as therapeutic options may become limited in severe cases.

This study aims to generate a database on the status of the existing risk factors, such as multidrug-resistant and pathogenic *Vibrio* spp., to support regulatory intervention, or policy update, for knowledge-based safe consumption of seafood in maintaining and improving the health of Canadians.

MISSION STATEMENT OF PROJECT: The outcome of this project will help Canadian seafood consumers to make safe and healthy decision, based on knowledge and regulatory updates.

2.03 A Pilot Survey of 2- and 3-Monochloropropanediol and Glycidol Fatty Acid Esters in Foods on a Canadian Market

A. Becalski[1], S. Feng[1], B. P.-Y. Lau[1], and T. Zhao[1]

[1] Food Research Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Recent studies have identified the presence of 2- and 3-monochloropropanediol (2- and 3-MCPDEs) and glycidols (GEs) in many refined fats and oils and also food products manufactured with fats and oils, such as cookies. These substances may be formed during processing/refining of commercials oils.

MISSION STATEMENT OF PROJECT: Health Canada's Food Directorate is responsible for providing standards, advice and information that translates into policies for safety and nutritional value of food. The data presented in this study will be used to update exposure estimations and risk assessment for 2- and 3-MCPD and glycidol esters in food.

2.04 Revised Estimates of the Burden of Food-Borne Illness in Canada

M.K. Thomas[1], R. Murray[1], L. Flockhart[1], K. Pintar[2], F. Pollari[1], A. Fazil[2], A. Nesbitt[1], and B. Marshall[1]

[1] Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, PHAC, Guelph, ON
[2] Laboratory for Foodborne Zoonoses, PHAC, Guelph, ON

PLAIN LANGUAGE SUMMARY: In 2008, the Public Health Agency of Canada (the Agency) estimated that 11 million episodes of food-borne illness occur each year in Canada. Although the best estimate at the time, it was determined using older methods and data.

The main goal of this study was to calculate a more accurate estimate of food-borne illness in Canada using current data and more robust methods than the 2008 estimate.

The Agency calculated estimates for 30 known pathogens and unspecified agents – known agents with insufficient data to make estimates, undiscovered agents and unrecognized food-borne agents – using data from Canadian surveillance systems (for years 2000-2010), international literature and the 2006 Canadian census population.

From this analysis, the Agency estimates there are 4.0 million episodes of domestically acquired, food-borne illness each year in Canada (i.e. unrelated to international travel) with 1.6 million episodes from 30 known pathogens and 2.4 million episodes from unspecified agents. This means that approximately 1 in 8 Canadians get sick each year from the food they eat.

The revised estimates are more accurate than the 2008 estimate because they were derived from current data and more robust methods. This allowed the Agency to calculate pathogen-specific estimates for the first time. Policy makers, industry, academia and other organizations can use these revised estimates to better inform policy, research, food safety risk assessments, education campaigns and other prevention and control activities. Pathogens which cause the greatest amount of illness can be prioritized for intervention activities.

MISSION STATEMENT FOR PROJECT: These pathogen specific estimates better enable prioritization of pathogens and food-borne illness prevention and control activities.

2.05 Higher Intakes of Calcium Worsen Magnesium Deficiency in Rats Fed an Inadequate Magnesium Diet

J. Bertinato[1], C. Lavergne[1], L.J. Plouffe[1] and H. Abou El Niaj[1]

[1] Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Many Canadians have inadequate intakes of magnesium suggesting a possible problem of magnesium deficiency in the Canadian population. Calcium supplementation is common in Canada for the prevention of calcium deficiency and maintenance of bone health. Calcium is added to many food products. Some studies have suggested that high intakes of calcium decrease intestinal magnesium absorption increasing the risk of magnesium deficiency. This study investigated whether small increases in dietary calcium worsen magnesium deficiency in rats fed an inadequate magnesium diet. Rats fed diets containing 150–400% of the recommended amount of calcium had lower magnesium content in bone indicating poorer magnesium status.

These results show that even small increases in dietary calcium can decrease magnesium status. Data from this study provide information on the health risks associated with increasing calcium intakes and could influence the development of guidelines and regulations on calcium supplementation and addition of calcium to foods.

MISSION STATEMENT FOR PROJECT: This research investigated health risks associated with higher calcium intakes that could influence nutrition guidelines and regulations on calcium supplementation and fortification.

2.06 Formalizing an Evidence Review Cycle for Dietary Guidance

H. Lowell[1], K.J. Faloon-Drew[1], S. Olson[1], J.A. Gilbert[1], and A. Ellis[1]

[1] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Health Canada develops evidence-based guidance on healthy eating. This guidance is currently communicated through Canada's Food Guide, the Prenatal Nutrition Guidelines, and Nutrition for Healthy Term Infants.

As there is no formal schedule to review Health Canada's guidance on healthy eating, a new Evidence Review Cycle is being implemented. The Cycle involves the assessment of evidence in three key areas: scientific basis (updated nutrient standards, and research on diet and health); use of existing healthy eating guidance (for example, results from the Outcome Assessment of Canada's Food Guide - see separate poster presentation); and relevance in the Canadian context (for example, the changing food supply and population demographics).

Reviewing the evidence on a cyclical basis will help identify any future actions that may be required to ensure Health Canada's healthy eating guidance is scientifically sound, relevant and useful. However, it does not imply that a revision of Canada's Food Guide will be undertaken. The Cycle will also help inform other federal actions such as the promotion of healthy eating messages to Canadians. The method for communicating results of this work to Canadians on a regular basis is being developed. The first communication is planned for 2014.

MISSION STATEMENT FOR PROJECT: The formalized Evidence Review Cycle will strengthen Health Canada's ability to provide credible and reliable advice on healthy eating for Canadians.

2.07 Detection of Foodborne Pathogens by On-Chip PCR through a Novel Microfluidic Platform

N. Corneau[1], G. Marchand[1], C. Luebbert[1], M. Duplessis[2], S. Bidawid[1], J.M. Farber[1], K. Morton[3], X. Dai Hoa[3], L. Clime[3], M. Geissler[3], D. Brassard[3], and T. Veres[3]

[1] Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Director General's Office, Food Directorate, HPFB, Health Canada, Ottawa, ON
[3] Life Sciences Division, Medical Devices Portfolio , National Research Council, Boucherville, QC

PLAIN LANGUAGE SUMMARY: Available methodologies for active surveillance of agri-food systems and processing environments for foodborne pathogens are lengthy, require trained technicians and a microbiological containment/laboratory setup. Traditional culture-based approaches can take up to several days for the isolation and detection of bacteria such as *Listeria monocytogenes* or verotoxigenic *E. coli*. An automated microfluidic-based device is currently being developed. This Lab-on-a-chip system includes platforms for the isolation and the detection of foodborne pathogens through PCR amplification and microarray hybridization. This technology can detect and identify foodborne pathogen(s) within one day with a simple read in confined equipment. An amplification chip was designed out of polymer material. Successful amplifications were achieved with conventional PCR reagent concentrations from bacterial genomic DNA template.

We are able to amplify DNA in a multiplex fashion with results similar to that of a benchtop thermocycler for both *L. monocytogenes* and *E. coli*. The incorporation of Cy3 labelled dCTPs in the PCR mix which is used for the identification of the species serovars was achieved and a successful amplification of the target genes was obtained. The following step is the detection of Cy3 labelled PCR products with microarray and the evaluation of the detection level (bacterial concentration) of this protocol.

MISSION STATEMENT FOR PROJECT: Rapid diagnostic for foodborne pathogens.

2.08 New Regulatory Process for the Efficient and Timely Approval of Food Additives

R. Awadia[1], M. Bauder[1], B. Bertrand[1], R. Billingsley[1], M. Boruk[1], J. Bouchard[1], D. Boudreau[1], B. Buchanan[1], D. Covonev[1], R. Duhaime[1], D.K. Edwards[1], D. Fournier[1], J. Garrah[1], F. Geraghty[1], K. Hislop[1], M.-F. Huot[1], B. Junkins[1], D.K. Lee[1], J. LeGarignon[1], D. McGuire[1], L. McVeigh[1], R. O'Leary[1], T. Paolasini[1], R. Smith[1], C. Strowbridge[1], A. Whitfield[1], B. Lee[1], and A. Papadopoulos[1]

[1] Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: On October 25, 2013, Health Canada took a major step in making approvals for food additives more timely and efficient once it has completed a relevant scientific assessment. A food additive is any chemical substance that is incorporated in food during preparation or storage and either becoming part of the food or affecting its characteristics. Examples of food additives include colouring agents, preservatives, and sweeteners.

Using new legislative authorities provided under the *Food and Drugs Act* as part of the *Jobs, Growth and Long-term Prosperity Act* (Bill C-38), the Minister of Health enacted 15 new food additive ministerial regulations (officially known as "marketing authorizations") that incorporate by reference 15 lists of permitted food additives found on the Health Canada website.

Previously, permitted food additives were prescribed in regulation in 15 tables found in Division 16 of the *Food and Drug Regulations*. As prescribed tables, any changes to their content, such as the addition of a new additive or an extension of the use of an established additive, necessitated a regulatory amendment - a lengthy process requiring 18-24 months to complete following the scientific assessment. This resulted in a system where regulatory rules did not reflect the latest science and innovation nor could be amended efficiently in response to an emerging health risk.

By contrast, having the additive lists incorporated by reference means that changes to the lists may be done administratively once the scientific assessment and relevant public notifications are completed, all without the need for lengthy regulatory amendments or cabinet approval.

MISSION STATEMENT FOR PROJECT: This innovative approach to ensuring that food safety regulations accurately reflect the most up-to-date science available has ensured much speedier access to food additives that have undergone a thorough and rigorous assessment and been proven safe for Canadians.

2.09 Food Sources of Magnesium and Potassium in the Canadian Diet

I. Massarelli[1], L. Nguyen[1], and I. Rondeau[1]

[1] Bureau of Food Surveillance and Science Integration, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Data from the Canadian Community Health Survey (CCHS) 2004 was used to see which foods contribute to the magnesium and potassium intake of Canadians.

Foods contributing to magnesium and potassium intakes of Canadian aged 19+ were determined using the first 24-hour food recalls derived from the CCHS Nutrition 2004. After classifying the data by Canada's Food Guide (CFG) food groups, we find that the Vegetables and Fruit group is the greatest source of both magnesium and potassium for Canadians. Bananas, fruit juice, potatoes and tomatoes are the top contributors. The meat and alternatives group is the next best source. Milk is the top source for both nutrients in the Milk and alternatives group. Coffee is also an important source of magnesium and potassium.

According to data from the CCHS 2004, more than 34% of Canadians over the age of 19 consumed magnesium in quantities below the estimated average requirement (EAR).

Food guide analysis has shown that Canadians don't meet the recommended Food Guide serving of fruits and vegetables. Consuming more fruit and vegetables would help adult Canadians meet both EAR and CFG recommendations.

(ref. http://hc-sc.gc.ca/fn-an/surveill/nutrition/commun/art-nutr-adult-eng.php)

MISSION STATEMENT FOR PROJECT: Inform nutrition surveillance activities.

2.10 Is there Contamination from the Fukushima Accident in Beluga?

T.J. Stocki[1], L. Losetto[2], M. Gamberg[3], E. Pellerin[1], L. Bergman[1], J.-F. Mercier[1], L. Genovesi[1], M.W. Cooke[1], B. Todd[1], J. Whyte[1], and X. Wang[4]

[1] Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON
[2] Department of Fisheries and Oceans, Winnipeg, MB
[3] Gamberg Consulting, Whitehorse, YK
[4] Environment Canada, Burlington, ON

PLAIN LANGUAGE SUMMARY: This project examined the levels of radioactive contaminants in Canadian Arctic caribou and beluga whale, both before and after the Fukushima Daiichi Nuclear Power Plant accident, which began on March 11, 2011. The purpose of this study was to determine whether contaminant levels in these food resources have changed since the accident. It turned out that the eastern Beaufort Sea beluga whale population that winters in the Bering Sea was not affected by radionuclides released from the Fukushima Daiichi accident on March 11, 2011. Arctic beluga continues to be a healthy food choice for northern Canadians, with respect to radioactivity in it. The safety of an important food source for northern Canadians has been reassessed with respect to radioactivity levels to determine the potential effects from the Fukushima Daiichi nuclear accident.

MISSION STATEMENT FOR PROJECT: This project will reassure northern Canadians that two of their traditional foods (caribou and beluga) have not been affected by the Fukushima accident.

2.11 Association of Vitamin B12 Supplement Use and Dose with Vitamin B12 Status in the Canadian Population

A.J. MacFarlane[1], L.S. Greene-Finestone[2], and Y. Shi[2]

[1] Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON
[2] Social Determinants and Science Integration Division, PHAC, Ottawa, ON

PLAIN LANGUAGE SUMMARY: While high intake levels of vitamin B12 have not been shown to be toxic, they have also not been proven to provide additional benefit to consumers. Using data from the Canadian Health Measures Survey, cycle 1, we determined the association between vitamin B12 supplement use and dose and vitamin B12 status. We found that children (6-12 y), adolescents (13-19 y) and older adults (60-79 y) in the general population do not gain additional benefit in terms of vitamin status from supplemental vitamin B12 intakes greater than 10 µg/day. Adults aged 20-59 y had increased vitamin status up to 25 µg/d. The data indicate that vitamin B12 supplement doses greater than 25 µg/day, although unlikely to pose harm, do not benefit the general population.

MISSION STATEMENT FOR PROJECT: Our aim is to identify the determinants of nutrient status of Canadians to inform regulations and public health policy.

2.12 Male Dietary Folic Acid Intake Alters Choline Metabolism in their Descendants

J.W.R. Zinck[1], N.A. Behan[2], C.L. Yauk[3], M. Caudill[4], and A.J. MacFarlane[2]

[1] Social Determinants and Science integration Directorate, PHAC, Ottawa, ON
[2] Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON
[3] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[4] Division of Nutritional Sciences, Cornell University, Ithaca, NY

PLAIN LANGUAGE SUMMARY: Folic Acid (FA), an essential B vitamin, is added to flour to reduce the incidence of neural tube birth defects, such as spina bifida. As a result, the general Canadian population, including men and children, are consuming increased amounts of folic acid. Folic acid intake in one generation may change the risk for chronic disease in subsequent generations. To examine possible consequences of high folic acid intakes on non-target populations and their offspring, we examined changes in gene expression using microarray analysis in the descendants of male mice fed folic acid deficient, sufficient or supplemented diets. We found that the descendants of male mice exposed to low or high levels of dietary folic acid had altered choline metabolism, a semi-essential nutrient. Our data indicate that current fortification policies may affect the nutritional requirements, not only of those directly exposed, but of future generations as well.

The results of this research will be used by Health Canada to formulate new folic acid nutritional recommendations and guidelines for non-target human populations, specifically males and children.

MISSION STATEMENT FOR PROJECT: Our aim is to understand the health consequences of fortification programs in the general population.

2.13 Parental Folic Acid Intake Influences the Expression of Birth Defect Related Genes in Male Descendants

N.A. Behan[1], J.W.R. Zinck[2], C.L. Yauk[3], and A.J. MacFarlane[1,4,5]

[1] Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Social Determinants and Science integration Directorate, PHAC, Ottawa, ON
[3] Mechanistic Studies Division, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[4] Department of Biology, Carleton University, Ottawa, ON
[5] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Folic Acid (FA), an essential B vitamin, is added to flour to reduce the incidence of neural tube birth defects (NTDs). The two most common NTDs are spina bifida and anencephaly NTDs and they occur at a rate of approximately 0.4 in 1000 live births in Canada since fortification was mandated. As a result of fortification, Canadians are consuming an increased amount of folic acid. Folic acid intake in one generation may change the risk for chronic disease in subsequent generations due to its influence on gene expression. We found that the descendants of male mice exposed in early development or in the post-weaning period, to low or high levels of dietary folic acid had changed the expression of genes that are associated with increased risk for neural tube defects, suggesting that the nutritional status of one generation can influence the risk for developing birth defects in their descendants.

MISSION STATEMENT FOR PROJECT: Our aim is to understand the health consequences of food fortification programs in the general population.

2.14 The Development of a Short Sodium Screener (Short Diet Questionnaire): Metholological Considerations

M. Cooper[1], R. Klutka[1], and J. Randall Simpson[2]

[1] Nutrition Research Division, Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa ON
[2] Department of Family Relations and Applied Nutrition, University of Guelph, Guelph, ON

PLAIN LANGUAGE SUMMARY: In accordance with the Health Canada mandate to help the people of Canada maintain and improve their health, we have developed a Short Sodium Screener (questionnaire) to identify high and low consumption in order to regularly assess sodium intakes in the population. A main component of this process was to ensure that the correct groupings of foods were selected for inclusion on the screener. Data from the Canadian Community Health Survey – Nutrition was used to group foods into general categories (e.g. snack foods) to serve as the basis of screener questions (e.g., 'How often in the past 4 weeks have you consumed snack foods such as chips, crackers, popcorn, pretzels, rice cakes, etc?'). The data from this survey formed the foundation for the 43 questions on the Screener. A typical serving size and sodium value has been assigned to each question. The use of Canadian Survey Data has ensured the creation of a questionnaire that reflects typical Canadian consumption patterns. Health Canada will use the results of this methodological development to assess this nutrition tool against a standard method to ensure that this has future use for Canadian population nutrition surveys.

MISSION STATEMENT FOR PROJECT: To improve the understanding of the methodology involved in developing dietary questionnaires used for population nutrition surveys.

2.15 Inactivation of Soy Bean Trypsin Inhibitor (SBTI) Remaining in Commercial Soy Beverages and Adverse Effects of Active SBTI in Rats

C.W. Xiao[1,2], E. Mantil[1], and C. Wood[1]

[1] Nutrition Research Division, Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Consumption of soy foods/products containing high levels of soybean trypsin inhibitors (SBTI), anti-nutritional factors, results in decreased protein digestibility and nutritive value, and even causes pancreatic problems in certain species. We have recently showed that many of the commercial soy beverages contain high levels of active SBTI. However, the upper safe levels of active SBTI in the foods have not been established and regulated.

This study aimed to optimize the SBTI inactivation conditions in commercial soy beverages, and to examine the potential adverse effects of intake of active SBTI. Results shows that dietary active SBTI remarkably increased pancreatic weights and cell secretions of proteases in rats, and heating at 121°C, 15 psi for 6 min lowered the residue SBTI activity to the safe level of consumption.

This information is important for the development of guidelines for the manufacturing process of soy products and the establishment of upper safe levels of SBTI, which is consistent with Health Canada's mission of ensuring the Canadian food supply is safe and meets nutritional requirements.

MISSION STATEMENT FOR PROJECT: This information is useful in the development of guidelines for the manufacturing processes of soy products and the eablishment of upper safe levels of anti-nutritional factors, which is consistent with Health Canada's mission of ensuring the Canadian food supply is safe and meets nutritional requirements.

2.16 The Inertial Microfluidic Separation of *Cryptosporidium spp.* and *Giardia Duodenalis* from Contaminated Food Samples

K.R. Ganz[1], J.M. Farber[1], N. Corneau[1], L. Clime[2], T. Veres[2], and B. Dixon[1]

[1] Parasitology Laboratory, Bureau of Microbial Hazards, Food Directorate. HPFB, Health Canada, Ottawa, ON
[2] Life Science Division, National Research Council Canada, Boucherville, QC

PLAIN LANGUAGE SUMMARY: *Cryptosporidium* spp. and *Giardia duodenalis* are enteric protozoan parasites which infect a wide range of vertebrate hosts, including humans, and can be transmitted through foods. The detection and surveillance of these parasites from various foods is critical in establishing health risk assessments. Current detection methods elute the parasites from the surface of the foods; giving rise to a parasite suspension which contains a low concentration of parasites and high concentration of interfering food particles.

The goal of the research is to develop a specific concentration method which separates the parasites from the food particles in the suspension. This new method is more successful in removing unwanted background particles and recovers comparable amounts of parasites to current techniques. A concentrated and clean parasite suspension improves detection through the elimination of potential false negatives and/or false positives thus allowing for a more accurate health risk assessment.

MISSION STATEMENT FOR PROJECT: Increase the detection and analysis of protozoan parasites from foods to provide an accurate health risk assessment.

2.17 New Methodology for Sample Preparation Toward Efficient Sr-90 Analysis of Milk Samples in Emergency Scenarios

P. Czechura[1], J.-F. Mercier[1], and M.W. Cooke[1]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Strontium-90 (Sr-90) is formed in nuclear reactors and during nuclear tests, and can find its way into the environment, the food chain, and people. Sr-90 tends to concentrate in our bodies, with a high affinity for human tissue, especially bone and teeth. Since Sr-90 is well retained and exhibits high-energy particle emission during its decay, its presence can lead to disease such as cancer. Monitoring Sr-90 concentration in food is thus important. This is especially true for milk, since the soil to milk pathway for Sr-90 incorporation is efficient.

The National Monitoring Section of the Radiation Protection Bureau is responsible for routine and emergency analysis of Sr-90 in samples obtained from across Canada. The goal of this project was to make our Sr-90 analysis of milk better suited to the high sample volume and time constraints anticipated with a nuclear emergency. To this end, we have addressed the time-consuming aspect of sample preparation by developing a new method that is fast, efficient and requires minimal manipulation. The method expands our processing capabilities for expected large sample numbers in order to more quickly assess potential health hazards to Canadians in case of a nuclear incident.

MISSION STATEMENT FOR PROJECT: The National Monitoring Section of the Radiation Protection Bureau has developed a new sample preparation procedure for emergency analysis of strontium-90 in milk. The method provides capability for fast and high-throughput sample processing and thus expands our toolbox for emergency preparedness.

2.18 The Outcome Assessment of Canada's Food Guide

C. Bonetta[1], B. McIntyre[2], V. Dorais[1], H. Lowell[1], S. Olson[1], J. Zeitouny[1], S. Ramsay[1], and K. LaForce[1]

[1] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON
[2] Health Promotion and Disease Prevention Division, FNIHB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Millions of Canadians have received Canada's Food Guide and yet there is limited information on how it is being used. An assessment was undertaken by Health Canada to better understand how Canada's Food Guide is used by consumers and professionals. The Assessment included *Eating Well with Canada's Food Guide* and *Eating Well with Canada's Food Guide – First Nations, Inuit and Metis*.

The purpose of the assessment was to provide information on who is using Canada's Food Guide, how it is being used, and how it is being integrated into policies, programs and initiatives at the federal, provincial, territorial, and local levels.

An evaluation framework was developed and information was gathered through various lines of evidence such as: a review of documents, interviews with professionals and consumers, discussion groups, surveys of stakeholders and consumers, and case studies.

Findings from the assessment will provide baseline information on how the Canada's Food Guide is used and whether it is effectively achieving its objectives. As well, the assessment will inform dietary guidance work, program decision-making and increase overall accountability.

MISSION STATEMENT FOR PROJECT: The Outcome Assessment will inform the work of the "Evidence Review Cycle for Dietary Guidance" being conducted by the Office of Nutrition Policy and Promotion to help determine if and when changes to dietary guidance are needed.

In addition, the results of the assessment will provide baseline information related to healthy eating and will inform program accountability frameworks (eg. performance measurement framework).

2.19 A Closer Look at the Diets of Canadians in 2004 Relative to *Eating Well with Canada's Food Guide*

L.-A. Elvidge[1], L. Dumais[2], K. Esslinger[1], E. Jones-Mclean[3], E. Mansfield[2], M.-F. Verreault[2], M. Villeneuve[2], D. Miller[1], J.-A. Gilbert[1], and S. St-Pierre[1]

[1] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON
[2] Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON
[3] Health Promotion and Chronic Disease Prevention Branch, Social Determinants and Science Integration Directorate, PHAC, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The aim of this project was to assess the diets of Canadians relative to the recommendations made in Canada's 2007 Food Guide, *Eating Well with Canada's Food Guide* (CFG).

This was done using a newly revised classification system that classifies the foods listed in the Canadian Nutrient File as either "Foods in line with CFG guidance", "Foods partially in line with CFG guidance" or "Foods not in line with CFG guidance". The Canadian Nutrient File is a database used to analyze nutrition survey data.

The amount and type of foods consumed by Canadians in the Canadian Community Health Survey, cycle 2.2, were examined with the classification.

Results show that across all ages (2 yrs +), "Foods in line with CFG guidance" represented 89% (95% Confidence Interval [CI]: 88, 89) of the Vegetable and Fruit servings consumed and 71% (CI: 70, 72) of Grain Product servings. In contrast, these foods accounted for only 42% (CI: 41, 43) of Milk and Alternative servings and 33% (CI: 32, 34) of Meat and Alternative servings. This shows that Canadians could especially improve the quality of their Milk and Alternative and Meat and Alternative choices.

The findings will serve as a basis for comparison with the next national nutrition survey and help inform nutrition policy and promotion activities within Health Canada.

MISSION STATEMENT FOR PROJECT: The results from the analysis will support research and foster relationships with researchers across the country. It will also help inform Health Canada's Evidence Review Cycle for Dietary Guidance and Health Canada's nutrition promotion activities.

2.20 Assessment of Key Food Skills among Canadians: Results from the Canadian Community Health Survey (CCHS) Rapid Response Modules on Food Skills

J.-A. Gilbert[1], V. Dorais[1], J. Zeitouny[1], D. Gibson[1], and S. St-Pierre[1]

[1] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Higher food skills contribute to healthier eating habits; yet, some studies suggest that these skills are declining over time. Data describing Canadians' food skills had never been collected at the national level; a rapid response survey was conducted to gather this information.

The questionnaire measured Canadians' ability to cook, transferring skills from adults to children, meal planning, food shopping practices and mechanical cooking skills. With regards to cooking ability, most Canadians are able to prepare most meals by themselves or with a recipe. About 15% of Canadians reportedly do not participate in meal preparation. The main reasons provided for not getting involved in meal preparation was "not my responsibility" and lack of time or skills. Most adults share a family meal with their children "almost every day" or "every day". In addition, in households with children, most respondents reported involving children in meal preparation, making suggestions for meals or grocery shopping. When buying foods, most Canadians plan meals in advance and use grocery lists and nutrition labels.

These baseline findings provide a better understanding of the state of food skills in Canada and are used in the development of Health Canada's Healthy Eating Awareness and Education Initiative.

MISSION STATEMENT FOR PROJECT: By addressing current gap related to the status of food skills in Canada, the results from this survey will inform Health Canada's nutrition policy and program intervention. Specifically, they will help guide the development of the Healthy Eating and Awareness Initiative which focuses on food skills to improve healthy eating practices and reduce the risk of chronic disease.

2.22 Industrial Trans Fatty Acids are Gradually Disappearing from Canadian Human Milk

W.M.N. Ratnayake[1], E. Swist[1]. R. Zoka[1], C. Gagnon[1], W. Lillycrop[2], and P. Pantazapoulos[2]

[1] Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Food Laboratory Division, Ontario Region, Health Canada, Scarborough, ON

PLAIN LANGUAGE SUMMARY: In Canada for a long time, partially hydrogenated vegetable oils were used in commercial baking, frying and also in preparation of variety of processed foods. Trans fatty acids (TFA) are formed during partial hydrogenation and consumption of these industry produced fatty acids increase the risk of coronary heart disease. In order to reduce the TFA content in the Canadian diet, Health Canada in 2003 mandated TFA labelling on pre-packaged foods and furthermore, in 2007 called on the industry to voluntarily reduce the levels of TFA in processed foods.

To assess the impact of these efforts, the concentration of TFA in 639 human milk samples collected nationwide in 2009, 2010 and 2011 were measured. Human milk TFA reflects the TFA in the mother's previous day diet; therefore, human milk is a convenient biological source for establishing dietary levels of TFA. The mean TFA contents were 2.7%, 2.2% and 1.9% of total milk fat for samples collected in 2009, 2010 and 2011, respectively. These values are considerably lower than the value of 7.2% found in Canadian human milk in 1992 and suggest that the efforts taken by Health Canada have resulted in significant reductions in the TFA levels in Canadian human milk and the Canadian diet.

Future studies need to address the possible benefits to cardiovascular health of Canadians.

MISSION STATEMENT FOR PROJECT: Health Canada's mission is to ensure that the Canadian food supply is safe of nutritional hazards and meets nutritional requirements. The results of this study further confirm that the current Canadian food supply is safe as far as the levels of industrial trans fats are concerned.

2.23 Targeted Survey of Di-2-Ethylhexyl Adipate and Phthalate Plasticizers in Samples of Meat, Fish and Cheese

X.-L. Cao[1], W. Zhao[1], R. Churchill[1], and C. Hilts[1]

[1] Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Di-2-ethylhexyl adipate (DEHA) and phthalates are commonly used as plasticizers to soften polyvinyl chloride (PVC) products. Since DEHA and several phthalates have been identified as priority chemicals for assessment of human health risk under the Government of Canada's Chemicals Management Plan, a comprehensive targeted survey was conducted to investigate the occurrence of DEHA and eight selected phthalates in a total of 118 samples of meat (beef, pork, chicken), fish, and cheese packaged mostly in cling films. DEHA was detected in all food samples packaged in DEHA-plasticized cling films, with the highest levels found in cheese. Di-2-ethylhexyl phthalate (DEHP) was also detected in a few cheese samples, but the other seven phthalates were not detected in any of the food samples. The results from this study will complement the on-going Total Diet Study for exposure and risk assessment to ensure that chemicals are not present in foods at levels that would pose an unacceptable risk to health of Canadians.

MISSION STATEMENT FOR PROJECT: This study was conducted to ensure that chemicals are not present in foods at levels that would pose an unacceptable risk to the health of Canadians.

2.24 Welcome to the A-List: An Introduction to the Automated *Listeria in Silico* Typer

A.W. Pightling[1], N. Petronella[2], D. Brulé[2], and F. Pagotto[1]

[1] Listeriosis Reference Service, Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON Food Directorate, HPFB, Health Canada, Ottawa, ON

[2] Bureau of Food Surveillance and Science Integration, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Foodborne illness continues to have significant health and economic repercussions for Canadians. Consumption of ready-to-eat foods contaminated with *Listeria monocytogenes* may result in listeriosis, a disease with symptoms that range from fever, muscle-aches and gastroenteritis to blood poisoning, meningitis and death. To mitigate the consequences of listeriosis, we must continually improve the safety of our food supply with early detection of *L. monocytogenes* in food production environments and rapid identification of the sources of clinical illnesses.

Analysis of an organism's full genome sequence (genomics) has proven to be a valuable tool for short- and long-term epidemiological investigations. Furthermore, advances in DNA sequencing technologies and reduced costs have made whole-genome sequence (WGS) data readily available. However, automated platforms required for rapid and accurate computational analysis of WGS data are lacking for most human pathogens. We present the automated *Listeria in silico* typer (a-List), a computational workflow that automatically assembles, identifies and analyses entire *L. monocytogenes* genomes in approximately three hours. Since the workflow is fully automated, it is accessible to a wide range of users and it yields exactly reproducible results, providing the means to use WGS data to respond to sporadic and outbreak cases and to inform policy decisions.

MISSION STATEMENT FOR PROJECT: This work provides in-house capacity to use genome sequence data to establish science-based policy for tracking and preventing the emergence of pathogens in the food production system.

2.25 The Impact of Menu Labelling on Calories Selected or Consumed: A Systematic Review and Meta-Analysis

S.E. Sinclair[1], M. Cooper[2], and E.D. Mansfield[1]

[1] Nutrition Standards and Regulation Division, Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Nutrition Research Division, Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Menu labelling is an important issue to Canadians. Many people believe that menu labelling is an effective way to help consumers make informed decisions when eating out. Some restaurants have post calorie labels on their menus. Others have posted calories plus contextual/interpretive information, such as daily requirements or traffic light symbols, to make the calorie amounts more meaningful to consumers. The purpose of this review was to find out if menu-based calorie labels affect the amount of calories that consumers choose or eat. Whether or not more information was added was also examined to find out if it had an impact on calories chosen and eaten. Menu labelling with calories alone did not decrease the amount of calories chosen or eaten at point of purchase. When information was added to help make the amount more meaningful, fewer calories were chosen and eaten (-67 Calories, p=0.008 and -81 Calories, p=0.007, respectively).

The findings of this review support calorie labels with additional contextual/interpretive information to help consumers select and/or consume fewer calories when eating in restaurants.

MISSION STATEMENT FOR PROJECT: Since 2003, recommendations and requests for expansion of Canadian nutrition labelling regulations from public health and consumer advocacy groups have been made at both the federal and provincial level. In the US, the FDA has been considering menu labelling since 2010 and final rule on *Nutrition Labelling of Standard Menu Items at Chain Restaurants* is expected in 2013. The results of this work will help support the design and development of a voluntary menu labeling approach for use in restaurants and foodservices throughout Canada.

2.26 Development of a Diagnostic Tool for the Identification of Antimicrobial Resistance in *N. gonorrhoeae*

P.H. Links[1], I. Martin[2], M.G. Links[3], J.Wu[1], and T. Wong[1]

[1] Professional Guidelines and Public Health Practice Division, Center for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, PHAC, Ottawa ON

[2] Bacteriology and Enteric Diseases Division, National Microbiology Laboratories, Infectious Disease Prevention and Control Branch, Public Health Agency Of Canada, Winnipeg MB

[3] Bio-Products and Bioprocessing, National Science Program, Science and Technology Branch, Agriculture and Agri-Food Canada, Saskatoon, SK

PLAIN LANGUAGE SUMMARY: *Neisseria gonorrhoea* (NG) infections remain the second most common bacterial sexually transmitted disease in Canada and USA; if left untreated infections can result in serious health problems including infertility. Current diagnosis of NG infection is performed by polymerase chain reaction (PCR) on urine samples which may take days to confirm infection. This diagnosis provides no information about antibiotic resistance. As strains resistant to third generation cephalosporins, cefixime, and ceftriaxone, azithromycin and other antibiotics become more common there are few antibiotics left for treatment. Using whole genome sequencing and bioinformatics we have compared the single nucleotide polymorphisms (SNPs) present in sensitive and resistant NG. This approach, allows us by computer to distinguish NG strains which are sensitive or resistant to cefixime, and ceftriaxone. A rapid PCR diagnostic is being developed which will be capable of distinguishing candidate SNPs common to sensitive and resistant NG isolates. The tests will then be transferred to the National Microbiology Laboratory (NML) where incoming patient samples will be used to further validate the assays.

A new rapid genotypic resistance assay could inform the use of the most appropriate treatment for gonorrhea. This will ensure correct medications are prescribed, limiting the spread of drug resistant infections by preventing treatment failure.

MISSION STATEMENT FOR PROJECT: To improve our ability to rapidly diagnose antimicrobial resistance in *N. gonorrhoea.*

2.27 Foodbook: Canadian Food Exposure Study to Strengthen Outbreak Responses

T. Terefenko[1], V. Morton[1], A. Nesbitt[1], Foodbook Team[1], Food Directorate[2], Canadian Food Inspection Agency and P/T Enteric Disease Representatives

[1] CFEZID, PHAC, Guelph, ON
[2] Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: A key step in identifying the source of a foodborne illness outbreak is to identify foods eaten by more cases than expected when compared to foods eaten by the general population. Outbreak investigators require food exposure data describing what Canadians eat over a time period relevant to enteric diseases. Currently, these data do not exist. Nutrition-focused 24 hour dietary recall surveys cannot be extrapolated to longer exposure periods and do not target foods that are high risk for foodborne infections. The Public Health Agency of Canada in consultation with federal, provincial and territorial partners designed Foodbook to fill this important data gap. Foodbook is a population-based telephone survey that will assess Canadians' exposure to specific foods and key enteric illness risk factors over a seven-day period.

Data will be used to direct outbreak investigators to foods most likely to be the cause of a foodborne illness outbreak and will be used to build the weight of epidemiological evidence required to remove the source from the marketplace. In addition, data will be collected on consumer food safety knowledge and practices, and prevalence of acute gastrointestinal illness.

MISSION STATEMENT FOR PROJECT: This project will provide data to inform enteric outbreak investigators, who will use this information to build the weight of evidence required to remove the source from the marketplace. This will be crucial for timely and effective response, reducing the impact of outbreak events on the health of Canadians.

2.28 Evaluation of Agar Media for the Isolation of Verotoxigenic *Escherichia coli*

A. Gill[1], G. Huszczynski[2], M. Gauthier[2], and B. Blais[2]

[1] Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Ontario Laboratory Network, Canadian Food Inspection Agency, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Verotoxin producing *Escherichia coli* (VTEC) are bacterial pathogens spread by contaminated food and water. An estimated 40-50% of VTEC illness is caused by VTEC of the O157:H7 serotype (serotype is a method of categorising bacterial isolates on the basis of antibody reactions to specific carbohydrate molecules on the cell surface), but 50-60% is caused by other VTEC serotypes. There are reliable methods of analysis for *E. coli* O157:H7, but not for other VTEC because they are difficult to distinguish from non-pathogenic *E. coli*. Analysis for VTEC is necessary to ensure accurate diagnosis, support risk assessment and to identify sources of contamination of food and water. Isolation on agar media is a key part of any methods of analysis for bacteria.

In this study eight agar media were assessed for their suitability for the isolation of VTEC. Of the media evaluated in this study, three media were highly inhibitory to the growth of VTEC, preventing the growth of 20 to 30%of the strains tested. The results of this study will be of value in informing testing for VTEC for the purposes of clinical diagnosis, public health surveillance and regulatory enforcement.

MISSION STATEMENT FOR PROJECT: The aim of this study is to provide information to inform the choice of methods for VTEC testing in the context of clinical diagnosis, public health surveillance and regulatory enforcement.

2.29 Surveillance of Verotoxin-producing *Escherichia coli* in Ground Beef, Cattle and Surface Waters: Implications for Interventions

R.P. Johnson[1], K. Pintar[2], and F. Pollari[3]

[1] Laboratory for Foodborne Zoonoses, PHAC, Guelph, ON
[2] C-Enternet, Centre for Foodborne and Environmental Zoonotic Infectious Diseases, PHAC, Ottawa, ON
[3] C- Enternet, Centre for Foodborne and Environmental Zoonotic Infectious Diseases, PHAC, Guelph, ON

PLAIN LANGUAGE SUMMARY: *Escherichia coli* O157:H7 and other *E. coli* known as Verotoxin-producing *E. coli* (VTEC) are bacteria shed in the manure of healthy cattle that can cause severe diarrhea and kidney failure in humans. Historically, most human VTEC infections have been considered foodborne, with ground beef as the most common exposure source. However, produce, water and contact with cattle and farms are known but lesser sources of human exposure. Monitoring of VTEC in these sources can identify changes in their prevalence that may increase or decrease the risks of human exposure and reveal opportunities to control these risks.

Over the past 14 years we have periodically and more recently under the C-Enternet program, regularly tested retail ground beef, cattle manure and impacted waters for VTEC using methods for *E. coli* O157 and other VTEC. During the past three to five years the prevalence of VTEC in ground beef has decreased by more than 50%, probably due to improved beef processing. This decrease may be reflected in an observed similar decrease in the number of human infections in the C-Enternet program. In the same period, testing of cattle manure has indicated healthy cattle continue to carry VTEC at high frequency, and water testing has revealed much higher than expected prevalence of VTEC. Together these results suggest that the risk of human exposure through ground beef is reduced and that dissemination of VTEC from cattle manure into farm environments and impacted waters carries a proportionally greater risk of transmission to humans. Accordingly, strategies to control VTEC in cattle and on the farm can potentially reduce the risks of human VTEC illness from sources other than ground beef.

MISSION STATEMENT FOR PROJECT: This study supports the need for an integrated animal/environmental/human approach to control of zoonotic foodborne and waterborne infections, as has been embraced by the “One Health” concept that addresses the broader aspect of the public health significance of interactions between animals, humans, microbes, food and their environments in zoonotic diseases in general.

2.30 Establishment of a Transparent Process for Reviewing Dietary Reference Intake Values

V. Dorais[1], K. Esslinger[1], D. Hayward[2], and A.J. MacFarlane[2]

[1] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON
[2] Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Dietary Reference Intakes (DRIs) are evidence-based values for nutrient adequacy and safety that underpin nutritional guidance, policies and regulations in Canada and the United-States. Some DRI values have not been re-visited since 1997. A process was needed to ensure these values continue to be accurate and founded on current evidence.

A Canada-US Joint working group was established to develop a process to identify and prioritise nutrients for review.

A nomination process was developed to engage DRI users from within and outside government, making the identification of candidate nutrients open and transparent.

The 90-day nomination period ended July 31, 2013, with 26 nominations submitted on nutrients linking diet, health, and chronic disease. Nominations will be assessed on the availability of significant, new, and relevant data as well as relevance to public health concerns. This proactive approach ensures that only nutrients deserving of a review will be considered further.

This work also reinforces the strong, collaborative relationship between both governments on this file, which has been fostered for over 15 years.

This is an innovative and cost-effective mechanism which will ensure that DRI values continue to be based on the best available evidence and are updated in a timely and appropriate manner.

MISSION STATEMENT FOR PROJECT: The governments of Canada and the United States have jointly undertaken the development of harmonized Dietary Reference Intake (DRI) values since the mid-1990s. Maintaining DRIs up-to-date ensures that Canadians' nutritional health and safety is best protected by having current and evidence-based food and nutrition guidance, policies and regulations.

2.31 The Role of Sanitizers in Controlling *Listeria monocytogenes* on Stainless Steel Surfaces

F. Pagotto[1,2], and K. Hébert[1,2]

[1] Research Division, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON
[2] Listeriosis Reference Service for Canada, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: A primary objective of the Bureau of Microbial Hazards within the Food Directorate is to minimize public health risk from consumption of contaminated foods. Proper maintenance and sanitization of food-contact and non-food-contact surfaces remains a high priority for the food industry in helping to ensure that their final products will be safe from a microbiological point of view. *Listeria monocytogenes*, a foodborne pathogen found in ready-to-eat foods and capable of causing serious illness such as meningitis, spontaneous abortions and death, is often present in factory environments and needs to be controlled to avoid contamination of final product. The effectiveness of commonly used sanitizers was tested against *Listeria* to verify their effectiveness in controlling this important foodborne pathogen. Sanitizers used at recommended concentrations and contact duration were deemed effective for the food industry in being able to control the survival of *Listeria*.

MISSION STATEMENT FOR PROJECT: This study demonstrated that sanitizers are effective in controlling *Listeria* on stainless steel surfaces when proper adherences to protocols were maintained. Misuse of sanitizers can allow the organism to survive on food-contact surfaces such as stainless steel and possibly make its way into the final food product.

2.32 Cloth-Based Hybridization Array System (CHAS) for Identification and Confirmation of *Listeria monocytogenes* and other *Listeria* Species

F. Pagotto[1], J. Xue[2,3], and B. Blais[3]

[1] Listeriosis Reference Service, Bureau of Microbial Hazards, Food Directorate, Health Canada, Ottawa, ON
[2] Department of Biology, Carleton University, Ottawa, ON
[3] Canadian Food Inspection Agency, Ottawa, ON

PLAIN LANGUAGE SUMMARY: *Listeria monocytogenes* is an important food-borne pathogen whose presence as a contaminant in foods and the food manufacturing environment is a major public health concern. The 2008, the largest Canadian listeriosis outbreak in ready-to-eat meat raised many issues over the safety and reliability of the national food supply. Three of the recommendations of the Weatherill, a comprehensive and independent investigation mandated to make recommendations to strengthen the Canadian food safety system as a result of this outbreak, specifically focused on the improvement and validation of methods in order to enhance responsiveness to foodborne emergencies.

Current detection techniques involving enrichment culture in order to allow for the target organism to grow to sufficient numbers prior to attempting isolation, followed by a variety of biochemical tests to help confirm the identify. These are time-consuming and labour-intensive. The purpose of this work was to develop a rapid test that would allow for confirmation of isolated bacteria as either *Listeria* species or *Listeria monocytogenes*, thereby allowing regulatory agencies to be able to make evidence-based decisions on the safety of the product in question.

MISSION STATEMENT FOR PROJECT: The work presented here supports the use of the LmCHAS as a reliable tool for the identification of food borne *L. monocytogenes*, significantly reducing the turnaround time for reporting results. In this assay, the genes acting as the basis for the species-specific markers are key elements in the pathogenic mechanism of *L. monocytogenes*, and their discernment in food-borne isolates will contribute significantly to risk-based regulatory decision making.

2.33 Inter-Laboratory Validation on an Enhanced Multiple-Locus Variable-Number Tandem Repeat Analysis (MLVA) Protocol for Subtyping *Listeria monocytogenes* from Food, Clinical and Environmental Sources

F. Pagotto[3], S. Saleh-Lakha[1], V. Allen[2], J. Li[1], J. Odumeru[4], E. Taboada[5], B. Blais[6], D. Ogunremi[6], G. Downing[7], C. Nadon[8], S. Lee[1], A. Gao[1], and S. Chen[1]

[1] Laboratory Services, University of Guelph, Guelph, ON
[2] Public Health Ontario, Toronto, ON
[3] Listeriosis Reference Service, HPFB, Health Canada, Ottawa, ON
[4] Ontario Ministry of Environment, Etobicoke, ON
[5] Public Health Agency of Canada, Lethbridge, AB
[6] Canadian Food Inspection Agency, Ottawa, ON
[7] Ontario Ministry of Agriculture and Food (OMAF), Guelph, ON
[8] National Microbiology Laboratory, PHAC, Winnipeg, MB

PLAIN LANGUAGE SUMMARY: *Listeria monocytogenes* is the causative agent of listeriosis, a rare and often fatal human infection. The majority of human cases of Listeriosis have been linked to the consumption of contaminated foods, especially ready-to-eat foods that require little to no preparation prior to consumption. Time to results is everything, especially when *Listeria* bacteria contamination is suspected. Public health and food inspection agencies need to act quickly to know what kind of *Listeria* they are dealing with, to stop potential outbreaks from occurring at the source while protecting the Canadian food supply. *L. monocytogenes* needs to be identified and characterized in a timely manner in order to diagnose infection, identify clusters and outbreaks, address environmental persistence, and help to mitigate any ongoing risks through the food chain. Genetic fingerprinting of bacteria, a DNA profiling approach to identify a specific individual pathogen from another, has been widely employed in recent years to determine the how similar bacteria are in various investigations to identify the precise source of the contamination.

This study aims to refine a novel approach, called multi-locus variable number of tandem repeats (or MLVA), to provide a rapid genetic fingerprint of strains of *Listeria* isolated along the farm-to-fork continuum.

MISSION STATEMENT FOR PROJECT: PulseNet is a critical surveillance system used to quickly identify and respond to foodborne disease outbreaks. A standardized laboratory method allows different laboratories to compare genetic fingerprints of foodborne pathogens and allows consistent communication of information about foodborne illnesses, indicating a common source of food contamination. By integrating the use of MLVA into the PulseNet system, it will be possible to further enhance molecular epidemiology, source attribution and outbreak investigations of important foodborne pathogens such as *L. monocytogenes*.

Toxicology

3.01 New Methods for the Analysis of Mutations in Sperm

M.A. Beal[1], J.M. O'Brien[1], F. Marchetti[1], and C.L. Yauk[1]

[1] Mechanistic Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Health Canada is leading international efforts to develop improved methods for identifying chemicals that induce mutations in germ cells (eggs and sperm) in order to protect the health of future generations. Mutations in germ cells can be inherited and cause adverse effects in offspring. Currently, there is a lack of effective tools to identify chemical agents that induce heritable mutations. Here, we describe two methods that we are developing for quantification of chemically induced mutations in the sperm of mutagen-exposed mice. The first method explores microsatellites, a type of unstable DNA, as a new target to detect changes in sperm following exposure to N-ethyl-N-nitrosourea (ENU), a well-characterized germ cell mutagen. We confirm that microsatellite mutation frequencies are elevated in mouse sperm following ENU treatment. Second, we adapted an existing method that uses mice containing a mutation 'reporter' gene to study mutation frequencies in somatic cells (i.e., any cells other than germ cells). We applied this method to analyse the sperm of mice exposed to benzo(a)pyrene, a classic mutagen.

We confirm that we can measure induced mutation in sperm using this approach. These new methodologies are much higher-throughput and use fewer animals than existing methods. We propose that these may be suitable alternatives to existing germ cell tests.

MISSION STATEMENT FOR PROJECT: This project will improve our ability to detect heritable mutations and allow for better regulation of environmental agents that may pose a risk to future generations.

3.02 Select Toxicant Yields and Salmonella Mutagenicity of Mainstream Smoke Emissions from Canadian “Super Slim” Cigarettes

R.M. Maertens[1], N. Mladjenovic[2], E.C. Soo[2], and P.A. White[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Office of Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Super slim cigarettes have a significantly smaller circumference than all other Canadian cigarettes and have the potential to be perceived as less harmful. This project examines the impact of the super slim design on levels of toxic chemicals in cigarette smoke (emissions) and on smoke toxicity. Smoke from 5 brands of super slim cigarettes was analyzed for select toxic chemicals and was tested for its ability to cause damage to bacterial DNA. The levels of chemicals measured in the smoke from the super slim cigarettes were often lower than the reference cigarettes and a best-selling regular sized brand. However, the super slim cigarettes containing mixed blend tobacco, as opposed to Virginia flue-cured tobacco, often had comparable or higher levels of some toxic chemicals relative to the references and best-seller. These mixed blend tobacco super slim cigarettes also caused similar or higher levels of DNA damage compared to the references.

This study provides insights into the effect of the super slim design on toxic smoke emissions and product toxicity. Based on this work, super slim cigarettes should not be considered ‘less harmful’ cigarettes. These findings support the public health consensus that there is no risk-free level of exposure to tobacco smoke.

MISSION STATEMENT FOR PROJECT: These findings support the current scientific and public health consensus that there is no level of exposure to tobacco smoke that is without risk.

3.03 A Health Risk Assessment of Carcinogenic Volatile Organic Compounds in Windsor, Ontario

A. Khanchi[1], C. Hebbern[1], and S. Cakmak[1]

[1] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: We investigated the excess cancer cases associated with personal exposure to carcinogenic volatile organic compounds (VOCs) in Windsor, Ontario where air pollution is a main concern. The personal concentrations used in the study were significantly higher than outdoor concentrations for most selected VOC species. As a result, outdoor concentrations underestimated the adverse effects. Personal concentrations of acetaldehyde and chloroform had the highest carcinogenic effects. We identified five possible sources for the chosen carcinogens: mobile, indoor, water, industrial and dry cleaning. In risk analysis of the sources, the industrial source (acetaldehyde, 1,2-dichloroethane) presented the highest cancer risk while the indoor environment (vinyl chloride, dichloromethane) had the lowest risk of adverse effects.

Our results help to understand the hazardous effects of VOCs on persons living in a Canadian city and are important for policy purposes.

MISSION STATEMENT FOR PROJECT: Canadian Air Quality Health Index uses outdoor central measurements to monitor air quality. Our study shows that outdoor measurements would significantly underestimate the carcinogenic effects of the pollutants. Meanwhile, focused effort is required to minimize exposure to VOCs with most carcinogenic adverse effects.

3.04 Cell Death and Regenerative Proliferation in Hepatocellular Carcinoma: The Effect of Furan on B6C3F1 Mouse Global Gene Expression in Liver

A.F. Jackson[1,2], A. Williams[1], L. Recio[3], M.D. Waters[3], I.B. Lambert[2], and C.L. Yauk[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Department of Biology, Carleton University, Ottawa, ON
[3] ILS, Inc., Research Triangle Park, NC 27709, USA

PLAIN LANGUAGE SUMMARY: Furan is a chemical that causes liver cancer in mice and rats. Understanding the effects of furan on biological systems is important because furan is a known contaminant in heat-treated foods and therefore might pose a threat to human health. The liver is a unique organ in that it has the capacity to regenerate itself upon injury. Regeneration occurs because the remaining, healthy liver cells are able to divide and replace damaged cells. The previously proposed mechanism for furan-induced liver carcinogenicity is chemically-induced liver injury followed by excessive liver regeneration, ultimately leading to tumour formation. This process has been previously observed by studying liver tissue and cells using microscopes, but it has not been studied using modern molecular biology approaches. Here we study how all of the genes in the mouse liver respond to furan treatment using modern 'genomics' technologies, in order to understand what changes are brought about by furan inside liver cells on a molecular scale. We observed cellular changes that are consistent with the previously proposed mechanism of furan carcinogenicity and gained a much more in-depth understanding of how this type of chemical affects cellular biology.

We also used furan as a case study to demonstrate how Health Canada regulators can use this type of state-of-the-art data to assess human health risk of this and other potential human carcinogens.

MISSION STATEMENT FOR PROJECT: We used furan as a case study to demonstrate how Health Canada regulators can use genomics data to support human health risk assessment of this and other potential non-genotoxic human carcinogens.

3.05 The Development and Implementation of a Workflow for RNA-Seq Data Analysis

R. Gagné[1], and C.L. Yauk[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: mRNA (messenger ribonucleic acid) is an early molecular product of a gene. Toxicogenomics measures changes in mRNA levels (known as gene expression) in response to chemicals and is becoming a standard analytical endpoint that's examined in toxicology. Scientists in the Mechanistic Studies Division (MSD) currently use DNA microarray technology for toxicogenomics. This technology is known to have numerous limitations including: 1) the technology is unable to analyse changes in mRNA that have not been included on the microarray; and, 2) the technology relies on changes in the fluorescence of probes and thus is not quantitative.

A new technology, Next Generation Sequencing (NGS), has emerged that resolves many of the microarray limitations and is now comparably priced. NGS RNA-sequencing (RNA-Seq) consists of reading in parallel, one nucleotide at a time, millions of fragments of RNA contained in a sample. Although powerful, the analysis RNA-Seq data is challenging and computationally extensive. We have developed a workflow for RNA-Seq data analysis that performs data quality control, mapping of RNA fragments to genes, and statistical modeling to calculate gene expression changes. Our pipeline will be useful to scientists at HC seeking to apply RNA-Seq in their experiments.

MISSION STATEMENT FOR PROJECT: This workflow provides an analytical approach for evaluating the quality of RNA-Seq data, mapping data to the genome, and analysing expression changes for HC scientist.

3.06 Integration of Metabolic Activation with a Predictive Genomics Signature to Classify Genotoxic Versus Non-Genotoxic Chemicals in Human TK6 Cells

J.K. Buick[1], I. Moffat[1,2], C.D. Swartz[3], A. Williams[1], D.R. Hyduke[4,5], L. Recio[3], A.J. Fornace Jr.[5], J. Aubrecht[6], and C.L. Yauk[1*]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Water, Air and Climate Change Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON
[3] Integrated Laboratory Systems, Research Triangle Park, North Carolina, USA
[4] Department of Bioengineering, University of California San Diego, La Jolla, California, USA
[5] Lombardi Comprehensive Cancer Center, Georgetown University, Washington, District of Columbia, USA
[6] Drug Safety R & D, Pfizer Inc., Groton, Connecticut, USA

PLAIN LANGUAGE SUMMARY: Health Canada is responsible for evaluating the health risks posed by chemicals to the Canadian population. Chemicals that are genotoxic (i.e., damage DNA) can cause adverse outcomes such as cancer and inherited genetic diseases. As such, genotoxicity testing is used to determine whether or not a chemical is able to damage DNA and is a critical component of chemical safety testing.

In this study, Health Canada collaborated with the Health and Environmental Sciences Institute (HESI) to determine whether changes in the regulation of genes (gene expression) can be used to predict genotoxicity. Gene expression changes provide an indication of cellular response to a chemical. We confirm that human cells in culture exposed to genotoxic and non-genotoxic agents exhibit changes in gene expression that accurately predict genotoxicity. We demonstrate that these changes are highly correlated with measures of DNA damage and cell survival. In addition, we confirm that the strength of the gene expression response can be used to predict the concentration at which genotoxicity begins to occur.

While further testing and refinement of this method are necessary, preliminary data suggest that this approach has the potential to add significant value to the existing genotoxicity testing system.

MISSION STATEMENT FOR PROJECT: The intent of this study is to develop a metabolically competent in vitro model for predictive toxicogenomics that provides rich mechanistic data to complement the standard genotoxicity testing strategy. This will allow for more effective regulation of genotoxic chemicals. This genomic biomarker is currently under formal evaluation by the US Food and Drug Administration as a first step in accomplishing a more integrated genotoxicity testing battery to better inform human health risk assessment.

3.07 Integrating Male Germ Cell Analysis into the Transgenic Rodent Mutation Assay

J.M. O'Brien[1], M.A. Beal[1], C.L. Yauk[1], and F. Marchetti[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: An identified testing gap in chemical risk assessment is the lack of practical methods for identifying agents that cause DNA mutations in germ cells (sperm or egg). Germ cell mutations may be inherited and cause adverse health outcomes in unexposed offspring. The transgenic rodent (TGR) mutation assay is a method recently endorsed by the international risk assessment community for testing the ability of chemicals to induce DNA mutations, and is now routinely used to screen chemicals for mutagenicity in numerous somatic (non-germ) tissues including lung, liver, and colon. However, the experimental design (i.e., timing of dosing and tissue collection) for somatic cell testing is not suitable for the analysis of male germ cells. Here we assess three strategies for integrating male germ cell analysis into the TGR mutation assay. Our results indicate that all three strategies are capable of detecting chemically-induced DNA mutations in male germ cells, but vary in terms of sensitivity, specificity, economic feasibility, and technical complexity. These strategies integrate male germ cell testing into an internationally recognized method for detecting induced DNA mutations, can be easily incorporated into the current risk assessment program, and ultimately improve Health Canada's ability to protect future generations from chemically-induced heritable mutations.

MISSION STATEMENT FOR PROJECT: The presented strategies integrate male germ cell testing into an internationally recognized method for detecting chemically-induced DNA mutations, can be easily incorporated into the current hazard identification/risk assessment program, and ultimately improve Health Canada's ability to protect future generations from heritable mutations caused by chemical exposure.

3.08 Rodent Developmental Neurotoxicity (DNT) Study Paradigm: Consultation and Development Process for Establishing Additional Guidance for Regulatory Reviewers

F. Bailey[1], and W. Bowers[2]

[1] Toxicology Re-evaluation Section-1, Health Evaluation Directorate, PMRA, Health Canada, Ottawa, ON

[2] Environmental and Radiation Health Sciences Directorate, Health Environments and Consumer Safety Branch (HECBS), Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The rodent Developmental Neurotoxicity (DNT) study paradigm has evolved over time with the most recent test guidelines updated in 2007 with the introduction of Organizations for Economic Co-operation and Development (OECD) guideline 426. Despite this, there has been a continued interest in developing additional guidance for reviewers responsible for evaluating chemicals that trigger this kind of an assessment. As this study is labour and resource intensive and the results are important to the regulatory process when the study is required, an initiative was created to retrospectively look at the DNT protocol from a regulatory context, in order to re-establish and re-iterate the study parameters that are crucial to the assessment of DNT. Identification of these parameters was a NAFTA-inspired multi-governmental initiative that involved consultation with both governmental and non-governmental stakeholders. Following an extensive consultation process, a joint USEPA-PMRA intergovernmental group was formed to create a document that would serve as a Standard Evaluation Procedure (SEP) for regulatory reviewers in both countries.

Health Canada has undertaken this initiative to provide better context to key parameters necessary for the review of a DNT study, not only for the individual behavioural tests, but for their integration into the weight of evidence for the entire study and for the ultimate assessment of hazard and risk. The SEP document will be the net result of this process.

MISSION STATEMENT FOR PROJECT: The development of additional guidance for reviewers who are responsible for evaluating DNT studies will improve the efficiency of assessment while maintaining or improving the scientific defensibility and human health protectiveness of regulatory pesticide risk assessments.

3.09 Analysis of Tea Samples for Radiocesium Contamination by Gamma Spectroscopy

M.C. Cook[1], B. Todd[1], W. Zhang[2], M.J. Stukel[2], S. Kiser[1], J.-F. Mercier[1], and M.W. Cooke[1]

[1] National Monitoring Section, Radiation Surveillance Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

[2] Verification and Incident Monitoring Section, Radiation Surveillance Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: As part of an ongoing Total Diet Study (TDS), the National Monitoring Section (NMS) of the Radiation Protection Bureau (Health Canada) routinely analyzes a wide variety of food products collected by the Canadian Food Inspection Agency for radionuclide content. As a result of this ongoing surveillance, several dried tea samples were shown to contain radiocesium originating from the March 11, 2011 Fukushima Daiichi nuclear disaster. Radiocesium, due to its high volatility and chemical reactivity, is rapidly dispersed into the environment and readily enters the food supply thus creating a potential health concern.

In this investigation, gamma spectroscopy was used to determine both the level and the source of radiocesium contamination of imported dried tea samples from Japan. In addition to the samples received from the CFIA, ten additional Japanese tea samples were purchased locally in Ottawa and analyzed for radiocesium content. The most active dried tea sample was also treated with boiling water to determine how much radiocesium is extracted during the typical preparation of a cup of tea.

The ratio of radiocesium isotopes measured in the tea indicated contamination from the Fukushima-Daiichi nuclear incident. Approximately 50-60% of the radiocesium was extracted from the tea during preparation. The ongoing monitoring of food products by NMS helps to safeguard the health of Canadians in accordance with Health Canada's mandate.

MISSION STATEMENT FOR PROJECT: This project illustrates the capacity of the National Monitoring Section to detect radiological contamination at levels far below intervention guidelines, ensuring that the Canadian food supply is safe.

3.10 Method Development for the Separation and Analysis of Radio-Strontium and Radio-Yttirum in Milk by Ion Chromatography

M.C. Cook[1], A. Botti[1], P. Czechura[1], J.-F. Mercier[1], and M.W. Cooke[1]

[1] National Monitoring Section, Radiation Surveillance Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The National Monitoring Section (NMS) of the Radiation Protection Bureau (Health Canada) routinely analyzes milk for radiostrontium (Sr-90) contamination. Sr-90 emits beta-particles and is generated during nuclear energy production and nuclear testing and is found in reactor waste. Since it is chemically very similar to calcium, it readily accumulates in bone thus posing a serious health concern. The current method is lengthy and a new method was developed to rapidly analyze milk samples for Sr-90 and its decay product, radioyttrium (Y-90). In the event of a nuclear emergency and for routine analysis, the new method will allow rapid screening of samples for Sr-90/Y-90 content.

MISSION STATEMENT FOR PROJECT: This project augments the emergency response capabilities of the NMS by enhancing its capacity to analyze a high volume of samples that would be anticipated in such an event, thus helping to ensure the safety of the Canadian food supply.

3.11 Antimicrobial Susceptibilities of *Neisseria gonorrhoeae* Isolated in Canada, 2010-2012

G. Liu[1], P. Sawatzky[1], V. Allen[2], L. Hoang[3], B. Lefebvre[4], M. Lovgren[5], D. Haldane[6], P. Van Caeseele[7], G. Horsman[8], R. Garceau[9], S. Ratnam[10], T. Wong[11], and I. Martin[1]

[1] Bacteriology and Enteric Diseases Program, National Microbiology Laboratory, PHAC, Ottawa, ON
[2] Public Health Ontario Laboratories, Toronto, ON
[3] British Columbia Centres for Disease Control Public Health Microbiology & Reference Laboratory, Vancouver, BC
[4] Laboratoire de santé publique du Québec, Ste-Anne-de-Bellevue, QC
[5] Provincial Laboratory for Public Health, Edmonton, AB
[6] Queen Elizabeth II Health Sciences Centre, Halifax, NS
[7] Cadham Provincial Laboratory, Winnipeg, MB
[8] Saskatchewan Disease Control Laboratory, Regina, SK
[9] Hôpital Dr. G.L. Dumont, Moncton, NB
[10] Newfoundland Provincial Laboratory, St. John's, NF
[11] Centre for Communicable Diseases and Infection Control, PHAC, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Public Health Agency of Canada's National Microbiology Laboratory performs testing on isolates of gonorrhea to see if they show resistance to antibiotics. The isolates are sent by provincial or hospital laboratories that have either found the isolate to have antibiotic resistance or did not test it for resistance. Antibiotics tested for gonococcal resistance at the NML include penicillin, tetracycline, spectinomycin, erythromycin, ceftriaxone, ciprofloxacin, cefixime and azithromycin.

The percentage of isolates of gonorrhea with decreased susceptibility to cefixime increased 0.9% from 3.3% to 4.2% between 2010 and 2011 but decreased by 2.0% to 2.2% in 2012. The percentage of isolates with decreased susceptibility to ceftriaxone decreased by 1.0% from 7.2% to 6.2% between 2010 and 2011 and decreased another 0.7% to 5.5% in 2012. The percentage of all isolates tested between 2010 and 2012 (9,366) that were resistant to penicillin, tetracycline, erythromycin or ciprofloxacin ranged from 23% to 31% while the percentage of azithromycin resistance was 0.8%. This data is used to inform the Canadian Guidelines on Sexually Transmitted Infections, which are treatment guidelines for sexually transmitted infections to help ensure that gonorrhea is treated with effective drugs.

MISSION STATEMENT FOR PROJECT: The Canadian Guidelines on Sexually Transmitted Infections rely on the surveillance of antimicrobial resistance of *Neisseria gonorrhoeae* in Canada to ensure effective treatment of gonorrhea.

3.12 Microbial Composition and Cytotoxicity of a Model Consortium Intended for Bioremediation Applications

G. Coleman[1], J. Crosthwait[1], P.S. Shwed[1], D. Ashby[2], and A.F. Tayabali[1]

[1] Biotechnology Laboratory, Mechanistic Studies Division, Environmental Health Science and Reearch Bureau, HECSB, Health Canada, Ottawa, ON

[2] Biotechnology Section, CEPA New Substances Assessment Division, New Substances Assessment and Control Bureau, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Our laboratory studies the potential virulence characteristics of microorganisms for input into screening assessments conducted by Health Canada and Environment Canada evaluators. Here, we summarize the complex nature of a mixture of microorganisms known as a consortium using microbiological, toxicological, and genomic tests.

The results show that the microbial population changes over time. Molecular biology methods were able to identify the closest related species. Toxicity was relatively low towards cultured human cells. Additionally, susceptibility to ten clinically relevant antibiotics was tested. The preliminary information provided here gives insight into the complex nature of consortia and the challenges associated with characterizing their composition and toxicity.

MISSION STATEMENT FOR PROJECT: To study the pathogenic potential and virulence characteristics of a microbial commercial product for input into screening assessments conducted by Health Canada and Environment Canada evaluators.

3.13 Exposure to Carbon Black Nanoparticles Induces Chronic Inflammation, Affects Smooth Muscle Contraction and Induces DNA Damage Response in Mouse Lungs

M. Husain[1], Z.O. Kyjovska[2], J. Bourdon[3], A.T. Saber[2], K.A. Jensen[2], N.R. Jacobsen[2], A. Williams[1], H. Wallin[2], S. Halappanavar[1], U. Vogel[2], and C.L. Yauk[1]

[1] Mechanistic Studies Division, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] National Research Centre for the Working Environment, Copenhagen, Denmark
[3] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Nanoparticles (NPs) are very small particles with dimensions of 1-100 nanometers (10 million nanometers = 1 centimetre). Carbon black nanoparticles (CBNPs) are NPs that are used extensively in consumer products. As such, there is a potential for environmental and occupational exposures to CBNPs. Our previous work showed that CBNPs induce various adverse effects in exposed rodents including inflammation one, three and 28 days after the initial exposure. However, effects at very early (initiating) or late (persistent) post-exposure time points are unknown.

To understand the series of molecular changes that occur in cells/tissues to respond to a CBNP exposure, and to understand what effects may persist for long periods of time, we exposed mice to CBNP and collected lung tissues 3 hours, and 1, 2, 3, 4, 5, 14 and 42 days post-exposure. We examined changes in the regulation of genes at all of these times to provide comprehensive insight into the immediate and sustained biological effects. Our data show that CBNP immediately induces inflammation and has a number of sustained effects in the lungs associated with muscle contraction and inflammation. These results will be used by Health Canada to further our understanding of particle-induced lung effects and direct further research on NP-induced long term effects.

MISSION STATEMENT FOR PROJECT: The results of this study will be used by Health Canada to direct further research on nanoparticle-induced long term effects to help better assess the health risks from nanoparticle exposures.

3.14 Systemic Effects of Exposure to Titanium Dioxide Nanoparticles Include Translocation to Heart and Activation on the Complement Cascade

P. Gupta[1], D. Wu[1], M. Husain[1], A. Williams[1], Z.O. Kyjovska[2], A.T. Saber[2], U. Vogel[2], H. Wallin[2], and S. Halappanavar[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] National Research Centre for the Working Environment, Copenhagen, Denmark

PLAIN LANGUAGE SUMMARY: Nanoparticles (NP) are materials that measure 1-100 nm in size and are extensively used in industrial biomedical, and consumer applications. Titanium dioxide (TiO_2) NP are the most extensively produced NP and are readily used in paints, tissue implants and cosmetics. TiO_2 NP can induce toxic effects in lungs and can translocate from lungs to blood and other organs in animals. However, the biological effects of such translocation are not understood. In this study, mice were exposed to TiO_2 NP by direct lung deposition and the effects of translocation of TiO_2 NP from lungs to blood, liver and heart were assessed 24 hours following exposure. Results confirmed translocation of TiO_2 NP from lungs to liver and traces of TiO_2 NP to blood and heart. Expression levels of several genes and proteins involved in inflammation and the immune system were altered in heart and blood. On the contrary, liver showed no effects.

These results shed new light on responses of the cardiovascular system to particle translocation, which will provide guidance for future research in the field and support the risk assessment and management of NP-induced health effects.

MISSION STATEMENT FOR PROJECT: The results of the study provide insight into the mechanism of action of NP of titanium dioxide, and will help form a baseline level of understanding that will help in the interpretation of other studies of the health impacts of NP. In the long term, this work will identify markers of exposure to NP that will facilitate the assessment of health risks associated with novel NP.

3.15 The Establishment and Validation of an *In Vitro* Mutagenicity Assay Based on Primary Hepatocytes from the Muta™ Mouse

J.A. Cox[1,2], E.P. Zwart[3], M. Luijten[3], and P.A. White[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Department of Biology, University of Ottawa, Ottawa, ON
[3] Laboratory for Health Protection Research, National Institute for Public Health and the Environment, Bilthoven, Utrecht, The Netherlands

PLAIN LANGUAGE SUMMARY: Health Canada routinely uses cultured animal cells to assess chemical toxicity. The increasing use of cells grown in the laboratory reflects a global shift away from toxicity testing in experimental animals. Induction of genetic (DNA) damage is correlated with a chemical's ability to cause cancer, and assessment of genetic toxicity is an important component of regulatory evaluations. Unfortunately, genetic toxicity assessment in cultured cells is technically challenging. One problem is a lack of physiologic similarity between the cultured cells and healthy animal tissue. For example, the cells employed are often similar to cancerous tissue, rather than normal tissue. Additionally, some chemicals that cause genetic damage must be metabolized in organs like the liver, and this metabolic processing is difficult to simulate.

To address these issues, and provide an improved system for genetic toxicity assessment, we have developed a system based on primary liver cells isolated from a strain of mouse known as the Muta™Mouse. The cells behave like normal liver cells, are capable of metabolizing chemicals, and permit the use of the reliable Muta™Mouse mutation scoring system. Once fully characterized and validated, the test will be a valuable tool for the regulatory assessment of potentially dangerous chemicals.

MISSION STATEMENT FOR PROJECT: Once completed, this project will provide Health Canada and the regulatory toxicology community in general, with a valuable tool for efficiently assessing the hazards posed by new and existing chemicals in Canada.

3.16 Development of an *in vitro* Screening Regime for Evaluating the Differential Effects of Different Zinc Oxide Nanoparticles

Y.M. Zhang[1], K.C. Nguyen[1], D.E. Lefebvre[2], P.S. Shwed[1], J. Crosthwait[1], G.S. Bondy[2], and A.F. Tayabali[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Materials composed of zinc oxide nanoparticles (ZnO-NPs) are used and sold commercially for cosmetic, food, medical and industrial applications. The widespread use of ZnO-NPs means that evaluators and policy makers must have a solid understanding of their chemical and physical characteristics and potential toxic effects. However, there is a scarcity of literature data on ZnO-NPs, whose characteristics and biological effects may be completely different from their bulk or atomic form. Thus far, this study has characterized the materials for size, shape and elemental content and evaluated their toxicity in mouse and human cells.

The results revealed that all materials were highly clumped and were capable of causing cell damage in a dose-dependent manner. Some cell types were more sensitive than others, and only some tests could demonstrate a difference in toxicity between various types of materials. This study has implications for the design of assays used in hazard evaluation of nanomaterials. The next stage of analysis will extend the work to immunological effects in animal exposures, and also testing of ZnO-NP containing consumer products.

MISSION STATEMENT FOR PROJECT: This study has implications for the design of assays used in hazard evaluation of nanomaterials, also provides useful scientific information for risk assessment and management of nanomaterials at Health Canada.

3.17 Identification of Potential Mechanisms of Neurotoxicity of Benzo(*a*)pyrene by Toxicogenomics Approach

N. Chepelev[1], A.S. Long[1], R. Gagne[1], W. Bowers[1], V. Arlt[2], P.A. White[1], and C.L. Yauk[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Analytical and Environmental Sciences Division, MRC-HPA Centre for Environment and Health, King's College London, UK

PLAIN LANGUAGE SUMMARY: Benzo(*a*)pyrene (BaP), a known human carcinogen, is a polycyclic aromatic hydrocarbon (PAH) formed during the incomplete combustion of organic matter. Exposures of laboratory animals to BaP and occupational exposures of humans to BaP, elicits a reduction in performance on neurobehavioural tests, suggesting that BaP exposure impairs learning and memory. Our recent review of the scientific literature suggests that the potential to induce behavioural alterations (neurotoxicity) may be more relevant to assessments of adverse human health impact than carcinogenicity. However, the mechanisms underlying the neurotoxicity of BaP are poorly understood.

Our goal was to investigate how BaP exposure can lead to adverse neurological effects in mice. We exposed adult mice to three consecutive daily oral doses of BaP alongside solvent control that are known to cause neurotoxic effects and examined changes in gene expression and the frequency of BaP-induced DNA damage in the brain. Our results indicate that BaP alters the expression of genes that are involved in the transmission of nerve impulse. The findings improve our understanding of the mechanisms underlying the neurotoxicity of BaP, and moreover, highlight neurological changes that may serve as indicators of neurotoxicity during regulatory evaluation.

MISSION STATEMENT FOR PROJECT: This research will ultimately permit the integration of neurotoxicity biomarkers into regulatory assessment of PAHs and other potential neurotoxins.

3.18 Application of Toxicogenomic Methods to the Investigation of Mechanisms Underlying the Immunotoxicity of the Potent Carcinogen Dibenso(*a,l*)pyrene

N. Chepelev[1], A.S. Long[1], A. Williams[1], B. Kuo[1], V. Arlt[2], P.A. White[1], and C.L. Yauk[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Analytical and Environmental Sciences Division, MRC-HPA Centre for Environment and Health, King's College London, UK

PLAIN LANGUAGE SUMMARY: Dibenzo(*a,l*)pyrene (DalP) is the most carcinogenic polycyclic aromatic hydrocarbon (PAH) examined to date. It undergoes metabolism in mammals to generate reactive products that can damage DNA. Preliminary experiments revealed that acute exposures of experimental animals to DalP cause a dramatic reduction in spleen size. This work employed global profiling of gene expression to identify the mechanisms by which DalP exposure leads to spleen atrophy. Understanding the mechanisms of DalP-induced spleen atrophy will facilitate the development of more refined approaches to identify immunotoxicity for risk assessment of PAHs. We exposed adult mice orally to DalP daily for three days. We measured gene expression and the frequency of DalP-induced DNA damage events in the spleen. DNA damage in the spleen increased with increasing dose, suggesting direct exposure of the spleen to DalP metabolites. Gene expression analyses revealed that DalP exposure alters the expression of a variety of genes that collectively control cellular growth and proliferation.

The findings are consistent with known biological processes leading to organ atrophy, and illustrate the utility of gene expression measurements for identifying the mechanisms of toxicity. sSpleen weight is routinely used to access adverse effects on the immune system.This work highlights the utility of incorporating assessments of gene expression changes into (geno)toxicity assessments of PAHs and other substances that may threaten the immune system.

MISSION STATEMENT FOR PROJECT: Our research highlights the utility of incorporating toxicogenomics into (geno)toxicity assessment of PAHs and other potential immunotoxicants.

3.19 Bisphenol A (BPA) Induces Differentiation of Human Preadipocytes in the Absence of Glucocorticoid and is Inhibited by an Estrogen-Receptor Antagonist

J.G. Boucher[1], A. Boudreau[1], and E. Atlas[1]

[1] Environmental Health Science and Research Bureau, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Obesity in Canada has increased significantly resulting in serious public health implications. While diet and physical activity impact weight gain, environmental pollutants such as endocrine-disrupting chemicals (compounds that affect hormones) have the potential to affect obesity. Currently, not enough information exists on the potential health problems associated with endocrine-disrupting chemicals to inform government policy decisions. We have developed BPA as a model chemical to assess the effect of endocrine-disrupting chemicals on the fat cell differentiation.

Our data show that BPA induces differentiation and fat accumulation in adipocytes. Using this model, it will be possible to screen additional environmental chemicals for their potential role in obesity and fulfill Health Canada's mandate.

MISSION STATEMENT FOR PROJECT: This project will help develop a human model to facilitate screening of environmental/industrial chemicals on obesity and adipocyte biology.

3.20 Phylogenetic Characterization and Differentiation of Total and Viable Microbes in Complex Microbial Mixtures

J. Crosthwait[1], G. Coleman[1], K. Curtis[1], G. Arya[1], A.F. Tayabali[1], and P.S. Shwed[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The risk assessment and monitoring of biotechnology products containing microorganisms is part of Health Canada's mandate. Several industrial products consist of mixtures or consortia of different microorganisms working together to produce a desired function. This project involves the evaluation/development of methods for identifying the components of products containing microbial consortia, with the focus on screening for pathogenic bacteria which may be harmful, as a means of supporting product assessments. Genetic material from one such product was isolated following treatment with a chemical which destroys the genetic material from dead organisms so that only live cells would be identified.

Over 20 different bacterial species were identified from sequencing of a marker gene indicating the mixture was highly complex and the treatment significantly altered the profile of organisms detected. The results of this study will be used to optimize future protocols for the analysis of more complex microbial mixtures.

MISSION STATEMENT FOR PROJECT: The development and optimization of methods to support the risk assessment of biotechnology products containing microorganisms.

3.21 *In Vivo* Assessment of Toxicity and Pathogenicity of a Model Microbial Consortium Product

K.C. Nguyen[1], Y.M. Zhang[1], K. Kittle[2], D. Patry[2], D. Ashby[3], M. Breton[3], K. Yambao[3], and A.F. Tayabali[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[3] New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Microorganisms have been shown to play crucial roles in environmental biotechnology applications including bioremediation, biofuel production, and as biopesticides. Microbial consortia, defined as a complex unformulated natural combination of microorganisms, have been of particular interest in these environmental technologies. Although bacterial consortia have been widely used in biotechnology, they might pose potential hazard and are required to be evaluated for their impacts to human health and the environment under the Canadian Environmental Protection Act (CEPA, 1999).

In this study, we applied an animal testing regime using a mouse model to assess the toxicity of a model consortium product that is used for cleaning oil contamination. Our results revealed lung immune responses, as well as effects in the blood and liver of mice exposed to this consortium product. The study provides evidence on the early immune effects and potential toxicity of the consortium and helpful data for screening assessments conducted by Health Canada evaluators.

MISSION STATEMENT FOR PROJECT: The study provides information on the pathogenicity potential of microorganisms used in biotechnology, which is helpful for risk assessments conducted by evaluators at Health Canada.

3.22 Toxicological Evaluation of OECD Reference Silver Nanoparticles

K.C. Nguyen[1], L. Richards[1], P. Rippstein[2], and A.F. Tayabali[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] University of Ottawa, Heart Institutes, Ottawa, ON

PLAIN LANGUAGE SUMMARY: With the increasing use of nanoparticles (NPs) in a wide range of applications and consumer products, screening for potential toxicity of nanoparticles is essential at Health Canada to ensure the health and safety of Canadians and the environment. Owing to their antimicrobial properties, silver nanoparticles (Ag-NPs) have widely been used in consumer, medicine, and cleaning products, leading to increased human exposure. Yet, information on their human health impacts is limited. This study investigates the toxicity of NM300K Ag-NPs, which is a representative manufactured NP under the Organisation for Economic Co-operation and Development (OECD) sponsorship program. Our results showed that at the test doses employed, NM300K induced toxic effects in mammalian cells by causing decreased cell viability, alteration of subcellular structures, inflammation and cell stress, leading to cell death.

This study presents evidence of the potential toxicity of silver nanoparticles. The data will ultimately be helpful for improving the understanding of nanomaterials for their risk assessment and risk management at Health Canada.

MISSION STATEMENT FOR PROJECT: These data may provide a better understanding for their risk assessment and risk management at Health Canada.

3.23 Tissue Biodistribution and Toxic Effects of Quantum Dot Nanoparticles in a Mouse Model

K.C. Nguyen[1,3], Y.M. Zhang[1], J. Todd[2], D. Parks[2], D. Patry[2], M. Lalande[2], M. Navarro[2], L. Casavant[1], L. Richards[1], W.G. Willmore[3], and A.F. Tayabali[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[3] Department of Biology and Institute of Biochemistry, Carleton University, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Nanomaterials (NMs) possess novel properties that lead to their widespread use in biotechnology applications and consumer products. The heightened production and use of NMs will result in greater exposure to consumers and workers. Therefore, the hazards associated with NMs need to be assessed. Health Canada is responsible for regulating the products of nanotechnology to ensure the health and safety of Canadians. Much research at Health Canada is needed to understand the behaviour and effects of NMs when they are introduced into biological systems. Quantum dots are a class of nanoparticles that, because of their unique optical and electrical properties, have been widely used in a variety of applications including electronics, computing, biomedical imaging, and therapeutics. However, the toxicity of these nanoparticles has not been thoroughly investigated.

This work examined the tissue distribution of cadmium telluride quantum dots (CdTe-QDs) in mice and what health consequences followed after they were intravenously injected into test animals. Preliminary data obtained from a pilot study showed that at the highest test doses, CdTe-QDs affected animal health/wellness. Effects included mild difficulty in breathing, dehydration and body weight loss. CdTe-QDs were observed in the blood, lung, liver, spleen, and brain. The results reveal the potential toxic effects and a preference for certain target tissues. The data provides preliminary information on the behaviour of NMs within living organisms, potential health effects, and insights into methodology which will be helpful in the risk assessment of NMs.

MISSION STATEMENT FOR PROJECT: The study provides preliminary information on the behaviour of nanoparticles within living organisms and their potential health effects, which should be helpful for risk assessment and management of nanomaterials at Health Canada.

3.24 Human Exposure Factors for Cosmetics and Personal Care Products

L. MacKinnon[1], M. Patel[1], C. Chun[1], B. Lo[1], R. Moore[2], M. Shaw[1], and A. Zidek[1]

[1] Existing Substances Risk Assessment Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

[2] New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Humans use a variety of cosmetics and personal care products every day. The way people use these products, such as how much they apply and how often, are important when estimating exposure to substances that may be present in these products. The Existing Substances Risk Assessment Bureau (ESRAB) and the New Substances Assessment and Control Bureau, have reviewed and assessed existing use pattern data for cosmetics and personal care products (PCPs). This data is used in exposure assessments conducted under Canada's Chemicals Management Plan (CMP). Use pattern data for cosmetics and PCPs were collected from the published literature and existing guidance documents. This information was analyzed using a rating system and resulted in the recommendation of exposure factors for approximately 30 cosmetics and PCPs for various age groups.

This is the first time this type of data specific to PCPs have been compiled across such a wide range of product types and subpopulations including adults, adolescents, children and infants for regulatory use. This work will provide a consistent approach and strengthen exposure assessments conducted under the CMP. Future work includes the evaluation of 16 additional cosmetics and PCPs in 2013/14.

MISSION STATEMENT FOR PROJECT: Development of exposure factors for estimating potential exposure to substances present in cosmetics and personal care products using a rigorous, systematic process provides a consistent and up-to-date source of information. This in turn supports and strengthens ongoing risk assessment work under the Chemicals Management Plan as well as other programs assessing or managing risks associated with this product sector.

3.25 Developmental Effects of Legacy Brominated Flame Retardants from House Dust in Rats

E.W.Y. Tung[1], A. Kawata[1], M. Rigden[1], B.F. Hales[2], and M.G. Wade[1]

[1] Hazard Identification Division; Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] Department of Pharmacology and Therapeutics, McGill University, Montreal, QC.

PLAIN LANGUAGE SUMMARY: Brominated flame retardants (BFRs) are extensively used as additives in commercial products including electronics, textiles, and polyurethane foam. Some forms of these have recently been banned from use in Canada following similar bans elsewhere. Because of the very widespread use of these banned forms, all Canadians will continue to be exposed as they are released into our homes and workplaces from the furnishings and consumer products that contain them. We initiated a series of studies to determine if the continued presence of BFRs in everyday environments constitutes a hazard.

The current study examined how exposure to an environmentally relevant mixture of BFRs during pregnancy and lactation may impact long-term health. Pregnant rats were exposed to a mixture of BFRs during gestation and lactation by diet. General markers of postnatal development including body weight, food consumption, developmental markers, and onset of puberty were monitored. At various time points, tissues were collected and assessed. Dam evaluations showed no differences among treatment groups, except increased liver weights. Results from offspring suggest that higher doses influence infant development but lower, more environmentally-relevant doses have no effect. These results do not indicate a need for aggressive removal of legacy BFRs from home and work environments.

MISSION STATEMENT FOR PROJECT: This project will help determine if there is a need for further action to limit exposure to legacy flame retardants (PBDEs and/or HCBD) that remain in the built environment as components of furnishings, consumer products, and building materials.

3.26 *In Vitro* Cellular Responses to Silica Nanoparticles: Genotoxic Potential

S. Prasanna Mukherjee[1], D. Wu[1], M. Johnston[2], S. Bernatchez[3], M. Hill[3], and S. Halappanavar[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Centre for Vaccine Evaluation, Biologics and Genetic Therapies Directorate, Health Canada, Ottawa, ON
[3] New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Nanoparticles (NP) measure ≤100 nm in any one dimension and may exhibit distinct size-associated properties. Silica nanoparticles (SiNPs) are widely produced and are used in electronics, solar cells, cosmetics, and for drug delivery. Heath Canada (HC) is responsible for regulating products on the Canadian market and for assessing potential human health risks. The current HC study has been undertaken to provide insight into the capabilities of SiNP of different sizes to cause DNA damage (genetic toxicity) and reveal how size plays a role in induced toxicity. In this study, mouse lung cells derived from normal Muta™mouse (a mouse model designed to investigate genetic toxicity) were exposed to various concentrations of commercially available SiNPs of nanometer (small) and micrometer (large) sizes.

Results revealed dose- and size-dependent responses, with the smallest SiNPs showing the highest amount of genetic toxicity, suggesting that their potential to induce genetic toxicity may be size-dependent. These findings will help build a comparative database that will aid in the assessment of the health risks of various types and sizes of SiNP.

MISSION STATEMENT FOR PROJECT: Silica nanoparticles (SiNP) are one of the most commonly produced nanoparticles and are used in many commercial applications in Canada. The results of the study provide insight into the genotoxic capabilities of SiNP of different sizes and reveal how size plays a role in induced toxicity. These findings will help build a comparative database that will aid in the assessment of the health risks of various types and sizes of SiNP.

3.27 Characterization of the Cytotoxicity Profile of Neutraplex Nanoparticles in Human Monocyte/Macrophage THP-1 Cells for HIV Reservoir Targeting

E. Berrger[1], D. Breznan[2], R. Vincent[2], and C. Lavigne[1]

[1] National HIV & Retrovirology Laboratories, National Microbiology Laboratory, PHAC, Ottawa, ON
[2] Environmental and Radiation Health Sciences Directorate, HECSB, HC, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Following infection, HIV virus hides within tissues or cells such as macrophages that are inaccessible to optimal levels of antiretroviral drugs, thus escaping the action of treatment. Nanotechnology-based vehicles represent new potential strategies to transport therapeutic molecules through natural barriers to targeted cells. In this study we wanted to investigate the potential of the lipid-based nanosystem named Neutraplex as a delivery strategy for antiviral drugs to target HIV in macrophages. More specifically we were interested in determining the safety of this nanosystem by evaluating its toxicity profile using human macrophage cells and various cytotoxicity assays.

Our microscopy studies showed that Neutraplex nanoparticles are rapidly and efficiently taken up by macrophages and are still abundantly found in the cells 48h following exposure. Nanoparticles were not found toxic for the cells. Therefore, this indicates that the Neutraplex nanosystem shows potential to transport drugs into macrophages to target HIV sequestered in these cells or to prevent or treat diseases affecting these important immune cells. Next, the Neutraplex nanoparticles will be used to better understand the molecular basis of the persistence of the virus in macrophages in order to aid in the design of novel nanotherapeutics aimed at purging HIV-1 infected patients of quiescent virus.

MISSION STATEMENT FOR PROJECT: The results of this research provide information on the efficiency and safety of nanoparticles as drug delivery systems for nanomedicine application.

3.28 Rapid Analysis of DNA Damage for Biological Dosimetry Using New Imaging Flow Cytometry Technology

L.A. Beaton[1], C. Ferrarotto[1], and R.C. Wilkins[1]

[1] Consumer and Clinical Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Dicentric Chromosome Assay (DCA), considered to be the gold standard for biodosimetry, has been adapted for use in emergency triage situations for biological dose estimates. The limiting factor has traditionally been the time required to prepare samples for the microscope-based method. A more rapid analysis of DNA damage is desirable for improved triage, and the use of new imaging flow cytometry technology will increase sample throughput. The imaging flow cytometer combines the sensitivity of microscopy with the increased statistical power of conventional flow cytometry.

Whole blood samples were drawn and irradiated to the prescribed doses. Post-irradiation, white blood cells were isolated and cultured. After incubation, the chromosomes were stained with fluorescent labels for centromeres and DNA content. Stained chromosomes were analyzed by imaging flow cytometry on the ImageStream^x (EMD Millipore).

Using the imaging flow cytometer, individual chromosomes could be identified and chromosomes with one or more centromeres could be counted. A dose response curve was generated. Details of the method and preparation of the dose response curve will be presented and compared to traditional microscope scoring as well as conventional flow cytometry.

In conclusion, the imaging flow dicentric chromosome assay (FDCA) allows for the rapid, semi-automated analysis of fluorescently labelled chromosomes. The assay requires further optimization but has the potential for fully automated, high throughput analysis for mass casualty events.

MISSION STATEMENT FOR PROJECT: This project aims to increase Health Canada's capacity for fully automated, high throughput analysis for biological dose estimates, in the case of a mass casualty event involving radiological or nuclear material.

3.29 Hepatic Gene Expression Microarray Profiles from Male Rats Exposed *In Utero* and/or During Lactation to Complex Mixtures of Environmental Contaminants

C. Cummings-Lorbetskie[1], G.-h. Xiao[1], K. Leingartner[1], A. Rowan-Carroll[1], M. Husain[1], A. Williams[1], C.L. Yauk[1], and D. Desaulniers[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Exposure to chemicals such as methylmercury and organochlorines, continue to raise health concerns for developing infants, since they persist particularly in food sources of Northern Canadians and have been detected in human tissues.

Mixtures of these contaminants were composed to mimic the levels detected in human blood. To determine the important time window of exposure, some rat litters were exposed prenatally and/or after birth during lactation. The genetic expression profiles of male offspring livers were characterised at pre-puberty and adulthood.

Various gene expression perturbations, which could initiate disease onset, were detected at pre-puberty; however these specific changes did not persist through adulthood. Different genetic changes with uncertain health effects were detected in adult offspring livers. Prenatal exposure to chemical mixtures caused minimal effects while exposure during lactation contributed the most to genetic profile alterations.

This research suggests that postnatal and not prenatal exposure to contaminant mixtures can affect liver gene expression, that these changes do not persist, and that the expression of different genes were altered during adulthood, but with uncertain biological consequences. These animal data can assist epidemiologists in refining developmental research strategies and bring awareness to regulators of the complexity of potential developmental origin of liver dysfunction.

MISSION STATEMENT FOR PROJECT: To highlight to epidemiologists and regulators the potential developmental origin of liver dysfunction following exposure to persistent bioaccumulative and toxic chemicals.

3.30 Automated Analysis of the Cytokinesis-Block Micronucleus Assay for Radiation Biodosimetry Using Imaging Flow Cytometry

M.A. Rodrigues[1,2], L.A. Beaton[1], B.C. Kutzner[1], and R.C. Wilkins[1]

[1] Consumer and Clinical Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON
[2] Department of Physics, Carleton University, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Following a radiation accident hundreds of casualties may need to be assessed for radiation exposure. One method to estimate dose is the cytokinesis-block micronucleus (CBMN) assay, performed via microscopy, which correlates the number of micronuclei (MN) to dose. While accurate, its use is impractical following a mass casualty event and automation of the method for higher throughput is desirable. With the development of new technologies such as the imaging flow cytometer, automation of the CBMN assay is now possible in a form that is free of user intervention.

Whole blood samples were irradiated and cultured, then analyzed on the ImageStream^X (EMD Millipore), an imaging flow cytometer. The ImageStream^X allows some of the sensitivity of microscopy to be maintained when quantifying relatively large radiation doses (> 1 Gy) and adds the increased throughput of flow cytometry.

Results indicate that binucleated cells (BNCs) and MN can be identified, imaged and scored automatically by imaging flow cytometry. Details of method development, gating strategy and dose response curves generated are presented.

The CBMN assay has been adapted for use with an imaging flow cytometer. Further optimization is required but the potential for high throughput analysis following a mass casually event is illustrated.

MISSION STATEMENT FOR PROJECT: This project aims to broaden Health Canada's capacity to perform fully automated, high throughput biodosimetric analyses to estimate biological dose following a mass casualty event involving radiological or nuclear material.

3.31 The Bureau of Food Surveillance and Science Integration Bioinformatics Lab

N. Petronella[1], and A.W. Pightling[1]

[1] Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Bureau of Food Surveillance and Science Integration Bioinformatics Lab (BL) was recently built to provide a flexible and powerful computer lab capable of offering Health Canada access to current and cutting edge computationally based research methods, effectively supporting genomics research and regulatory policies.
The BL is currently sustaining the Food Directorate's (FD) next generation sequencer (NGS), a machine that is capable of outputting entire genomes from isolated DNA within a few hours. It is primarily for this reason that NGS technologies are quickly becoming the standard in biological research.

As a result of being a novel technology, there is limited research establishing a thoroughly tested methodology for analyzing bacterial NGS results. Using the BL and simulated NGS data, a series of programs were rigorously tested to not only analyze their accuracy at assembling genomes and detecting mutations but also to establish a standard procedure for NGS research.

The BL is also collaborating on numerous other projects within and outside the department. One of which involves supplementing, innovating and increasing the efficiency of current research methods required for FD's *Clostridium botulinum* project.

MISSION STATEMENT FOR PROJECT: The Bureau of Food Surveillance and Science Integration Bioinformatics Lab offers Health Canada access to current and cutting edge computationally based research methods, effectively supporting genomics research and regulatory policies in addition to increasing innovation and reducing research costs.

3.32 The Genotoxicity of PAHs and Complex PAH Mixtures: Employing the *In Vivo* Muta™ Mouse TGR Assay to Evaluate the Assumption of Response Additivity

A.S. Long[1,2], C.L. Lemieux[3], C. Aroche[1,4], and P.A. White[1,2]

[1] Mechanistic Studies Division, Environmental Health Science and Research Bureau, Health Canada, Ottawa, ON
[2] Department of Biology, Faculty of Graduate and Postdoctoral Studies, University of Ottawa, Ottawa, ON
[3] Air Health Science Division, Water and Air Quality Bureau, Health Canada, Ottawa, ON
[4] Department of Biochemistry, Faculty of Science, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Humans are regularly exposed to complex mixtures of polycyclic aromatic hydrocarbons (PAHs) in the environment, many of which are carcinogenic. The process of assessing the health risks associated with exposure to complex mixtures of PAHs generally focuses on only a few targeted compounds, with the assumption that the expected incremental effects of each compound can simply be added (response additivity). This study evaluated this "additivity" assumption by examining the ability of selected PAHs and complex PAH mixtures to damage mouse DNA (i.e., produce mutations). Mice were exposed to 8 PAHs and 2 PAH mixtures, and the frequency of mutations was evaluated in bone marrow, liver, glandular stomach, small intestine, and lung. The response of the mixtures was then compared with that predicted using the tissue-specific responses of the individual PAHs and their respective concentrations in the mixtures. The results to date indicate that the observed effect of the complex mixture on bone marrow is less than would be predicted using the additivity assumption (sub-additive).

For other tissues, the observed mixture effect is more than would be predicted (supra-additive). These results provide a valuable evaluation of the approach commonly employed to assess the risk of adverse health effects posed by PAH-contaminated matrices.

MISSION STATEMENT FOR PROJECT: The ultimate goal of this study is to improve the confidence in the risk assessment process for PAH-contaminated matrices.

3.33 Developmental Neurotoxicity in Primary Neural Cell Culture using Gene Expression Markers

M. Singh[1], B.K. Padhi[1], and G. Pelletier[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Exposure to toxic chemicals during early life can injure immature brain and impair neurological functions. This is a matter of concern, since the potential neurotoxicity of most marketed chemicals remains untested. The use of laboratory animals to assess the potential effects of chemicals on foetal and infant's brain development is extremely costly and time-consuming, so developing alternative methods to screen and prioritize chemicals requiring further testing is a real need to protect children's brain health. To meet this necessity, we developed an alternative *in vitro* method that uses gene expression patterns in neuronal cells isolated directly from the juvenile rat brain. These cells are ideally suited for this assay as they mimic critical biological programs occurring in the developing brain.

The usefulness of this cell-based method as a predictor of neurotoxicity hazard will be further assessed by testing well-known neurotoxic pesticides acting through different molecular mechanisms along with non-neurotoxic compounds. This approach will hopefully lead to a useful method for the rapid screening of chemicals and for the prioritization of the ones that require further testing using animal models.

MISSION STATEMENT FOR PROJECT: Protecting the health of vulnerable populations is a part of Health Canada's mandate. The development and validation of this alternative *in vitro* neurotoxicity assay will improve the identification of potentially neurotoxic chemicals.

3.34 Identification of Splice Variants by Comparative Gene Sequence Analysis and Application to Toxicant-Induced Differential Gene Expression

B.K. Padhi[1] and G. Pelletier[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: In mammals, most genes can produce more than one transcripts by the selective retention or removal of specific sequence fragments by a process called “alternative splicing”. Rat is widely used as a model in toxicological studies, but alternative splicing is not well characterized in this species. Investigation of gene expression without proper consideration of undescribed gene splice variants can lead to erroneous results. To overcome this issue, we developed an approach where rat gene sequences are compared to sequences from other species where alternative splicing is better characterized to derive information on potential alternative gene splicing in rat. This approach was applied to the assessment of two genes involved in the formation of myelin sheets (which ensure proper conduction of nerve impulse) in rat brain following exposure to methyl mercury, a well-known neurotoxicant. We predicted and then confirmed the existence of undocumented splice variants of these myelin-associated genes in rat. Assessment of the expression of individual transcript variants of these genes in developing rat brain exposed to methyl mercury further confirmed that myelin producing cells are impacted by methyl mercury.

Application of this comparative sequence analysis approach has the potential to improve the quality and reproducibility of toxicogenomic studies, which in turn will benefit risk assessment.

MISSION STATEMENT FOR PROJECT: Health Canada is responsible for risk assessment of chemicals under chemical management plan. The application of comparative gene sequence analysis method will improve reproducibility of toxicogenomic studies and will ultimately benefit human health risk assessment.

3.35 Assessing Biomonitoring of Bisphenol A in Infants and Pregnant Women using Gestational Pharmacokinetic Models

A. Nong[1], D. Lefebvre[1], M. Fisher[1], and T.E. Arbuckle[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Concerns about exposure to various contaminants in the environment have led to efforts at gathering a growing database of chemicals measured in blood and/or urine taken from Canadians. These biomonitoring surveys provide a wealth of information on the extent of exposure to chemicals in the general population, but are less clear on susceptible populations such as pregnant women and infants. In the Plastics and Personal-Care Product use in Pregnancy (P4) Study, urine was collected from a small group of pregnant women and infants to measure levels of phthalates and their metabolites, bisphenol A, triclosan and triclocarban. Computer generated biological models can be used to describe the relationship between a person's exposure to a chemical and levels in their body.

At various life stages from infancy to adulthood, these models consider different biological processes that can affect the fate of a chemical in and out of the body. The aim of this work is to better describe the link between bisphenol A (BPA) levels in pregnant women and levels found in infants using data from the P4 study and computer based biological models. As a tool to support chemical health evaluation, these models will apply biomonitoring data to determine the exposure to pregnant women and the amount of environmental contaminants that can be transferred to their infants.

MISSION STATEMENT FOR PROJECT: This research tool will help interpret chemical exposure results from biomonitoring studies into a public health risk context for further evaluation and management actions.

3.36 Optimization of the VitroCell® Exposure System for *In Vitro* Toxicity Testing of Diesel Emissions at the Air-Liquid Interface

R. Greenan[1], T. Chan[2], M. Könczöl[3], J. Bourdon[1], D. Rosenblatt[2], M.-J. Poitras[2], and P.A. White[1]

[1] Mechanistic Studies Division, HECSB, Health Canada, Ottawa, ON
[2] Emissions Research and Measurement Section, Environment Canada, Ottawa, ON
[3] Department of Pharmaceutical Biology and Biotechnology, University of Freiburg, Germany

PLAIN LANGUAGE SUMMARY: Toxicity assessment of diesel combustion emissions and other aerosols is difficult and challenging. Combustion-derived aerosols are variable and contain highly complex mixtures of gases and particles; with a wide range of chemicals, both known and hitherto unidentified. Effective toxicological characterization of these mixtures requires complex animal inhalation exposures to diluted aerosols. The use of cultured animal cells for toxicity assessment of combustion emissions has often been regarded as unrealistic and impractical for regulatory decision-making. The VitroCell® exposure device permits exposure of cultured animal cells at an air-liquid interface, and thus provides a platform for real-time aerosol exposures and toxicity assessment. However, successful deployment of the device requires time-consuming optimization of exposure and toxicity assessment protocols.

Recent work involved optimization of cell culture and exposure conditions, as well adaptation of toxicity assessment procedures commonly employed to measure cell condition and viability. The results obtained to date confirm improvement of assessment performance and reliability. Optimized protocols will be used for comparative toxicity assessment of diluted diesel emissions generated from combustion of diesel, biodiesel, and diesel-biodiesel blends. The device and associated protocols will permit relatively efficient toxicity assessment of combustion emissions and other complex aerosols, which may assist in setting emissions standards to protect the health of Canadians.

MISSION STATEMENT FOR PROJECT: This project will culminate in the successful deployment of an aerosol toxicity assessment tool that can be used to generate data for comparative assessments of diesel emissions generated under a variety of engine design, fuel formulation and pollution-control scenarios. The data could influence policies related to use of alternative fuels and deployment of novel emission control devices.

3.37 Mass Spectrometry Analysis of DNA-Adducts

S. Mohottalage[1], A. Atwal[1], R. Vincent[2], and P. Kumarathasan[1]

[1] Analytical Biochemistry and Proteomics Laboratory, Mechanistic Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Inhalation Toxicology Laboratory, Hazard Identification Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Exposure to chemical components of environmental pollutants can bind to DNA resulting in alteration of DNA molecules along with many negative health outcomes in humans. Reliable methods to identify these altered DNA molecules (i.e., DNA adducts) can contribute to the assessment of possible mechanisms of chemical toxicity; and function as indicators of exposure. A common method used for detecting DNA adducts involves the use of toxic radio-chemicals; whereas our intention here was to develop a method that does not involve use of these toxic materials. We used an analytical instrument called a mass spectrometer to identify DNA adducts. Previously, we have shown that mass spectrometry could be used to identify adduct formation using two DNA damaging chemicals. Here we expanded the method to include the identification of adducts under more complex conditions.

Our results demonstrated that the methods developed here could be useful in mode of action and exposure assessments of these DNA damaging chemicals.

MISSION STATEMENT FOR PROJECT: The method developed in this project could enhance our knowledge necessary to improve existing environmental monitoring practices.

3.38 Maternal Proteomic Screening for Profiling and Pathways of Adverse Birth Outcomes

P. Kumarathasan[1], R. Vincent[1], D. Das[1], S. Mohottalage[1], E. Blais[1], K. Blank[1], S. Karthikeyan[1], N.Q. Vuong[1], T.E. Arbuckle[1], and W.D. Fraser[2]

[1] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] St-Justine Hospital, Montreal, QC

PLAIN LANGUAGE SUMMARY: Previous studies have linked mother's nutritional status and exposure to environmental pollutants including smoking during pregnancy to problematic pregnancies. However, biological mechanisms that are necessary to associate maternal exposures to pregnancy outcomes are not clear. For this purpose, Health Canada researchers have screened blood samples from pregnant women to identify biological changes such as protein changes that can explain the observed pregnancy outcomes. A small subset of third trimester blood samples were used from a mother-infant study (Maternal-Infant Research on Environmental Chemicals-MIREC) that was conducted under the National Biomonitoring and Surveillance Initiative of Health Canada. Blood plasma samples from mothers with low and normal birth weight babies were analysed for high content protein changes by mass spectrometry. Also, few known biologically significant proteins were analysed in the same samples by antibody-binding assays.

Our preliminary results exhibited that high content protein changes can allow identification of mothers who can be associated with negative pregnancy outcomes such as low infant birth weights. Information generated by the application of this approach can contribute to risk identification and to risk management by perhaps mitigation or intervention strategies.

MISSION STATEMENT FOR PROJECT: Information generated from this project will support the Department's biomonitoring efforts, risk assessment and regulatory processes.

3.39 Effects of Phthalates on DNA Methylation in Human Cells

C. Parfett[1], G. Zhou[1], D. Desaulniers[2], C. Cummings-Lorbetskie[2], and G.-H. Xiao[2]

[1] Mechanistic Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Hazard Identification Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Phthalates are a series of chemicals often used in medical and consumer products that have been shown, in animals, to affect DNA methylation, which is a physiological modification of DNA that regulates gene expression and genetic stability. The objective of the present work was to see if phthalates could affect global DNA methylation in human fetal-type liver cells grown in the laboratory. We used fluorescently modified antibodies specific for methylated DNA to measure changes in individual cells, caused by various phthalates. The measurement could be conducted relatively quickly (5 days) and over a range of concentrations for each phthalate. We show, for the first time in human cells, increases in DNA methylation caused by a phthalate, di-(2-ethylhexyl) phthalate. Greater increases in DNA methylation were caused by lower amounts of the primary metabolite that is formed in the liver (mono 2-ethylhexyl phthalate). Together with ongoing measurements of other phthalates, the test data shows that changes in DNA methylation may be a mode of action shared by many phthalates and their liver metabolites.

This is information that can be used to order the screening assessments of individual phthalates now being conducted under the Chemical Management Plan.

MISSION STATEMENT FOR PROJECT: The results will contribute to the human relevance of the assessment of the phthalate grouping of substances being assessed under the Government of Canada's Chemical Management Plan 3.

3.40 Sequencing Modification Site of a Chemical on DNA using Capillary Electrophoresis-Electrospray-Tandem Mass Spectrometry

L. D'Ulivo[1], and Y.-L. Feng[1]

[1] Exposure and Biomonitoring Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Studies on the mechanisms by which DNA damage is produced by chemicals are important for risk assessment because they allow the selection of the appropriate models for extrapolating from high levels of exposure used in lab experiments to the low levels found in the environment to which humans are exposed. DNA damage may also have merit as an indicator or biomarker of the level of human exposure to a chemical in the environment. The specific site that chemicals bind to DNA provides further mechanistic information that allows chemicals to be compared to one another. This study used capillary electrophoresis, a high resolution separation technique, and mass spectrometry to characterise the modification site and selectivity of chemicals to DNA. This method can provide precise information on which site on the DNA sequence is modified by the chemicals and which site is the preferred initial target of modification.

MISSION STATEMENT FOR PROJECT: This study was intended to develop new methods to identify how chemicals interact with DNA, which supports risk assessments by indicating potential toxicity modes of action and providing a potentially useful biomarker of human exposure to chemicals.

3.41 Evaluation of the Cytotoxicity Profile of Commercial Silicon Dioxide Nanaparticles

D. Breznan[1], D. Das[2], C. MacKinnon-Roy[1], D. Jurgens[1], A. Ha[1], J.M. O'Brien[1], S. Nimesh[1], N.Q. Vuong[1], S. Bernatchez[3], A. Afghan[3], M. Hill[3], P. Kumarathasan[2], and R. Vincent[1]

[1] Hazard Identification Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Mechanistic Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[3] New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Silica nanoparticles (SiNPs) have made their way into consumer products, everyday materials and medicine due to their novel properties compared to larger silica particles. However, these properties could also make them harmful to humans and/or to the environment. Therefore we need to determine how SiNPs may cause harm and which of their properties would be responsible. We studied the toxicity of three commercially available SiNPs in human lung epithelial cells, which line the lung air-exchange regions) and in human and mouse macrophages (cells which destroy foreign particles and bacteria in the body). We observed that SiNPs of similar size show different toxicity and that macrophages were more sensitive than epithelial cells. Next, we compared our toxicity data against a database that summarizes complex biological mechanisms and we identified biological pathways and molecules that are uniquely affected by the different particles. We then attempted to establish relationships between the biological measurements and the material properties of the SiNPs using statistical methods. We found that the most harmful SiNPs were the purest and the smallest. Our work will help evaluators to conduct human health assessments of SiNPs (and of other nanomaterials). In addition, this knowledge could help in the design of safer nanomaterials. This work was supported by Health Canada's EHSRB and NSACB funding.

MISSION STATEMENT FOR PROJECT: The project addresses priority knowledge gaps on the relationship between nanomaterial properties and toxicity to provide data required for evidence-based risk assessment of silica nanomaterials.

3.42 Key Considerations in Human Health Risk Assessment of Nanomaterials and Particles: Particle Toxicology, Molecular Toxicology, or Both?

M. Hill[1], A. Afghan[1], and S. Bernatchez[1]

[1] New Substances Assessment and Control Bureau, SED, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Particles come in all sorts of shapes, sizes and composition. Currently, particles are identified by nomenclature based primarily on chemical composition. One chemical name may represent a wide array of substances with the same composition but with varied physical-chemical characteristics (e.g., size distribution, shape, surface chemistry). Technological advances now allow the manipulation of matter at the nano-scale, resulting in the creation of novel substances with characteristics not always easily predicted from current knowledge. A substance with a fixed composition can now be engineered into many different forms (e.g., spheres, fibres, sheets) with varying physical characteristics. Although these different forms possess identical composition, changes in a particle's physical characteristics will influence the particle's physical-chemical and toxicological properties. The magnitude and specificity of this influence are currently impossible to predict in absence of particle specific test data. The near-limitless diversity of substances that can be engineered from one particular composition can result in some particles becoming toxic, some benign, while others may confer health benefits.

The goal of this work is to propose i) a logical paradigm for assessing particle human health risk under existing regulatory frameworks; and ii) a concern driven approach for focussing future toxicity testing requests for particles.

MISSION STATEMENT FOR PROJECT: To influence the paradigms used by Health Canada risk assessors when evaluating particles.

3.43 Impact of a Northern Contaminant Mixture (NCM) on Energy Metabolism and Cholesterol Homeostasis in the Liver of JCR Rats

R.J. Mailloux[1,2], M. Florian[1,2], Q. Chen[1], I. Petrov[1], M.C Coughlan[1], L. Mahemuti[1,2], M. Lalande[3], D. Caldwell[3], N. Li[4], W. Willmore[2], and X. Jin[1]

[1] Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Departments of Biology and Chemistry, Carleton University, Ottawa, ON
[3] Scientific Support Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[4] Hazard Identification Division, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Obesity, type 2 diabetes, and exposure to environmental contaminants can lead to the onset of fatty liver disease. To determine if and how simultaneous exposure to various environmental contaminants may play a role in the pathogenesis of obesity and other metabolic disorders observed in some Northern populations in Canada, rodents were exposed to a mixture of environmental contaminants to achieve levels of exposure similar to those found in some of the highly exposed human populations. The results show that at the exposure levels used, environmental contaminants exacerbate fatty liver disease in obese rats. This is achieved through disruption of mitochondrial metabolism and alteration the protein levels and function of various energy using pathways in the liver which induces the accumulation of fat and the onset of fatty liver disease.

These results illustrate that contaminant exposure can exacerbate fatty liver disease indicate that Northern Populations in Canada are more at risk for the development of fatty liver disease due to exposure to various toxins. These issues made HC understand that further work is needed to lessen the levels used.

MISSION STATEMENT FOR PROJECT: Results of this project will be reported to NCP.

3.45 Organ and Systemic Effects of a Northern Contaminant Mixture (NCM) in Obese and Lean JCR Rats Fed a Normal and High Fat/Sugar Diet

M. Florian[1,2], D. Patry[3], M.C. Coughlan[1], M. Laziyan[1,2], Q. Chen[1], M. Lalande[3], D. Caldwell[3], R.J. Mailloux[1,2], W.G. Willmore[2], and X. Jin[1]

[1] Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Departments of Biology and Chemistry, Carleton University, Ottawa, ON
[3] Scientific Support Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: We aimed to understand the role of diet, environmental pollutants and inherited genes in the development of metabolic and cardiovascular diseases. Obese and lean rats were exposed to a contaminant mixture at levels found in some of the highly exposed Northern populations. Concurrently, the rats were fed a normal or a high fat/sugar diet. Organ and systemic toxicity markers were measured at the end of the exposure. The results suggest that the liver and kidneys were affected by the contaminants the most severely, independently of the type of diet. In the liver, the contaminants disrupted lipid biosynthesis and/or transport, regardless of the type of rat and diet. However, the effects of contaminants on other parameters differed between rat strains and diets.The implications/relevance of these findings to Northern populations remains to be confirmed through epidemiological studies.

MISSION STATEMENT FOR PROJECT: Findings of this study will help to institute and implement additional strategies for contaminant control and health promotion among the populations in the Canadian North.

3.46 Strategic Genomic Characterization of Environmental *Bacillus megaterium* Strains to Yield Strain Specific Information

G. Arya[1], N. Petronella[2], J. Crosthwait[1], K. Curtis[1], and P.S. Shwed[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Bureau of Food Surveillance and Science Integration, Food Directorate, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Health Canada carries out the assessment of the potential for microorganisms used for biotechnology to adversely affect the health of Canadians. Many industrial microorganisms are closely related and derived from wild strains found in the environment. Understanding the shared and unique genes of the strains can provide information about how the strains function and if they may affect humans. This project involved comparing wild strains of one industrial microorganism by examining them in the lab on growth plates to the level of comparing fragments of their DNA contents. The industrial strain shared many features with most wild strains except one that featured different appearance and DNA fragment patterns. These two strains are now being compared in more detail for their entire DNA genome contents. The results of this study will help develop efficient procedures to provide bacterial strain genome specific information for risk assessment.

MISSION STATEMENT FOR PROJECT: To develop strategic methods that enable identification of genomic differences between biotechnology microbial strains. These methods will ultimately result in data that will be used in risk assessments conducted under CEPA (1999).

Biomonitoring, Therapeutics and National and International Policy

4.01 Analytical Survey of Liquid-Gel Products

J. Bellemare[1], P. Lacroix[1], F. Beraldin[1], K. Lebel[1], C. Taillon[1], C. Deschênes[1], A. O'Brien[1], S. Levesque[1], Y.-L. Trottier[1], and J. Gagnon[1]

[1] Inspectorate Laboratory, RAPB, Quebec Region, Regions and Programs Bureau, Health Canada, Longueuil, QC

PLAIN LANGUAGE SUMMARY: Soft gel capsules are an increasingly popular dosage form of pharmaceutical products. Consumers often prefer gelatine capsules because they have a neutral taste and aroma in addition to being easy to swallow. From a manufacturing standpoint, this type of formulation offers the advantages of better accuracy, uniformity of dosage, and stability due to less degradation.

When elaborating this survey, the Inspectorate Laboratory Programme considered some risk criteria: liquid-gel products have a short history of use, have not been surveyed yet, are susceptible to microbiological contamination, and are increasingly sold over the counter (not reviewed as thoroughly as prescription drugs). 20 products were submitted to the Inspectorate laboratories for microbiology testing. Each product was analyzed according to the company's method.

14 samples out of 20 were deemed satisfactory. The judgment was based on the documentation provided and the compliance of the sample to its specifications. Only one sample was judged unsatisfactory because of a bacterial contaminant (*Ralstonia mannitolilytica* as identified by biochemical tests with the Vitek 2 system). A Health Risk Evaluation was performed by the Therapeutic Product Directorate. It was determined that the presence of this organism represented a low risk considering that the product is administered orally and that the bacterial count was within the product's specifications.

In conclusion, there is no evidence indicating that liquid-gel formulations represent a higher risk than other formulations requiring enumeration tests and tests for specific microorganisms. The Inspectorate Programme will re-sample unsatisfactory products to verify whether compliance has been achieved and will continue to conduct surveys on products that require enumeration tests.

MISSION STATEMENT OF THE PROJECT: Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health.

To this effect, Health Canada verifies that the regulatory requirements relating to the safety, quality and effectiveness of health products are complied with, by carrying out risk assessments, which may take the form of surveillance activities, verification of the compliance and enforcement of the regulations. In addition, Health Canada provides information worthy of faith and evidence-based to Canadians and the health care professionals in order to enable them to make informed decisions.

The objective is to ensure that Canadians have access to health products safe, effective and of high quality.

4.02 Health Canada's "Information for Health Care Professionals-Cannabis and the Cannabinoids": A New, Comprehensive Monograph on the Science of Cannabis and the Cannabinoids and the Potential Therapeutic Uses of Cannabinoids and *Cannabis sativa*

H. Abramovici[1]

[1] Research, Synthesis and Dissemination Division, Office of Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Since 2001, Health Canada has managed a program that allows Canadians suffering from grave and debilitating illnesses to access marihuana (cannabis) for therapeutic purposes. Cannabis is not an approved therapeutic substance in Canada, and as such, no traditional medical information document has been published by any commercial sponsor. However, Health Canada has been publishing an information document on cannabis since 2003. Similar to the detailed information document destined for physicians, this document was created to provide some guidance to physicians on the potential therapeutic uses of cannabis.

In response to calls by the medical community for up-to-date and comprehensive information on the therapeutic uses of cannabis, Health Canada launched an international and Canadian-based expert review of the document. The updated product is the most comprehensive of its kind, containing in-depth information on the science and medicine of cannabinoids and cannabis. This information document will also serve as the basis for additional educational initiatives on the potential therapeutic uses of cannabis. It is hoped that together, these educational materials will help physicians in their discussions with patients on the subject of marihuana (cannabis) for medical purposes.

MISSION STATEMENT OF PROJECT: The "Information for Health Care Professionals: cannabis and the cannabinoids" document is Health Canada's principal information document for physicians on the potential therapeutic and adverse effects associated with the use of cannabis and cannabinoids. This document will help inform physicians on the science of cannabis for medical purposes and better support discussions between physicians and patients on this subject.

4.03 Adaptive Clinical Trials Designs: Challenges and Uncertainties

T. Salem[1], B. Li[1], S. Sultan[1] and C. Lourenco[1]

[1] Therapeutic Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The challenges associated with the regulation of drugs and their safety surveillance are common and worrisome. Unique safety issues with certain drug classes have also come to light when designing innovative clinical trials and capturing and measuring adverse events throughout the drug development process. “Adaptive Design*” in clinical trials is one of the emerging scientific topics in HPFB which requires carful assessment in the frame of the current risk management strategies.

The recent intense interest in the possibility in using adaptive features for the design of clinical trials has multiple safety concerns to physicians and drug regulators worldwide. Some of the features of the newly proposed adaptive clinical trials design are changes in design or analysis guided by examination of the accumulated data at an interim point in the trial; shorter trial duration; fewer patients; expecting broader dose response information.

Those designs represent various challenges like, but not limited to, complex computations such as those using Bayesian statistics, and complex non-traditional designs that cause challenges when implementing division 5 of the food and drug regulations.

In 2008 the department formed a branch wide working group to look into the newly emerging designs. In 2012 the working group produced a document entitled “consideration for adaptive CTDs” which did not reach the level of a guidance document due to multiple deficiencies. Currently the department do not contribute to, or advise sponsors when designing trials using adaptive designs, however once submitted they are assessed on a case by case basis.

MISSION STATEMENT OF PROJECT: The current stand of the regulatory agencies, as well as the pros and cons of using an adaptive approach for clinical trials in the drug discovery process will be improved.

4.04 Serious Side Effects of Drugs in the Digestive Tract

A.G. Craan[1], S. Hashim[1], S. Semalulu[1], R. Ing[2], and D. Vu[1]

[1] Marketed Biologicals, Biotechnology and Natural Health Products Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Faculty of Sciences, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Stomach ulcer and gut damage/rupture represent serious side effects (SEs) of drugs on the digestive system (DS). Can these SEs be avoided with sufficient analysis and evaluation of the benefits and risks of drug ingredients? We reviewed all pertinent information from industry, government, and scientific/medical journals in order to analyze/compare how these SEs occur and can be prevented. Anti-inflammatory biological/biotechnological drugs and painkillers (Cox-2 inhibitors or Coxibs) that inhibit the DS enzyme cyclooxygenase-2, do not cause stomach ulcer. In the gut, there are 3 major risk factors when taking some drugs: 1) the simultaneous presence of 2 or more drugs having an effect on one another, as observed when grapefruit juice ingredients interfere with drug action; 2) perforated bowel; and 3) ruptured bowel from severe constipation. While the first can be predicted before marketing, the other two are rare and more difficult to prevent. Unlike side effects on the heart or during pregnancy, SEs involving the digestive tract have only caused 2 drugs to be taken off the market.

Our findings suggest that the application of increased and improved knowledge to the life-cycle management of drugs, including post-market and patient compliance, can help prevent serious side effects in the DS.

MISSION STATEMENT FOR PROJECT: This project meets Health Canada's mandate for regulating the life-cycle management of drugs, particularly for post-authorization pharmacovigilance.

4.05 The Role Clinical Biomarkers in the Regulation of Biological Therapies

J.M. Sarjeant[1], J. Wang[2], and A.V. Klein[3]

[1] Clinical Evaluation Division, Hematology/Oncology, Centre for the Evaluation of Radiopharmaceuticals and Biologics (CERB), Biologics and Genetic Therapies Directorate (BGTD), HPFB, Health Canada, Ottawa, ON
[2] Clinical Evaluation Division – Hematology/Oncology, CERB, BGTD, HPFB, Health Canada, Ottawa, ON
[3] CERB, BGTD, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Clinical biomarkers are characteristics that can be measured in individual patients. The area of science called pharmocogenomics studies how a person's genetic material causes them to respond or react to a specific drug. For example, some patients may have experience the expected benefit of a certain drug with no side effects, while others experience no positive effect and suffer serious side effects from the same drug at the same dose. The constant evolution of scientific knowledge is making these biomarkers increasingly more relevant to our work. This poster will examine how clinical biomarkers are used in clinical cancer studies. It will also demonstrate how understanding pharmacogenomics is necessary for the authorization process of some biological medicines by the Biological and Genetic Therapies Directorate (BGTD). Some biomarkers that have been used in the analysis of clinical trial study data include HER-2 and KRAS. Case examples of biological medicines authorized by Health Canada where clinical biomarkers were considered will be examined.

Pharmacogenomics will play an increasingly important role in the design and interpretation of clinical trials in the future, and continuing knowledge transfer to reviewers is essential.

MISSION STATEMENT FOR PROJECT: Improve division knowledge in a rapidly advancing scientific field.

4.06 A New Mass Spectrometry Method to Quantify Key Proteins in Influenza Vaccines

D.G.S. Smith[1], G. Gingras[1], Y. Aubin[1] and T.D. Cyr[1]

[1] Centre for Vaccine Evaluation, Biologics and Genetic Therapies Directorate, Health Products and Food Branch, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Annual influenza vaccines are tested and approved for release by Health Canada. Quality control includes quantifying the key viral proteins (hemagglutinin (HA) from specific virus strains) against international reference standards, which are time-consuming to generate and difficult to reproducibly quantify using current methods. Here we present a rapid, reliable method for quantifying HA and other critical proteins in both influenza vaccines and reference standards using liquid chromatography (LC) and mass spectrometry (MS).

In this method, a control protein is added (spiked) to the vaccine at a known concentration. The resulting spiked vaccine is digested using trypsin, an enzyme that cuts proteins into specific short chains of amino acids (peptides). The peptides are analyzed by LC-MS and the three peptides generating the highest MS signal intensity ("Hi-3") from each protein are identified. Absolute protein quantities can be determined for most proteins by comparing average "Hi-3" signal intensities to that of the spike protein. To refine this approach a custom protein containing the "Hi-3" peptides from all proteins of interest was generated. This protein generates equal amounts of all peptides upon digestion allowing "Hi-3" correlation correction factors to be calculated and more accurate quantification of vaccine proteins to be achieved.

MISSION STATEMENT FOR PROJECT: To develop and test alternative methods to quantify proteins in influenza vaccines to augment/replace current outdated/less accurate methods. Approved methods can be integrated into internal lot release programs and/or quality control protocols for manufacturers of vaccine and reference materials.

4.07 Fentanyl: Recent Trends and Clandestine Production in British Columbia

S.A. Dubland[1], and R.R. Laing[1]

[1] Drug Analysis Service, HPL, RPB, Health Canada, Burnaby, BC

PLAIN LANGUAGE SUMMARY: Fentanyl, a potent synthetic opioid prescription drug that is approximately 100 times more potent than morphine, until recently was strictly a pharmaceutical product. As a result of the increasing occurrence of fentanyl in illicit drugs in BC associated with overdose deaths, this issue has been brought to national media attention. In 2011, Health Canada Drug Analysis Service chemists in Vancouver, whose mandate is to assist Canadian police forces in the enforcement of the *Controlled Drugs and Substances Act* through identification of controlled substances and by providing scientific and technical expertise regarding drugs and drug syntheses, attended the first two fentanyl clandestine laboratories to be identified in Canada. Since the time of these lab seizures fentanyl has been encountered in seized police exhibits as counterfeit pharmaceutical products and more recently found in street heroin exhibits.

The purpose for this study is to establish a suitable method for the identification and quantification of fentanyl in the presence of other drugs since very low levels of the potent opioid in the presence of other drugs provides for difficult analyses.This poster will provide details on the types of samples observed with fentanyl, the analytical challenges to verifying its presence along with the results of quantifying fentanyl in submitted samples as well as a common method for clandestine synthesis of fentanyl. Identification and quantitation of low level fentanyl in illicit drugs will improve public safety and enable enforcement agencies to track recent trends in seized drugs.

MISSION STATEMENT FOR PROJECT: Identification and quantitation of low level fentanyl in illicit drug samples will allow for better reporting and identification of illicit drug trends.

4.08 Update of the Canadian Guidelines for Protective Actions during a Nuclear Emergency

L. Bergman[1], D. Beaton[1], and J. Chen[1]

[1] Radiation Protection Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. In accordance with this mandate, Health Canada has a role in nuclear emergency preparedness and response. Health Canada is the Canadian federal department responsible for the Federal Nuclear Emergency Plan (FNEP). One of Health Canada's responsibilities under the FNEP is to prepare guidelines for protective actions during a nuclear emergency. Currently, there are two relevant Health Canada guidelines, *The Canadian Guidelines for Intervention During a Nuclear Emergency* (2003) and *The Canadian Guidelines for the Restriction of Radioactively Contaminated Food and Water Following a Nuclear Emergency* (2000). With the recent update of the FNEP (2012) new guidelines have been prepared which have combined the guidelines for protective actions and food and water controls in one cohesive and functional document. Lessons learned from the application of the previous guidance during the accident at the Fukushima Daiichi Nuclear Power Plant have been taken into account during the revision. Health Canada's new guidance has also adopted the latest recommendations from both the International Atomic Energy Agency (IAEA) and the International Commission on Radiological Protection (ICRP).

The new guidance takes an approach based on an overall protection strategy, consisting of one or more protective actions, and provides multiple options for decision making. The updates to the Health Canada guidance and the new recommended values on which to base decisions will be discussed.

MISSION STATEMENT FOR PROJECT: The document being discussed will replace two previous Health Canada guidance documents, specifically *The Canadian Guidelines for Protective Actions During a Nuclear Emergency* (2003) and *The Canadian Guidelines for the Restriction of Radioactively Contaminated Food and Water Following a Nuclear Emergency* (2000).

4.09 Knowing Hybrid SPECT/CT Imaging Modality as a Clinical Reviewer

W. Zeng[1], D.A. Hoffman[1], A.V. Klein[1], and J. Wang[1]

[1] CED-HO, CERB, BGTD, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The field of medical imaging is rapidly changing with continued innovation in technology. A new imaging method, called Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT), which assesses both function and anatomy of whole body or part of the body, has rapidly become the state-of-the-art imaging tool in daily nuclear medicine service. The new tool could be used to detect variety of diseases, including cancer, infection, trauma, lung clots, and coronary artery disease. In this presentation we will update the current standard of care in diagnostic nuclear medicine with important indications for SPECT/CT. We will show improved disease diagnosis with the new imaging method.

The goal of the abstract is to educate clinical evaluators reviewing submissions associated with radiopharmaceuticals and nuclear medicine imaging. In particular, the reviewers assessing clinical trial designs could benefit from the knowledge of SPECT/CT applications.

MISSION STATEMENT FOR PROJECT: Assuring the clinical assessments of radiopharmaceuticals is in line with the current clinical practice.

4.10 A Rapid, Quantitative LC-MS/MS Screening Method for 71 Active and 11 Natural Erectile Dysfunction Ingredients Present in Potentially Adulterated or Counterfeit Products

P. Lebel[1,2], J. Gagnon[2], A. Furtos[1], and K.C. Waldron[1]

[1] Department of Chemistry, Université de Montréal, Montreal, QC
[2] Inspectorate Laboratory Programme, RPB, Health Canada, Longueuil, QC

PLAIN LANGUAGE SUMMARY: Erectile dysfunction (ED) drugs are available on the illegal market (i.e., counterfeit Viagra) and in herbal or dietary supplements as adulterants. Suppliers add these synthetic compounds without declaring them, claiming to enhance sexual abilities in a safe, healthy way. Tablets from disreputable sources made in unsanitary environments may contain more ED drugs than recommended or be mislabelled, potentially leading to dangerous health effects. Therefore, a method to rapidly analyse tablets, herbal medicines and dietary supplements for a wide range of ED drugs and compounds suspected to enhance sexual performance was developed. Using liquid chromatography with tandem mass spectrometry (LC-MS/MS), two chemical separation techniques capable of identifying many components in a complex mixture, 71 active and 11 natural ED ingredients were resolved from a single mixture in only 10 min. Extraction of ED drugs from tablets or supplements was achieved using the solvent methanol with an efficiency of 92% and above.

The ED drugs could be quantified reproducibly at very low concentrations (< 1 ng/mL). The developed high throughput screening method capable of resolving 82 analytes in 10 min was 2-3 times faster than conventional methods for similarly complex samples and was 100% reliable based on comparison of real samples also analysed by the conventional methods. The rapid method was successfully applied to screen 32 seized samples for ED drugs.

MISSION STATEMENT FOR PROJECT: This project allows faster throughput and more comprehensive analysis of seized erectile dysfunction samples in that 71 active and 11 natural erectile dynsfunction ingredients may be identified simultaneously.

4.11 Rapid LC-MS/MS Screening Method for 24 Synthetic and Natural Cannabinoids Present in Potentially Adulterated or Counterfeit Products

P. Lebel[1,2], J. Gagnon[2], K.C. Waldron[1], and A. Furtos[1]

[1] Department of Chemistry, Université de Montréal, Montreal, QC
[2] Inspectorate Laboratory Programme, RPB, Health Canada, Longueuil, QC

PLAIN LANGUAGE SUMMARY: Narcotics (cannabis-like) remain amongst the most frequently used illicit drugs. Some manufacturers include them in herbal smoking mixtures, incense sticks, serum and other matrices, often with no indication of their presence. These herbal mixtures, which create marijuana-like psychotropic effects when smoked, are illegal to sell. They can be made in unsanitary environments or the active ingredients (cannabinoids) can be mislabelled. A rapid analysis method based on liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS), two techniques that permit chemical species in a mixture to be separated for identification, has been developed to simultaneously separate 20 synthetic cannabinoids and 4 natural cannabinoids in only 8 min. The 24 compounds have closely related chemical structures which makes their separation a challenge. The method was powerful enough to resolve overlapping compounds and some isomers, compounds having the same chemical formula. Methanol extraction of the drugs from various real matrices resulted in 95% or better recovery. The method was very sensitive, allowing detection at lower than 1 ng/mL.

Our high throughput screening method capable of resolving 24 compounds in 8 min compares favorably to conventional methods that take up to 25-30 min for similarly complex samples and to reported rapid separations where at most 12 drugs were monitored. Our LC-MS/MS method for cannabinoids was successfully applied to 11 seized samples.

MISSION STATEMENT FOR PROJECT: This project will allow faster throughput of seized samples where 24 synthetic and natural cannabinoids may be identified simultaneously.

4.12 The Extrapolating of Indications in the Review and Authorization of Subsequent Entry Biologics (SEBs)

B.J. Scott[1], A.V. Klein[1], and J. Wang[1]

[1] Clinical Evaluation Division – Hematology/Oncology, Centre for the Evaluation of Radiopharmaceuticals and Biotherapeutics (CERB), Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Biologics are medical products synthesized by biological processes. SEBs are biologic products that come to market subsequent to a biologic drug already authorized and marketed in Canada, termed a reference biologic drug (RBD). It is intended for SEBs to be highly similar to the RBD. Many biologic products, for which SEBs are being developed, hold indications for multiple diseases in multiple populations. The sponsors of SEBs are generally seeking authorization for all of the indications and populations granted to the RBD. However, in general, clinical trials are not carried out with the SEB in every disease and population for which authorization is sought. Thus, the regulator must decide when, and under what conditions, data generated in one or more indications can be extrapolated to support the authorization of multiple indications and clinical uses. General recommendations are made regarding the appropriate use of comparative quality and clinical data generated using an SEB and the conditions that should be met in order to support the application of such data to indications not studied for the SEB.

MISSION STATEMENT FOR PROJECT: The project will help clinical review staff identify information that is critical to determining the feasibility of extrapolation in the review of SEBs.

4.13 Ipilimumab Induced Immune-Mediated Advserse Drug Reactions

J. Ning[1], J. Wang[1], and A.V. Klein[1]

[1] Clinical Evaluation Division – Hematology/Oncology Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Yervoy (ipilimumab) is a novel new biological drug (manufactured in a living system, e.g. a microorganism or cells) used for the treatment of melanoma (a type of skin cancer). It specifically modifies the human immune system by turning off the inhibitory mechanism to allow cytotoxic T cells to continue destroying cancer cells. Yervoy is authorized in Canada based on an improved overall survival in patients with advanced melanoma. Through its specific effect on immune system, ipilimumab also induces unique adverse drug reactions which do not resemble any other authorized biologic anti-cancer drugs currently on the Canadian market. This is a scientific/regulatory challenge for conducting an adequate risk assessment and ensuring appropriate risk communication and management.

This review summarizes the underlying mechanisms and clinical manifestations of ipilimumab-induced specific “immune-mediated” adverse drug reactions (im-ADRs). The differences between “immune-related” and “immune-mediated” adverse drug reactions are summarized and discussed. Heath Canada’s approaches to ensure adequate risk communications and risk mitigation/management for im-ADRs are reviewed. Appropriate risk communication and mitigation for patient protection were achieved successfully. Scientific/Regulatory challenges regarding appropriate assessment of ipilimumab induced tumor response are also discussed.

MISSION STATEMENT FOR PROJECT: This is a good example of handling new challenges from submissions of immune therapies.

4.14 The Current Status of Orphan Drug Regulation in Health Canada, with Perspectives on the Challenges of Designing, Conducting and Evaluating Clinical Trials for Market Authorization of Orphan Drugs

Y. Sheng[1], W. Mooney[1], and A.V. Klein[2]

[1] Clinical Evaluation Division – Autoimmunity/Endocrinology, Centre for Evaluation of Radiopharmaceuticals & Biotherapeutics, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON
[2] CERB, BGTD, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: With rapid developments in biomedical technologies, a rapid increase in the number of new treatments of rare serious diseases ["Orphan Drugs" (ODs)] is expected. Challenges with evaluating benefits and risks for ODs (e.g., very small clinical trials; novel statistical methods; and defining clinically meaningful improvement in seriously ill patients) are described. Health Canada (HC) guidelines for ODs are being drafted, and will help strengthen development, evaluation and approval of these treatments. Industry is strongly encouraged to discuss with HC when designing and conducting clinical trials for rare diseases, to ensure study design, statistical plans and eventually efficacy and safety data are sufficient for review and subsequently for authorising the sale of these drugs in Canada. Each OD submission must be carefully considered on a case-by-case basis.

MISSION STATEMENT FOR PROJECT: The project will improve Health Canada's regulation and assessment of submissions for Orphan Drugs, and provide a significant benefit for Canadians with rare and serious diseases by facilitating access to new treatments with positive benefit/risk profiles.

4.15 Development of a Screening Level PECsoil Calculation for Use in Environmental Risk Assessment of New Veterinary Drug Active Ingredients in Canada

A. Belknap[1], G. Rattray[1], G. Stringer[1], and S. Kullik[1]

[1] Environmental Impact Initiative, Policy, Planning and International Affairs Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: A regulatory framework has been developed specifically for active pharmaceutical ingredients (APIs) in human and veterinary drug products regulated by the *Food and Drugs Act* (F&DA) to assess their potential environmental effects. APIs in veterinary drugs used in food animals primarily enter ecosystems through the application of livestock waste to agricultural land. A means to derive predicted environmental concentrations (PECs) of APIs in soil (PECsoil) following application of manure from treated animals to land as fertilizer is required as part of a directed testing approach. Variability in agricultural practices and the complexity of screening-level PECsoil calculations can be a challenge for regulatory authorities. A science-based and transparent methodology to calculate PECsoils that incorporates drug label information and default values representative of typical Canadian confined animal husbandry and agricultural practices has been developed and will be used to identify new APIs in veterinary drugs that may require more detailed ecotoxicity and environmental fate studies. Default input values representing confined cattle, swine and poultry production and manure management practices in Canada were developed by leveraging national and provincial sources.

A comparison to US and EU PECsoil approaches was made with a subset of currently marketed veterinary drugs from a range of classes and, where possible, to measured environmental concentrations (MECs). PECsoil values were comparable; however, differences in how some animal subcategories are defined make direct comparisons difficult. The PECsoil values generally over-predicted MECs, which is appropriate considering they are used during the screening stage of the risk assessment. Finally this talk will explore how PECsoil values can be utilized to better direct the testing requirements for veterinary APIs within the proposed regulatory framework.

MISSION STATEMENT FOR PROJECT: To reduce environmental and indirect human health impacts of products regulated under the *Food and Drugs Act* by developing appropriate environmental assessment regulations for substances contained in these products.

4.16 Antibody-Drug Conjugates (ADCs) in Cancer Therapy: Scientific and Regulatory Challenges

A. Pen[1], A.V. Klein[1], and J. Wang[1]

[1] Clinical Evaluation Division – Hematology/Oncology, Centre for Evaluation of Radiopharmaceuticals & Biotherapeutics, BGTD, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Antibody-drug conjugates (ADCs) are a new class of therapeutics consisting of a carrier protein (monoclonal antibody) attached to toxic chemical molecules. This strategy allows a selective delivery of drugs to tumour cells while sparing normal tissues. Two ADCs have recently been authorized, but more ADCs are expected to be submitted to regulatory agencies in the near future. The aim of this project is to summarize the benefits of ADCs and to describe the scientific and regulatory challenges associated with this new class of drugs. Due to the hybrid nature of ADCs, regulatory guidelines for both small molecules and biologics have to be considered. Our limited experience with ADCs also raises new scientific/regulatory issues.

These challenges should be addressed and the market authorization of ADCs in Canada should be based on an overall positive risk/benefit ratio in order to ensure that ADCs are safe and effective to Canadians. With increasing knowledge in oncology and progress in the development of ADC technology, ADCs are at the forefront of new and promising cancer therapies.

MISSION STATEMENT FOR PROJECT: The hybrid nature of ADCs necessitates an approach that integrates small molecule drug and biologic regulatory considerations. Therefore, ADCs require a collaborative approach between BGTD and TPD for review, and a review guidance document may be considered to address specific challenges of ADCs.

4.17 Measuring the Impact of a Regionally Delivered Science Program

R. LeBlanc[1], and A. Iannantuono[2]

[1] Environmental Health Program, Health Programs East – Atlantic Region, RAPB, Health Canada, Halifax, NS

[2] Strategic Policy and Planning, Health Programs East – Ontario Region, RAPB, Health Canada, Toronto, ON

PLAIN LANGUAGE SUMMARY: RAPB's Environmental Health Program (EHP) is a national science-based program that is delivered regionally. It comprises 5 program areas: Federal Contaminated Sites Action Plan, Radon, Chemicals Management Plan, Environmental Assessment and Air Quality, and is delivered through 6 regional offices across Canada. In order to measure the effectiveness of this program, and to assess the program's contribution to Health Canada's mandate, EHP developed a program performance measurement framework (PMF). The PMF consists of a logic model (that outlines the work of each program and links together the common goals), program and region-specific indicators (that describe how the program will evaluate its success in meeting the goals) and data collection tools (electronic spreadsheets that track work being done in each program). EHP staff developed and validated the logic model, indicators and the monthly data collection model.

The data collection provided staff the opportunity to evaluate the program indicators' accuracy in measuring the influence of provision of expert scientific advice on stakeholders' awareness of risks, health impacts and mitigation strategies related to environmental factors. This PMF provides a new methodology for assessing the impact of horizontal program delivery that allows staff to work across program areas, and informs program policy and design.

MISSION STATEMENT FOR PROJECT: A staff-validated, pan-regional performance measurement framework for the Environmental Health Program aims to achieve excellence in program and service delivery through an integrated and horizontal approach focused on the delivery of a suite of national, science-based programs.

4.18 Serum Concentrations of Selected Organochlorine Pesticides in Human Maternal and Umbilical Cord Blood

L. Walrond[1], C. Kubwabo[1], and W.G. Foster[2]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Department of Obstetrics and Gynecology, McMaster University, Hamilton, ON

PLAIN LANGUAGE SUMMARY: Organochlorine pesticides (OCPs) have been used historically as insecticides in agriculture and disease control; most have been banned in Canada since the 1970s. OCPs break down slowly in the environment; they have the potential for long range transport and bio-accumulation. OCPs are known to be carcinogenic and to potentially interfere with the hormone system of humans and wildlife. The primary route of exposure in humans is through food. The goal of this study was to determine blood serum levels of OCPs in expectant mothers and their unborn children. Mothers' serum samples were evaluated at two time points, midway through pregnancy and at delivery while fetal exposure was determined using umbilical cord blood serum (UCB) collected at delivery.

Twenty-six OCPs were analyzed simultaneously in 30 paired maternal and UCB serum samples. Method detection limits (MDLs) ranged from 0.02 - 1 ng/mL depending on the OCP. Only one OCP (4,4'-DDE) was found above the MDL and it was detected at very low levels in all maternal and UCB serum samples. This study showed that 4,4'-DDE can cross the fetal-placental barrier during pregnancy resulting in exposure of the developing fetus; however, these data also indicate that the placenta provides a partial barrier to 4,4'-DDE.

MISSION STATEMENT FOR PROJECT: Despite having been banned for decades, OCPs remain within the environment. This study was aimed at assessing potention transfer of these chemicals from mothers to fetus.

4.20 Sublingual Immunotherapy for Allergenic Diseases: Challenges in Regulation and Evaluation of Clinical Trials for Market Authorization of Novel Allergy Products

L. Patrick[1], Y. Sheng[1], K. Kourad[1], W. Mooney[1], and A.V. Klein[2]

[1] Clinical Evaluation Division – Autoimmune/Endocrinology, Centre for Evaluation of Radiopharmaceuticals & Biotherapeutics, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

[2] Centre for Evaluation of Radiopharmaceuticals & Biotherapeutics, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: 20-30% of Canadians have allergenic diseases including hay-fever, which cost the economy ~$1.5 billion annually in medication and lost work. Immunotherapy with painful allergy shots is a standard treatment to lessen or stop symptoms.

Recently, Health Canada has received an increased number of submissions for new immune therapies which don't require injections, including **S**ub**L**ingual (under-the-tongue) **I**mmuno**T**herapy (**SLIT**). Unique regulatory challenges in the evaluation of these novel products, including assessing clinical trial design, treatment benefit, and side effects, are discussed.

Drug developers are encouraged to communicate early with Health Canada when designing and conducting clinical trials with new immune therapies, to help ensure study data are sufficient for review and potential approval for marketing in Canada.

This Review will explore assessment of novel allergy products, and help improve Health Canada's regulatory ability to review immunotherapy submissions. This will provide a significant benefit to Canadians with allergenic diseases, helping them maintain and improve their health by facilitating access to new therapies, and minimizing health risk while maximizing benefits.

MISSION STATEMENT FOR PROJECT: This study will improve Health Canada's review and assessment of novel treatments for allergies and benefit Canadians with allergenic diseases. This will provide a significant benefit to Canadians with allergenic diseases, helping them maintain and improve their health by facilitating access to new therapies, and minimizing health risk while maximizing benefits.

4.21 Determination of Volatile Organic Compounds in Blood

R. Aranda-Rodriguez[1], A. Cabecinha[1], Z. Jin[1], and J. Harvie[1]

[1] Exposure and Biomonitoring Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Humans are exposed continuously to volatile organic compounds (VOCs) as they are everywhere in the environment at very low concentrations. They originate from natural and human-made sources. The latter includes building materials, adhesives, coatings, dry cleaning chemicals, and tobacco smoke. Due to Canada's northern climate, Canadians spend most of their time indoors which can contribute to overall VOC exposure. Health Canada is currently participating in the Canadian Health Measures Survey (CHMS) to measure VOCs in the indoor air, tap water and blood of participants. These measurements are used, along with a questionnaire, to estimate baseline data on exposure to environmental contaminants and the potential factors/behaviours which contribute to this exposure. HC implemented the protocols used by the Center for Disease Control and Prevention laboratory (CDC) which is responsible for analysis of samples from a similar study in the USA, the National Health and Nutrition Examination Survey. As Health Canada follows the same protocols used by the CDC, it is possible to compare data from both studies.

This work addresses the difficulty in accurately determining the concentrations of VOCs in blood samples. It is especially challenging because VOCs like benzene, toluene, xylenes and styrene are present in samples at very low concentrations and can be masked by the background levels found in the laboratory.

MISSION STATEMENT FOR PROJECT: The Exposure and Biomonitoring Division is the only Canadian laboratory capable of analyzing VOC in the blood of the general population. The EBD follows protocols established by the US counterpart allowing comparison of population exposures across countries.

4.22 Drug Related Severe Cutaneous Adverse Reactions (SCAR): All Rashes are not Created Equal

S. Hashim[1], F. Omara[1], S. Semalulu[1], S Noruziaan[2], and D. Vu[1]

[1] Marketed Biologicals, Biotechnology and Natural Health Products Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Faculty of Sciences, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Most skin reactions such as hives, rashes and eczema are mild and temporary. However, SCARs sometimes occur in association with biological drug use and may be life threatening. They include Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Acute Generalized Exanthematous Pustulosis (AGEP). SCAR can manifest as fever, painful rash, skin eruptions and burn-like blisters, sometimes associated with increase in white blood cells. There may also be involvement of internal organs. Therefore, whenever drug related rash is suspected, it is necessary to properly identify it in order to rule out a serious drug reaction and to carefully monitor the patient.

Scientific/medical/regulatory literature search was performed and types and mechanisms of skin reactions to biological therapeutics are compared. Our knowledge and experience with skin reactions to drugs is changing with the introduction of new therapies. It is therefore important, that the product information identify and delineate SCAR and properly indicate them in risk management plans and to users of these biological products. For a rash can be an early sign of grave consequences.

MISSION STATEMENT FOR PROJECT: This project meets Health Canada's mandate for regulating the life-cycle management of drugs, particularly for post-authorization pharmacovigilance.

4.23 Infusion-Related Reactions: Challenge of Differentiating them in Biological Product Labels

S. Drmanic Storbeck[1], K. Kouassi[1], S. Semalulu[1] and D. Vu[1]

[1] Marketed Biologicals, Biotechnology and Natural Health Products Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY Safety information for biotherapeutic products is relatively limited in its description of infusion-related reactions. Infusion-related reactions are signs/symptoms experienced by patients during or around the first day of the infusion. They consist of localized injection site pain and swelling, redness, itching, low blood pressure or abnormal breathing. Severer forms include high fever, lowered blood pressure, swollen lips, tongue and mouth, anaphylactic or anaphylactoid reactions, which may be fatal. Most product labels contain general statements that do not distinguish the different abnormal states underlying these reactions. This generalization makes the diagnosis of these events difficult, which may lead to improper management, unnecessary discontinuation or re-exposure to patients for whom continued treatment may otherwise be unadvisable. Potentially grave consequences may result if infusion-related reactions are not clearly delineated in product labels.

This review examines biotherapeutics associated with infusion-related reactions to determine if a more specific description of these adverse events would be more informative in identifying these risks to the health care providers and patients. This is done to improve the product safety information, in support of Health Canada's mandate of transparency in protecting public health. Thus, patients and health care providers will be better informed regarding decisions on product usage.

MISSION STATEMENT FOR PROJECT: Setting in place clearer and specific identification and characterization of IRRs will improve product safety information, and ultimately the safety of biotherapeutic agents, which play a vital role in the treatment of many chronic diseases.

4.24 Statistical Methods for Values below the Limit of Detection with Application to Biomonitoring Studies

K.A. Davis[1], M. Malowany[1], J. Fu[1], V. Choeurng[1,2], S.H. MacPherson[1,2], C.L. Liang[1], L. Marro[1], M. Walker[1], T.E. Arbuckle[1], and M. Fisher[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Carleton University, Ottawa, ON

PLAIN LANGUAGE SUMMARY: To determine the extent to which Canadians are exposed to environmental chemicals, Health Canada has undertaken a number of studies to measure chemicals (e.g. lead, mercury, bisphenol A [BPA]) in blood and urine samples. Often, the chemical levels may be so low that they cannot be accurately measured in a laboratory analysis. In fact, the values are known to be somewhere between zero and the laboratory's detection limit. Such values are referred to as censored and warrant additional consideration in any statistical analysis. To date, most scientists have substituted a constant such as half the detection limit for these censored values and subsequently analyzed the data using standard statistical methods.

Such an approach may lead to biased and imprecise conclusions, thus more sophisticated statistical techniques to account for these censored values have been developed and applied in this work. Results from statistical simulations and the recent Maternal-Infant Research on Environmental Contaminants (MIREC) Study demonstrate that these more sophisticated techniques offer the advantage of additional statistical precision and rigour, and may be applied to future studies undertaken by Health Canada and other organizations.

MISSION STATEMENT FOR PROJECT: Research on the use of censoring methods for statistical analysis of environmental data subject to a limit of detection has wide applicability for laboratory analyses, is consistent with current literature, and leads to improved performance in terms of bias and precision of statistical conclusions.

4.25 Compliance Verification Review in the Health Product and Food Branch Inspectorate Program

J. Saint-Pierre[1], K. Dix[1], and A. Morrow[2]

[1] Health Products and Food Branch Inspectorate, Health Canada, Ottawa, ON
[2] Health Products and Food Branch Inspectorate, Health Canada, Toronto, ON

PLAIN LANGUAGE SUMMARY: The Health Products and Food Branch Inspectorate and the Regions and Programs Bureau are responsible for delivering a national compliance and enforcement program under the Food and Drugs Act (FDA) and its associated Regulations, for pharmaceutical drugs (human and veterinary), biologics and radiopharmaceuticals, medical devices and natural health products. Activities conducted by the Inspectorate program include establishment licensing, inspections, compliance verification (CV) activities, border integrity and supporting laboratory and other functions.

The Inspectorate CV Review Project was initiated to review, and provide recommendations for improvements to, the efficiency and effectiveness of the CV activities. Internal staff, branch partners, as well as domestic and international organizations with compliance and enforcement programs were consulted and interviewed to identify areas for improvement and solutions. Improved performance measurements were identified based on the development of an Inspectorate Logic Model. Findings were compiled and 33 recommendations were developed.

Key recommendations included the need to update and standardize risk and prioritization across product lines, improve the way low risk issues are handled, improve national trend analysis, and improved standards for uniformity of action and processing of complaints. Implementation of some recommendations was initiated before the end of the project. Adoption of the recommendations will improve the efficiency and effectiveness of the Inspectorate compliance verification program.

The Inspectorate is now in the process of implementing selected recommendations based on greatest impact. They are developing an improved risk characterization of all incoming complaints and recalls, which will include a triage function. A pilot trial is being designed to assess and measure the benefits of this new approach.

MISSION STATEMENT FOR PROJECT: The project will improve the efficiency and effectiveness of the Inspectorate program compliance verification activities.

4.26 Building Workforce Capacity in Canada: Demonstrating the Impact of the *Skills Online* Competency Development Program

K. MacDougall[1], J. Watson[1], and E. Wright[1]

[1] Centre for Public Health Capacity Development, Health Security Infrastructure Branch, Skills Enhancement for Public Health, PHAC, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The persistence of public health workforce issues including the lack of qualified public health professionals and access to skills development and training opportunities, especially in the north, emphasize the need to enhance public health workforce capacity. *Skills Online*, an internet delivered, competencies based continuing education program enables public health practitioners to acquire the knowledge, skills and attitudes necessary for effective public health practice. Since 2002, close to 8000 learners have completed at least one of Skills Online's 10 facilitated modules.

Multiple lines of evidence were used to evaluate the impact of participation in the *Skills Online* professional development program.

Findings indicate that participation in *Skills Online* has both individual and organizational impact. Learners gain an increased understanding of the breadth of public health and develop and strengthen public health competencies. In addition, learners increase their knowledge of available resources and information sources. By creating opportunities for learners to work together across disciplines and teams, *Skills Online* improves the way learners interact in their work environment and has an impact on front line public health practitioners' ability to transfer and integrate knowledge and skill to the workplace. Evaluation findings contribute to continuous program improvement including adaptations to increase accessibility.

MISSION STATEMENT FOR PROJECT: The *Skills Online* competency development program contributes to building the public health workforce in Canada.

4.27 Maternal Exposure to Bisphenol A and Triclosan: Results from the MIREC Study

T.E. Arbuckle[1], L. Marro[1], K.A. Davis[1], P. Bélanger[2], P. Ayotte[2], A. LeBlanc[2], G. Provencher[2], P. Dumas[2], R. Bérubé[2], É. Gaudreau[2], E.M. Faustman[3], E. Vigoren[3], A.S. Ettinger[4], M. Fisher[1], S.H. MacPherson[1], M. Dellarco[5], and W.D. Fraser[6]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Le centre de toxicologie, Institut nationale de santé publique Québec, Quebec City, QC
[3] Institute for Risk Analysis and Risk Communication, Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington, USA
[4] Center for Perinatal, Pediatric & Environmental Epidemiology, Yale School of Public Health, New Haven, Connecticut, USA
[5] The National Children's Study, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland, USA
[6] CHU Sainte-Justine Research Center, Mother and Child University Hospital Center, Montreal, QC

PLAIN LANGUAGE SUMMARY: One of the roles of Health Canada is to foster research on measuring exposure of the Canadian population to environmental chemicals, especially for susceptible populations such as pregnant women. The Maternal-Infant Research on Environmental Chemicals (MIREC) Study was designed to measure exposure to and potential health effects of elevated levels of environmental chemicals during pregnancy. Two of the chemicals for which there is limited data on levels in pregnant women are triclosan and bisphenol A (BPA). Triclosan is used as an antimicrobial in a wide range of cosmetics and personal care products, including non-prescription drugs. BPA is used to make a hard, clear plastic and is also found in epoxy resin linings on the inside of metal-based food and beverage cans. Thermal papers such as receipts and tickets may also be a source of BPA. These two chemicals were measured in a urine sample from approximately 1900 pregnant women participating in the MIREC Study. Approximately 70% of the pregnant women had detectable levels of BPA in their urine, with higher exposure among smokers and women born in Canada. Triclosan levels tended to be higher in women who had never smoked. These results will be used to estimate exposure to these chemicals for the Canadian population.

MISSION STATEMENT FOR PROJECT: Extensive biomonitoring data on BPA and triclosan in a susceptible population of pregnant women will be very useful in evaluating and updating the screening assessments of these chemicals by Health Canada and international agencies.

4.28 *In Vitro* Monocyte Activation Test for Quantitative Determination of Low Level Pyrogens in Influenza Vaccines

T. Shipley[1], Y. Adonsou-Hoyi[1], L. Lavigne-Brunette[1], A. Rinfret[1], and R. Isbrucker[1]

[1] Center for Vaccine evaluation, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: All biologics, including vaccines, must be tested prior to release for trace contaminants of bacterial origin which can cause fever (pyrogens). Current methods used are the rabbit pyrogen test and limulus (horseshoe crab) amebocyte lysate test; both of which have technical difficulties and require the use of animals or animal products.

A new method was recently developed for pyrogen testing which uses human derived white blood cell cultures; however, the method has not been tested for its ability to monitor pyrogen levels in vaccines. Test conditions were adapted for use with influenza vaccines and showed detection limits that are well below the allowable levels of pyrogens. When pyrogens were added into the vaccines at known concentrations, the detected concentration matched the concentration which was added, showing the vaccine did not interfere with the assay outcome or mask the presence of pyrogens. These results show this new assay is capable of detecting trace amounts of pyrogens with a high degree of accuracy, is cost-effective, and reduces the use of animals. Validation of the assay is planned prior to adoption into Health Canada's vaccine lot release program for influenza vaccines.

MISSION STATEMENT FOR PROJECT: Evaluation and adoption of new assay methods helps maintain the technical knowledge and skills required for an effective vaccine lot release program at Health Canada. The knowledge gained from this project will support the adoption of the monocyte activation test for pyrogenicity testing of other biologics.

4.29 Paradoxical Induction of Autoimmune Diseases by Treatment with Anti-Tumour Necrosis Factor (TNF-α) Agents

W. Huang[1], S. Semalulu[1], S. Noruziaan[2], and D. Vu[1]

[1] Marketed Biological, Biotechnology and Natural Health Products Bureau, HPFB, Health Canada, Ottawa, ON.
[2] Faculty of Science, University of Ottawa, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Autoimmune disease (AD) occurs when one's tissues are attacked by the body's own immune system. Certain cells, such as Tumor necrosis factor (TNF) and interferon (IFN), help the body to develop autoimmunity. Sometimes those cells are ineffective in performing this function, and medical intervention becomes necessary. Medical practitioners are increasingly prescribing anti-TNF agents, which are designed to specifically target selected harmful molecules in the cascade of events involved in autoimmunity. Unfortunately, increased and prolonged use of anti-TNF agents have resulted in a growing number of reports of the development of autoimmune conditions, such as drug induced systemic lupus erythematosus (SLE), vasculitis and psoriasis. In this study Health Canada describes the clinical and laboratory evidence needed to better support the diagnosis and effectively manage the risk of drug-induced AD. Proper labelling is also necessary to make this risk more prominent in the pertinent product safety information. Health Canada will use the results of this study to provide practitioners and patients with the tools necessary to more readily recognise and delineate drug induced autoimmune condition from the innate autoimmune diseases that these products are intended to treat.

MISSION STATEMENT FOR PROJECT: Appropriate product labeling for LLS, careful clinical and immunological evaluations are useful to inform health care professionals and patients, prior initiation of biological therapies.

4.30 Development of a Luminex-Aptamer/Antibody System

E.D. Bernard[1], K.C. Nguyen[1], M.C. DeRosa[2], A.F. Tayabali[1], and R. Aranda-Rodriguez[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Department of Chemistry, Carleton University, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Humans come into contact with a wide range of chemicals from environmental sources including air, water, soil, food, and consumer products. Some chemicals can cause detrimental biological effects that lead to conditions ranging from inflammation to chronic diseases such as cancer. This project supports Health Canada's mandates to assess and manage the risk that chemicals pose to Canadians through the development of a new high throughput method to detect proteins that are produced by the body after exposure to chemicals or other stressors. We are looking for alternative detection systems that use DNA or RNA sequences capable of selectively binding to proteins of interest.

Conventional methods use antibodies which are difficult to use in some cases. This project sought to incorporate short RNA chains into a system that normally uses antibodies for biomarker detection. Our first system was designed to detect C reactive protein (CRP). The concentration of CRP in serum can vary by two orders of magnitude and it has been used to identify inflammation processes or as a biomarker of cardiovascular disease. A wider range of concentrations of CRP could be measured with our RNA system compared to a commercial kit that uses antibodies. This allowed more accurate and reproducible measurements of biomarkers in serum since less sample preparation was required before analysis.

The next step will be to add more biomarkers to our system which will provide more information on human response to environmental contaminants.

MISSION STATEMENT FOR PROJECT: The incorporation of aptamers into the Luminex platform will support Health Canada risk assessment and risk management under the Chemicals Management Plan.

4.31 Canada's National Drugs Observatory: What's it all about?

J. Snider[1], and S. Desjardins[1]

[1] Office of Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Monitoring the drug situation in Canada is carried out by the country's National Drugs Observatory (NDO). Its structure is based on the model jointly developed by European Monitoring Centre for Drugs and Drug Addiction and the Inter-American Drug Control Commission of the Organization of American States. The NDO brings together data from many sources to start to paint a picture of drugs and drug addiction. Its activities are split into the three main areas. The first, an Early Warning System, comprises high risk population monitoring, tracking the introduction of new substances through monitoring of the internet, analyzing the Drug Analysis Service's drug seizure data for emerging substances, and monitoring media reports and scientific and medical literature. The second, Routine Monitoring, includes general population and student surveys, drug supply surveillance, emergency department monitoring and a network of drug and alcohol surveillance experts. The third, Dissemination of Information, consists of sharing of drug and drug addiction information both nationally and internationally. The NDO, once built, will be the cornerstone of Canada's drug monitoring and information sharing activities.

MISSION STATEMENT FOR PROJECT: The NDO, once built, will be the cornerstone of Canada's drug monitoring and information sharing activities. In addition to routine monitoring and reporting activities, the NDO's early warning system will be used to detect and report on the emergence of new substances in Canada and provide information on the potential harms associated with these substances. The results from the NDO's activities will be used in support of Canada's National Anti-drug Strategy and as evidence when regulating new substances.

4.32 Acetaminophen Safety in Canada: Are we Doing Enough?

A.J. Slot[1], V.G. Punch[1], J. Patel[1], J.M. Dai[1], A. Nanifard[1], S. Angione[1], A. Hamilton[1], and L. Galand[1]

[1] Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Acetaminophen is the most widely used non-prescription drug product in Canada, with over 4 billion tablets sold each year. Currently, there are over 450 different acetaminophen products sold in Canada. Serious liver injury is a potential side effect of acetaminophen use, most commonly seen with overdose. The product label and guidelines for its safe use in Canada were updated in November 2009; however, there are still uncertainties as to whether the risks could be reduced further. To better understand these risks and their causes, scientific and medical literature were reviewed and summarized for information on acetaminophen-related liver injuries. There is a clear gap in information on vulnerable groups of people, for example Native Canadians or those with alcoholic liver disease. Information from this study will be used with that of other areas of a working group on acetaminophen safety to help guide: a) the development of new product labeling instructions and guidelines for use; b) standards on maximum pill amounts and daily amounts of acetaminophen; and c) insight to best management practices for acetaminophen overdose.

MISSION STATEMENT FOR PROJECT: By providing consolidated safety information to both internal and external stakeholders, this working group's mission is to provide guidance as how to best manage and mitigate the hepatic safety risks surrounding acetaminophen use in Canada. The MHPD Acetaminophen Review Team aims to do this by:

1. Bringing together directorates and bureaus with a vested interest in both safety and efficacy concerns concerning the use of acetaminophen containing products in adults and children.
2. Facilitating interaction among various internal stakeholders.
3. Sharing information and methodologies, which may help different directorates and bureaus in their own future work.
4. Establishing transparency, among internal stakeholders, and by monitoring progression of the ongoing activities and actions regarding the file, and bring forward concerns.
5. Discussing and providing feedback on important issues regarding acetaminophen-containing products and the concerns at hand such as methodology, risk communications, external stakeholder interactions, and the Scientific Advisory Panel involvement.

As such, a cross-directorate collaborative effort surrounding the potential hepatic safety issues associated with the use of both prescription and non-prescription acetaminophen products in adults and children was formed in November 2010, primarily in light of the regulatory developments in the USA.

The results of this review, and working group at large, may impact the recommended maximum daily dose, dosing regimens, and prescription status of acetaminophen-containing therapeutics in Canada.

4.33 Recombinant Human Serum Albumin Expressed in *Oryza sativa* Displays Higher Stability, Reduced Drug Binding and Greater Heterogeneity than Recombinant Human Serum Albumin Expressed in Yeast

G.E. Frahm[1], D.G. Smith[1], A. Kane[1], T.D. Cyr[1], M. Girard[1], and M.J.W. Johnston[1]

[1] Centre for Vaccine Evaluation, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Human serum albumin (HSA) is the most abundant protein component of human plasma and due to its abundance and specific properties it is utilized for numerous laboratory studies and pharmaceutical applications. HSA obtained from human blood has been replaced in drug formulations due to the fear of disease transmission and shortages in supply. This has given rise to the development of recombinant versions of the protein (rHSA) produced in yeast and Asian rice. We investigated the properties of a number of rHSAs and determined that albumin produced in Asian rice displays higher stability and reduced drug binding than rHSA produced in yeast. This comparison of rHSA from varying expression systems could have implications for the use of rHSA in drug formulations and laboratory studies.

MISSION STATEMENT FOR PROJECT: Greater understanding of how different expression systems alter the properties of recombinant proteins.

4.34 Interpretation of Human Biomonitoring Data from the Canadian Health Measures Survey in a Risk-Based Contact

K. Werry[1], A. St-Amand[1], A. Nong[2], S.M. Hays[3], and L.L. Aylward[3]

[1] Chemical Surveillance Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[3] Summit Toxicology LLP, Lyons, CO, USA

PLAIN LANGUAGE SUMMARY: Since 2007, the Canadian Health Measures Survey (CHMS) has been measuring hundreds of chemicals in blood and urine of Canadians. For many chemicals, Health Canada has determined levels of exposure that are considered safe. Information about how the body absorbs and breaks down a chemical can be used to calculate the amount that is expected to be present in a person's blood or urine if they were exposed to a chemical at this level. This calculated amount is called a Biomonitoring Equivalent (BE) and is a screening tool which can help us to better understand the significance of finding concentrations of chemicals in Canadians. For a number of chemicals measured in the CHMS, we have compared the measured level in blood or urine of Canadians to the calculated BE. For the majority of chemicals, the results suggest that the current level of exposure in Canadians is below the BE. However, for arsenic and cadmium, levels in a portion of the population exceed the BE suggesting that these chemicals could be a higher priority for further investigation. This analysis may be used by scientists and regulators when focusing efforts on specific chemicals.

MISSION STATEMENT FOR PROJECT: BEs can be used to screen biomonitoring data from the CHMS and other population-level biomonitoring surveys and prioritize chemicals for follow-up by risk assessors and/or risk managers.

4.36 Acetaminophen Overdose: Contribution of Various Canadian Data Holdings

S. Aziz[1], S. McFaull[2], T. Wang[1], L. Galand[3], and J. Griffiths[1]

[1] Therapeutic Effectiveness and Policy Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Health Surveillance and Epidemiology Division, Centre for Chronic Disease Prevention, PHAC,Ottawa, ON
[3] Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON, on behalf of the other Intra-Directorate Acetaminophen Working Group Members

PLAIN LANGUAGE SUMMARY: Acetaminophen overdose is one of the leading causes of morbidity and mortality due to poisonings, in Canada. While the Canadian Institute for Health Information's (CIHI) Discharge Abstract Database is useful in determining the incidence of hospitalizations with acetaminophen overdose-related acute liver failure across Canada, mortality rate associated with acetaminophen-related overdose, occurring outside of hospitals, remained unknown. To investigate several supplementary Canadian data sources, regarding acetaminophen overdose-related medical incidents and deaths, which occur outside of hospitals. Data were extracted and analyzed from the following Statistics Canada, Public Health Agency of Canada and CIHI data holdings: the Canadian Coroner and Medical Examiner Database (CCMED), Canadian Hospitals Injury Reporting and Prevention Program (CHIRPP) and the National System for Incident Reporting (NSIR). Additionally, information from the Institute for Safe Medicine Practices (ISMP) was requested. Various combinations of search terms were used to obtain cases/deaths of acetaminophen overdose.

Preliminary investigations revealed that, each data source provided important information concerning acetaminophen overdose-related medical incidents and deaths. Each database had several limitations (to be discussed), that precluded their usefulness as stand-alone evidence, for clarifying acetaminophen's safety profile. However, from the perspective of overdose-related deaths that occur outside hospital important information can be obtained from CCMED.

MISSION STATEMENT FOR PROJECT: Health Canada will consider these data in its risk mitigation strategies to address the risk of liver injury associated with acetaminophen overdose.

4.37 Hospitalizations with Acetaminophen Overdose-Related Acute Liver Failure in Canada, 2004-2011

T. Wang[1], L. Galand[2], and J. Griffiths[1]

[1] Therapeutic Effectiveness and Policy Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

[2] On behalf of the other Intra-Directorate Acetaminophen Working Group Members, Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Canadian data on rate of acetaminophen overdose-related acute liver failure (ALF) are essential to develop an appropriate risk mitigation approach concerning acetaminophen overdose.

The Canadian Institute of Health Information's Discharge Abstract Database (DAD) and Hospital Morbidity Database-Québec (HMDB) were used to estimate the prevalence of acetaminophen overdose (accidental or intentional)-related ALF in Canadian hospital settings.DAD and HMDB capture administrative, clinical and demographic information collected upon hospital discharge. International Classification of Disease (ICD) codes from the first 15 diagnosis fields of DAD (2004-2011) and HMDB (2004-2010) were analysed. National, age-, gender-, and province-specific annual prevalence rates were determined. Trends in prevalence rates were also examined.

From a total of over 31 million hospitalizations between 2004 and 2011, the overall rate of acetaminophen overdose-related ALF remained stable, with Alberta showing the highest rate. Of the acetaminophen-associated ALF cases, a higher proportion involved intentional overdose than accidental overdose. However, the proportion of accidental overdose cases increased 2-fold over the 8-year time interval.

This is the first national study to assess acetaminophen overdose-related ALF from Canadian hospital data. Health Canada will consider these data in its risk mitigation strategies to address the risk of liver injury associated with acetaminophen overdose.

MISSION STATEMENT FOR PROJECT: Health Canada will consider these data in its risk mitigation strategies to address the risk of liver injury associated with acetaminophen overdose.

4.38 Measuring the Effectiveness of 'Dear Healthcare Professional Letters' using an Interrupted Time Series Analysis Study Method

M. Lebrun[1], R. Fry[2], S. Aziz[2], T. Wang[2], J. DiMuzio[1], Y. Ge[1], J. Griffiths[2], and V. Hogan[1]

[1] Office of Risk Management and Science, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Therapeutic Effectiveness and Policy Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Risk communication is an important tool to fulfill Health Canada's responsibilities of keeping Canadians informed on health issues. Effective risk communication improves the lives of Canadians by raising awareness and supporting decision-making. Studying risk communication effectiveness has been limited due to a lack of systematic methods. To fill this gap, the 'Evaluating the Effectiveness of Risk Communications' Project was designed to measure the effectiveness of Health Canada's health product risk communications in a systematic way. This was done using 13 different methods that looked at the reach, clarity or impact of each risk communication. The Interrupted Time Series Analysis was one of these methods. It was used to measure changes in the volume of drugs prescribed before and after issuance of a specific risk communication tool (the Dear Healthcare Professional Letter (DHPL)). More than 30 DHPLs were studied. Many of the DHPLs were associated with significant reductions in the volume of drugs prescribed, though external factors, like media coverage, could not be excluded.

This work describes a new method that decision-makers can use to measure the impact of certain risk communications. Together with other methods, this will create a systematic way of measuring the effectiveness of our risk communications. Future work will include publications and development of internal procedures to standardize the process.

MISSION STATEMENT FOR PROJECT: This project used ITSA and other evaluation approaches to evaluate the effectiveness of Health Canada's risk communications. Such efforts will allow for the development of policies to better leverage resources, improve efficiency and enhance focus on how risk communications are used as a risk minimization tool, in turn, directly supporting the Department's mandate.

4.39 A Federal/Provincial/Territorial (F/P/T) Initiative for Menu-Labeling in Restaurants and Foodservices

A. Sullivan[1], V. Lien[1], E. Mansfield[1], and N. Lee[1]

[1] Nutrition Standards and Regulation Division, Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Consumers want menus to be labelled with nutrition information to help them make food choices when eating out in restaurants and food services. While some restaurants put nutrition information on their menus there are concerns that not all population groups are equally served by the nutrition information being provided. A Federal/Provincial/Territorial (FPT) Task Group, formed in June 2011, is currently developing a simple and low-cost approach that consumers can understand and use to make food choices when eating out in restaurants. The approach resulting from this work will be one part of Canada's broad strategy to support healthy eating environments.

MISSION STATEMENT FOR PROJECT: This F/P/T project will result in a voluntary approach for provision of nutrition information that encourages health choices and can be widely and economically adopted by restaurants and foodservices in Canada.

4.41 Canadian Health Expenditures: Analyses, Forecasts and Simulations

A. Peluso[1], and E. Tipenko[2]

[1] Statistics Canada, Ottawa, ON (work was completed while the author was with Health Canada)
[2] Health System Research and Forecasting Division, Applied Research and Analysis Directorate, SPB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The growth of healthcare expenditures provokes constant comments and discussions, as countries battle the issues on cost containment and cost effectiveness. In this context, this study examines factors influencing Canadian health expenditures in each of the seven components (hospitals, physicians, drugs, other institutions, other professionals, capital, and public health) and relationships among the components. The study also estimates the impact of ageing on future healthcare expenditures and produces a forecast of healthcare expenditures.

The data for the study are obtained from the CIHI's report "National Health Expenditure Trends, 1975 to 2012".

We found that:

1. Expenditures for different components are affected by different economic factors, such as GDP, population, physician compensation, etc.

2. A change in one component leads to a change in other components, e.g., a sudden increase in physician expenditures is followed by significant and prolonged increases in all other components of expenditures.

3. The expenditures among seniors grow slower than they do for younger people. This suggests that many other studies overstate the impact of ageing effect.

4. This study forecasts about 6% growth of expenditures annually; this growth will not be seriously impacted by high or low economic growth (only about 0.5% – 1%). However, this growth would decline to about 3% if the recent slowdown in health spending continues.

Healthcare expenditure forecast is important to Health Canada for setting and administering Canadian health care system because a prior knowledge of a high forecasted growth rate can help policy makers to employ timely and appropriate policy tools to avert such growth rate which could threaten the sustainability of the publicly funded healthcare system in Canada.

MISSION STATEMENT FOR PROJECT: As countries battle the issues on cost containment and cost effectiveness of healthcare expenditures, it is important to forecast the healthcare expenditure and to understand the underlying factors that influence the growth to help shape policies that would contain the expenditure without compromising the health of the Canadians.

4.42 Regulatory Cooperation Council (RCC): Outcomes of a 2-Year Initiative on US and Canada Cooperation on Human Health Risk Assessment of Nanomaterials

M. Hill[1], A. Afghan[1], L. Chen[1], and S. Bernatchez[1]

[1] New Substances Assessment and Control Bureau, SED, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Advances in nanotechnology have resulted in commercialization of many nano-enhanced consumer products with novel applications and improved performance and durability. These products may be manufactured in Canada, or imported from other countries, including the United States (US). In 2011, Prime Minister Stephen Harper and President Barack Obama announced the creation of the Canada-US Regulatory Cooperation Council (RCC) to increase regulatory transparency and coordination between the two countries in several areas.

For the past 2 years Canada and the US have worked together under the RCC Nanotechnology Initiative to seek greater alignment in regulatory approaches to nanomaterials through the implementation of a Work Plan developed with input from stakeholders. The Nanotechnology Work Plan fosters the sharing of information as well as scientific and regulatory expertise, and promotes the implementation of consistent approaches to the assessment and management of nanomaterials. A Comparative Analysis of Regulatory Frameworks in the US and Canada was conducted in order to identify areas where alignment of regulatory approaches would be feasible and appropriate. Peer review of a multi-walled carbon nanotube (MWCNTs) risk assessment was conducted and risk assessment tools and conclusions were compared. A common approach for identifying additional testing requirements for nanoparticles was drafted.

MISSION STATEMENT FOR PROJECT: The work under the RCC has identified best practices in the conduct of risk assessments of nanomaterials in Canada and the US. Data gaps and research needs have been identified, and a better understanding of each other's approaches to risk assessment and risk management of nanomaterials will enable future cooperation and sharing of tools, research priorities and regulatory development.

4.43 Internal Consultation: Preliminary Analysis of Regulatory Oversight for Organism-Based/Derived Products of Synthetic Biology

Drafting Team: S. Allard[1], G. Arvanitakis[2], B. Foster[4], R. Lejmi-Mrad[5], J. Leppard-Smith[5], T. Tao[5], A. Atkinson[5], and M. Trainer[2]

Advisory Group: A. Baume[6], L. Bourbonniere[3], G. Cianciarelli[3], L. Gémar[5], R. Manion[7], D. McGuire[8], C. Pinsonnault[2], R. Sigouin[5], and S. Semalulu[91]

1 Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON
2 New Substances Assessment and Control Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON
3 Food Directorate, HPFB, Health Canada, Ottawa, ON
4 Therapeutic Products Directorate, HPFB, Health Canada, Ottawa, ON
5 Science Policy Directorate, SPB, Health Canada, Ottawa, ON
6 Inspectorate, HPFB, Health Canada, Ottawa, ON
7 Health Canada Legal Services, Department of Justice Canada, Ottawa, ON
8 Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
9 Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Synthetic biology is an emerging field of biological research that seeks to apply the principles of engineering to the design and manipulation of biological systems.

This document, intended to be the first of a modular series of Departmental analysis on the issue, was developed to seek a common understanding of how current HC regulatory frameworks apply to products of synthetic biology, and related issues across the Department.

Case studies were developed for specific products using information gathered from the public and scientific literature (e.g., *E. coli* for bioethanol production, yeast producing a chemical intermediate for the anti-malarial drug artemisinin, and a synthetic virus vaccine). Analysis of current regulatory oversight was conducted across participating regulatory programs to identify gaps, if any, at the operational level.

This analysis indicates that the existing regulatory frameworks are adequate for first-generation products of synthetic biology (e.g., insertion or modification of multiple genes and/or biochemical pathways, often using direct DNA synthesis). For second-generation developments for which feasible innovations and potential applications are not readily apparent (e.g., artificial life from scratch), additional gaps can be anticipated in the development of risk assessment approaches/tools for complex synthetic organisms with no clear reference organism for comparison.

Findings of this review suggest that the Department is adequately prepared for foreseeable products in the near future. Challenges posed by more speculative innovations in the future may require targeted and appropriate policies, where and if necessary.

Furthermore, by explicitly articulating the full continuum of potential synthetic biology applications, this document can inform the development of risk communications plans.

MISSION STATEMENT FOR PROJECT: Although synthetic biology is in its infancy, the potential commercial applications are tremendous and a number of products are already making their way along the R&D pipeline to Health Canada regulatory programmes. Given the rapid progress in this field, it is likely that Health Canada will begin to see increasing numbers of regulatory submissions for synthetic biology-derived products in the near future. This proactive foresight analysis ensures that the Department is ready to conduct evidence-based assessments of these products in a transparent and timely fashion.

4.44 The Diabetes and Pregnancy TeleForm Project (DPTP)

E. Enros[1], S. Khan[2], M. McCauley[2], V. Flynn[3], and C. Awadi[2]

[1] Health Promotion and Disease Prevention Division, Interprofessional Advisory and Program Support Directorate, FNIHB, Health Canada, Ottawa, ON
[2] Planning, Information, and Performance Measurement, Strategic Policy, Planning, and Information, FNIHB, Health Canada, Ottawa, ON
[3] E-Health Infostructure Program, Health Infrastructure Support, Regional Operations, FNIHB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: High rates of gestational diabetes mellitus (GDM) among First Nations women is a major health concern and may play a key role in the development of type 2 diabetes. This project's objective was to link risk factors, care processes and GDM-related outcomes among on-reserve First Nations, and build capacity to track and use information to improve programs and services.

The First Nations and Inuit Health Branch (FNIHB) worked with five communities to develop a data collection tool (TeleForm) to track prenatal risk factors, prenatal visits, screening, and outcomes related to diabetes and pregnancy. Additional information about programs and services on and off reserve was collected by meeting with communities and mapping the processes prenatal clients go through to access health services.

Data collected from 570 prenatal clients showed that greater or earlier contact with on-reserve health programs and services were associated with healthier gestational weight gains, lower GDM incidence, and fewer pregnancy complications.

This project has strengthened the ability of communities and FNIHB to collect, provide and use health information to improve programs and services. FNIHB will continue to refine the TeleForm process to support the availability of and access to high quality data to inform programs and policies.

MISSION STATEMENT FOR PROJECT: To promote evidence-based policy development, operational planning and decision making regarding federal funded health service delivery in on-reserve First Nations communities.

Clean Air Regulatory Agenda

5.01 Assessment of the Cytotoxic Potency Determinants of Industrial Particulate Emissions: Stress-Gene Responses of Human Lung Epithelial Cells to Chemically-Defined Surrogate Mixtures of Metals and Polycyclic Aromatic Hydrocarbons

F. De Rose[1], S. Karthikeyan[1], D. Vladisavljevic[1], D. Breznan[1], E. Thomson[1], C. MacKinnon-Roy[1], N. Vuong[1], P. Kumarathasan[1], E. Dabek[2], J.-P. Charland[2], J. Brook[3], and R. Vincent[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Analysis and Air Quality Section, Air Quality Research Division, Atmospheric Science and Technology, Environment Canada, Ottawa, ON
[3] Processes Research Section, Air Quality Research Division, Atmospheric Science and Technology, Environment Canada, Toronto, ON

PLAIN LANGUAGE SUMMARY: A clear link has been established between exposure to air pollution and adverse health outcomes, however the effects of air particle chemistry on toxicity is less understood. The source of particle emission greatly impacts the composition and toxicity of particles, making identification of key particle components crucial to industry regulation. Here we investigated the response of stress genes in human lung cells following treatment with chemical mixtures that were representative of particles derived from seven industrial locations across Canada. The chemical mixtures were comprised of a subset of water soluble metals and organic compounds found in the native particles. We found that gene responses were related to the abundance of specific metals, and therefore particle-specific industrial sources. This method will be valuable in the identification of interactions between various chemicals that contribute to particulate matter toxicity.

MISSION STATEMENT FOR PROJECT: This work provides a better understanding of gene responses relevant to particle chemistry, and in turn, to the source of ambient air pollutants. Such data will be relevant to the identification and regulation of sources of concern.

5.02 The Association between Traffic Related Air Pollution, Socioeconomics and Respiratory Health

S. Cakmak[1], and C. Hebbern[1]

[1] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Living near roadways is associated with increased respiratory illness. However, socioeconomic factors such as lower income levels can also negatively influence respiratory health. This study addresses the role that economic disparity plays in the relationship between proximity to roads and respiratory illness in children, and additionally examines the effect of aeroallergens on this relationship. We found that traffic and socioeconomic status together adversely affected respiratory health, and this worsened with decreasing levels of community income and education. By identifying factors that may cause children to be more vulnerable to traffic pollution, these findings will allow for more appropriate air quality standards to be set.

MISSION STATEMENT OF PROJECT: The findings from this study provide information on health risks from the transportation sector in Canada, meeting requirements of the Clean Air Regulatory Agenda (CARA),and will aid in cost /benefit risk assessment of air quality policies using the Air Quality Benefit Assessment Tool (AQBAT). Additionally, it will better identify influential factors that may cause a child to be vulnerable to traffic pollution and aeroallergens, and thus allow for better air quality standards to be set in order to protect such individuals.

5.03 Do Synoptic Weather Types and Aeroallergens Modify the Effect of Air Pollution on Hospitalisations for Asthma

S. Cakmak[1], and C. Hebbern[1]

[1] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The spatial synoptic classification is a system for categorizing ambient weather conditions into one of seven distinct weather types. Air pollution levels and the effect of air pollution on human health can both be modified by synoptic weather type. Similarly, aeroallergens can modify the effect of air pollutants on human health and are in turn modified by weather type. Previous studies have found associations between air pollution, aeroallergens, weather and hospitalisations for asthma; however, none of the studies investigated air pollution and aeroallergen interactions on asthma hospitalization under different synoptic scale weather types.

In this study, we investigated if the air pollution effect on asthma hospitalization rates is modified by aeroallergens and whether synoptic weather type plays a significant role in this effect modification. Aeroallergens were found to significantly modify asthma hospitalization due to exposure to most of the air pollutants, and the size of the modification is closely associated with synoptic weather type.

MISSION STATEMENT OF PROJECT: Health Canada, the provinces, and Environment Canada, have developed the Canadian Air Quality Health Index (AQHI). This study provides information on air pollution health effects in Canada, and also addresses whether current air quality guidelines are sufficient.

The findings from this study will be applicable to risk management decisions and the development of air pollution standards in Canada. Furthermore, the results can be used to: inform Canadians about the health risks of air pollution; help those with underlying diseases make decisions on how to minimize their exposure to air pollution and associated health risks; and help them to modify behaviour in response to AQHI health warnings. For example, recommending at-risk individuals remain indoors on days with extreme heat and high air pollution levels may reduce morbidity.

5.04 Risk Assessment for Cardiovascular and Respiratory Mortality Due to Air Pollution and Synoptic Meteorology in 10 Canadian Cities

C. Hebbern[1], S. Cakmak[1], and J. Vanos[2]

[1] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] The University of Texas, Texas, USA

PLAIN LANGUAGE SUMMARY: The spatial synoptic classification is a system for categorizing ambient weather conditions into one of seven distinct weather types. These synoptic weather types affect ambient air quality, influencing both human health and the level of exposure to air pollution. Weather types can therefore modify the relationship between air pollution and mortality. This study examined the relative risk of all-non accidental, cardiovascular, and respiratory mortality from four air pollutants over the period 1981 – 1999, in 10 Canadian cities. We found greater risk of dying from respiratory disease causes than cardiovascular causes in the majority of combinations of weather type, season, and pollutant. Moist tropical days and dry tropical days were of greatest concern in the spring and summer, with carbon monoxide and nitrogen dioxide the most harmful air pollutants. The health impact of air pollutants is dependent not only on the level of the pollutant but also the full ambient state of the weather at the time, and this can be explored by considering synoptic weather types.

This study demonstrates the usefulness of estimating short term health-pollution associations based on incoming synoptic weather patterns, and may aid in development of prevention strategies that can improve human health.

MISSION STATEMENT OF PROJECT: The findings from this study improve our understanding of the complex relationships between the ambient environment and human health and are applicable to risk management decisions and the development of air pollution standards in Canada. The epidemiologial evidence provided highlights the importance of considering incoming weather types in heat health warning systems and prevention strategies.

5.05 Analysis of Flame Retardants in Electronic Products used in Canadian Homes

P. Mochungong[1], G. Abbasi[2], M. Diamond[2], and J. Zhu[1]

[1] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa ON
[2] Department of Geography, University of Toronto, Toronto, ON

PLAIN LANGUAGE SUMMARY: Flame retardants are widely used in a variety of electronic products. This study measured both brominated diphenyl ethers (BDEs) and non-BDE flame retardants in selected electronic and other household consumer products collected from Canadian e-waste recycling plants. Specifically 14 BDEs and 8 non-BDEs were analysed using gas chromatography (GC) mass spectrometry (MS). TBBPA was the dominant non-BDE in all samples while BDEs, specifically tetra-BDEs and penta-BDEs, dominated in polyurethane foam (PUF) from indoor furniture. BDE209 levels in outer polymer components from TVs were magnitudes higher than that in polymer components from other products. BDE209 also dominated in fabric samples as well as in PUF from interior of cars.

This study indicated the presence of both traditional and novel flame retardants in electronic products used in Canada, making them potential emission sources to the indoor environment.

MISSION STATEMENT FOR PROJECT: This project reinforces our understanding of the sources and pathway of SVOCs in the indoor environment, which is important in the government's efforts of improving indoor air quality in residential and non-residential buildings.

5.06 Association of Ambient Air Pollution with Emergency Department Visits for Headache: A Multi-City Study

M. Szyszkowicz[1], and T. Kousha[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Clean Air Regulatory Agenda, Health Canada is mandated to investigate new health outcomes which may contribute to future risk assessment. Some studies have suggested that ambient air pollution (AAP) may contribute to triggering headache or migraine. Few studies have investigated the role of AAP in hospital admissions related to headache and migraine in the Canadian context. We conducted a multi-city (9 Ontario cities) study during the period of April 2004 to December 2011. We examined associations between emergency department (ED) visits for headache and migraine and AAP concentrations. ED visits for migraine and headache were retrieved from the National Ambulatory Care Reporting System. AAP measurements were taken from the National Air Pollution Surveillance program.

MISSION STATEMENT FOR PROJECT: Our findings support the associations between levels of AAP and the number of ED visits for headache and migraine. The associations were stronger for patients diagnosed with additional health conditions including cardiovascular and mental health problems.

5.07 Association of Air Quality Health Index with Emergency Department Visits for Asthma, Otitis Media and Urticaria in Windsor, Ontario

M. Szyszkowicz[1], T. Kousha[1], and G. Valacchi[2]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] University of Ferrara, Ferrara, Italy

PLAIN LANGUAGE SUMMARY: Health Canada is mandated to investigate new health outcomes which may contribute to future risk assessment under the Clean Air Regulatory Agenda. Health Canada and Environment Canada proceeded to develop a new air-health index to scale health risks in relation to ambient air pollutants (AAP) concentrations in 2001. Based on the combined effects on mortality of three AAP (ozone, nitrogen dioxide, and fine particulate matter with a median aerodynamic diameter of less than 2.5 μm) the Air Quality Health Index (AQHI) was defined. Health Canada investigates correlations between AQHI and Emergency Department (ED) visits for some non-respiratory diseases (urticaria and otitis media) and a respiratory disease (asthma) in Windsor area hospitals, Canada.

The findings support the associations between AQHI and the number of ED visits for all the three cases in Windsor.

MISSION STATEMENT FOR PROJECT: The pollutants investigated in this study are a part of the Air Quality Health Index (AQHI), AQHI is a tool which can be used by Canadians to reduce their risk of exposure to high levels of ambient air pollution by modifying their outdoor activities. This study supports the use of the AQHI as a tool to reduce risks of morbidity and also mortality.

5.08 Sources of Ambient Volatile Organic Compounds in Montreal

M. Szyszkowicz[1], and E. Porada[2]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Université du Québec, Québec, QC

PLAIN LANGUAGE SUMMARY: Among different air pollutants in ambient air there is a large group of so called volatile organic compounds (VOCs). There are many health concerns related with concentration levels of VOCs in air. VOCs also participate in forming other air pollutants by chemical reactions. For example ground-level ozone formation is driven by two major classes of directly emitted precursors: nitrogen oxides and VOCs. Thus identification of VOC sources in urban environment is important in shaping risk management measures. Using measurement data (every sixth day) from four fixed monitor stations in Montreal, 175 different VOC species have been associated with emission sources.

The results concerning the typical urban emissions show higher concentrations of long-lived heavy fractions—in comparison to reported results in China and in Mexico, where volatile and strongly reactive VOCs are more pronounced. Emissions specific to Montreal: natural and man-made emissions of aromatic terpenes, industrial emission from Montreal's pulp and paper plants, fine chemicals from biochemistry plants and pharmaceutical manufacturing. This research has been completed under the mandate of the Clean Air Regulatory Agenda.

MISSION STATEMENT FOR PROJECT: Identification and categorization of anthropogenic VOC sources in urban environment helps to develop regulation on industrial activities.

5.09 Association of Ambient Air Pollution with Emergency Department Visits for Epistaxis, Substance Use Disorders and Lower Respiratory Disease

M. Szyszkowicz[1], E. Thomson[1], R. Shutt[1], T. Kousha[1], I. Colman[2], and B. Rowe[3]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] University of Ottawa, Ottawa, ON
[3] University of Alberta, Edmonton, AB

PLAIN LANGUAGE SUMMARY: The term Ambient Air Pollution (AAP) refers to the pollution that all of us breathe every day. Although these levels are generally low in Canada, many different health conditions have been linked to exposure to AAP in Canada. The following ambient air pollutants were considered: carbon monoxide, nitrogen dioxide, sulphur dioxide, ozone, and particulate matter. Although some breathing problems have been linked to AAP levels, little research has been done looking at the nose (specifically nosebleeds), or the lower respiratory tract. Recent studies also have looked at the effects of AAP on mental health, but not at substance abuse specifically. In order to look at the relationship between these diagnoses and AAP, Health Canada used a database of emergency department (ED) diagnoses from Edmonton (1992-2002) for three health conditions. Statistical methods were applied to investigate the links between the levels of AAP at the time of admission for each of the diagnoses. Ozone levels were positively linked with nose bleed and lower respiratory tract disorders. Carbon monoxide and nitrogen dioxide (both gases generated by burning, including gasoline and diesel engines) were associated with increased substance use disorder diagnosis at the ED. Reducing one's AAP exposure, even by changing the timing of outdoor activities may be one way to positively influence these health problems.

The pollutants investigated in this study are a part of the Air Quality Health Index (AQHI), a tool which can be used by Canadians to reduce their risk of exposure to high levels of AAP, by modifying activities. This research has been completed under the mandate of the Clean Air Regulatory Agenda.

MISSION STATEMENT FOR PROJECT: The pollutants investigated in this study are a part of the Air Quality Health Index (AQHI), a tool which can be used by Canadians to reduce their risk of exposure to high levels of ambient air pollution, by modifying activities, and support the use of the AQHI as a tool to reduce risks of morbidity as well as mortality.

5.10 Health Canada's Urban Transport Exposure Study: Assessing the Personal Air Pollution Exposure of Canadian Commuters

K. Van Ryswyk[1], S. Weichenthal[1], L. Sun[1], and L. Wallace[2]

[1] Air Health Science Division, Water and Air Quality Bureau, HECSB, Health Canada, Ottawa, ON
[2] Consultant, Santa Rosa, California, USA

PLAIN LANGUAGE SUMMARY: Health Canada's Urban Transport Exposure study was designed to address the question of what levels of air pollution Canadians are exposed to while commuting. Commuting represents a short term but routine activity performed in an environment known as an air pollution source. The transport methods of light rail (subways), buses and private vehicles were targeted in several of Canada's major metropolitans. Three technicians monitored personal exposures for three weeks (two weeks for private vehicles) in summer and winter. Air pollution exposures were analysed within each transport method. Results suggest that commuter exposures in private vehicles are affected by road type and traffic. Exposures in buses were related to propulsion type and subway exposures to station and car design features.

The personal exposure data collected in this study will provide a benchmark of Canadian commuter exposure which will be compared to past and future levels to estimate benefits of any future actions designed to mitigate exposure to traffic related air pollution (TRAP). As TRAP has been strongly associated with respiratory and cardiac diseases, these reductions will contribute to the mandate of Health Canada which is to improve the health of Canadians. Epidemiological models will be developed for each pollutant and transport method combination. These will provide insight into the determinants of personal exposure while commuting in Canada. Lastly, UTES data will be combined with human activity pattern data collected by the initiatives of other federal departments to provide estimates of daily exposure attributable to commuting.

MISSION STATEMENT FOR PROJECT: The Urban Transport Exposure Study will apply methodologies developed in previous CARA air pollution exposure studies to characterize exposure levels in Canadian transport environments using real time air monitoring and geo-spatial measurements with the purpose of attaining current objectives of the Clean Air Regulatory Agenda such as the identification of sources of air pollutants on which future studies can be based.

5.11 Effects of Traffic-Related Air Pollution on Cognition: A Pilot Study

J. Curran[1], R. Shutt[2], L. Liu[2], and C. Carlsten[1]

[1] The Air Pollution Exposure Laboratory, Chan-Yeung Center for Occupational and Environmental Respiratory Disease, School of Population and Public Health, Faculty of Medicine, University of British Columbia, Vancouver, BC

[2] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the federal Clean Air Regulatory Agenda (CARA), Health Canada is assessing the health impacts of transportation-related air pollution (TrAP). Health Canada is also in the process of developing standards for ambient air quality. In support of ongoing risk assessment and regulatory activities, the current study investigated the effects of TrAP on the brain. TrAP has been linked to changes in brain function in animal studies. The purpose of this pilot study was to determine if subtle changes in the ability to concentrate and process information optimally, collectively called cognition, could be seen in a group of human subjects exposed to Diesel Exhaust (DE). The study procedure allowed for measurement of small temporary changes in cognition, and assessed the practicality of including functional brain imaging tests (fMRI) in the protocol. Six individuals were tested in the pilot study. High quality data were obtained and cognitive function test results showed strong trends towards significance despite the small sample size.

These results suggest that we will be able to detect subtle changes in cognition following moderate controlled DE exposure. Based on the success of the pilot, our next step will be to begin a full scale study using the piloted procedure.

MISSION STATEMENT FOR PROJECT: This novel study validates a methodology that will provide high quality, important data in support of the CARA mandate, including the acute health impacts of TrAP, specifically effects on cognition, and will support mechanistic determination of the neurotoxicology of acute TrAP exposure in humans.

5.12 Air Health Effects Assessment Division: Health Assessment Approach for Transportation Fuels and Technologies

M. Egyed[1], and M. Rouleau[1]

[1] Fuels Assessment Section, Air Health Effects Assessment Division, Water and Air Quality Bureau, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Transportation is a major contributor to air pollution in Canada, especially in urban areas. Exhaust and evaporative air emissions from vehicles powered by gaseous or liquid fuels contain a variety of harmful air pollutants. As Canadians are exposed to vehicle emissions daily, estimating their impacts on air quality and population health is important. This information can help regulators to identify and to evaluate the effectiveness of policies to reduce exposure to air pollutants and to improve the health of Canadians. The Air Health Effects Assessment Division (AHEAD) of Health Canada measures the risks associated with the use of transportation fuels and technologies in Canada.

The AHEAD approach, developed under the Clean Air Regulatory Agenda, relies on a review of the scientific literature (e.g., toxicology and epidemiology studies), and the use of computer models to estimate transportation emissions, air quality impacts and human health impacts associated with designated transportation scenarios, such as changes in vehicle efficiency or fuel quality. Models are a practical tool for comparing the benefits of different transportation-related policy options, for the present and future years. The AHEAD works in close collaboration with Environment Canada, and regularly contributes to regulatory impact assessments for fuels and vehicle-related regulations.

MISSION STATEMENT FOR PROJECT: To provide health-based scientific assessments to inform the development of sustainable transportation fuels/technologies in Canada.

5.14 Quantifying the Contribution of Outdoor Particles to Indoor Air: An Examination of the Infiltration Factor (F_{inf}) and the Ambient Component of Residential Indoor Fine Particles Acrosss Canada

M. MacNeill[1], J. Kearney[1], L. Wallace[2], and A.J. Wheeler[1]

[1] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON
[2] Consultant, Santa Rosa, California

PLAIN LANGUAGE SUMMARY: Exposure to particulate matter (a complex mixture of extremely small particles and liquid droplets) has been associated with a variety of adverse health effects, including an increase in the number of emergency room visits, an increase in hospitalizations of people with cardiac and respiratory disease and premature mortality. However, many of these studies have examined the health effects associated with particle concentrations measured from a centrally located outdoor monitor. Since people spend most of their time indoors, understanding the indoor-outdoor pollutant relationship is important for understanding the exposures of the Canadian population.

The contribution of outdoor particles to residential indoor air can be estimated by quantifying the infiltration factor (F_{inf}). This factor determines the fraction of outdoor particles that penetrate the building and remain suspended. F_{inf} estimates were determined for studies conducted three Canadian cities. The results suggest that regional factors such as climate, housing stock, air conditioning use and window opening can influence the contribution of ambient particles on indoor residential concentrations. This work enables quantification of Canadian's exposure to ambient particles that infiltrate indoors. It also helps Health Canada meet its mandate by improving our understanding of the health risks associated with particulate air pollution, and informing risk management strategies.

MISSION STATEMENT FOR PROJECT: Under CARA, Health Canada has committed to identifying specific sources of indoor air pollution and assessing/managing the risks associated with outdoor air pollution. This research enables quantification of Canadian's exposure to ambient particles that infiltrate indoors. It also contributes to a better understanding of the health risks associated with ambient particulate air pollution and can inform risk management strategies.

5.15 Source-Specific and Multi-Pollutant Air Risk Assessment for Point Sources

J. Willey[1], T. Hancock-Chen[1], T. Dinu[1], N. Lyrette[1], P. Raymond[1], G. Colas[1], and B. Jessiman[1]

[1] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Air quality has significant effects on human health in Canada. Risk management has reduced air pollution over the last 20 years, though remaining impacts are still significant. Recent changes to the way that air quality is managed places emphasis on reducing pollution from specific sources. Through the Clean Air Regulatory Agenda, Health Canada's role in this is to identify the most effective manner to reduce air pollution. The goal of the work presented here is to characterize the potential health impacts of several major industrial sources of air pollution in order to provide information that will assist in prioritizing risk management actions. Selected installations representing several major types of industry were modelled to provide a picture of the range of emitted pollutant concentrations and the resulting air quality effects in a 30 x 30 km area around each facility. Risk was then determined for populations residing within the study area surrounding the installations, with significant differences in modelled pollutant concentrations, and the resulting health risks, found both within and between certain sectors (industry types). In many cases, the exact source of a health risk within a facility study area was identified.

Overall, the results are expected to assist in both regulatory and non-regulatory aspects of risk management.

MISSION STATEMENT FOR PROJECT: The project is intended to identify sources of air pollution which have greater potential impact on Canadian populations. The results are intended to be used in the Air Quality Management System in order to identify the most cost-effective manner in which to manage air emissions. Both non-regulatory and regulatory outcomes are envisioned.

5.16 The Socio-Economic Benefits of Better Health: Analysis using the Air Quality Benefits Assessment Tool (AQBAT)

M. Donohue[1]

[1] Economics Division, Risk Management Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: When the health risks that people face go down, their quality of life goes up. But by how much? Quality of life is affected by income, physical health, environment, leisure time, and many other factors. How does a reduction in risks to health measure up against these other things that also impact quality of life? When developing a regulation, Treasury Board rules require that departments assess the costs and benefits of the regulation, to determine how its implementation is going to impact overall quality of life for Canadians. Therefore, we need to be able to quantify the impacts of a regulation on quality of life, and objectively compare the relative importance of different costs and benefits.

This presentation will discuss the economic basis for quantifying the impacts of health risks on quality of life (i.e. “valuing” good health), as well as recent research and analysis that has been undertaken to quantify quality of life benefits for several recent regulations using the Air Quality Benefits AssessmentTool (AQBAT), a computer simulation application designed within Health Canada to estimate the human health and welfare benefits or damages associated with changes in Canada’s ambient air quality

This work allows the department to develop regulations that are more economically efficient and that better protect and enhance the health and quality of life of Canadians.

MISSION STATEMENT FOR PROJECT: Ongoing research in this field (and on this model) will allow the department to develop regulations that are more economically efficient and that better protect and enhance the health and quality of life of Canadians.

5.17 The Association between the Canadian Air Quality Health Index and Cardiac Rate and Rhythm Characteristics During Ambulatory Electrocardiography

R. Dales[1], S. Cakmak[1], L.M. Kauri[1], R. Shutt[1], M. Green[2], L. Liu[1], M. Mulholland[2], and D. Stieb[1]

[1] Population Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] University of Ottawa Heart Institute, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Disturbances in the rhythm of the heart (arrhythmias) may alter the way that blood moves through the body, increasing the risk of heart attack, stroke or sudden death. On days of higher air pollution, more Canadians are hospitalized for heart disease. To look at the relationship between air pollution and heart rhythm disturbances, we compared the daily Air Quality Health Index (AQHI) value and cardiac rhythms recorded from about 9000 patients who underwent outpatient cardiac monitoring at the University of Ottawa Heart Institute.

The AQHI is a numerical summary of the outdoor air pollution level used to inform the Canadian public of health risks associated with outdoor air pollution. We found that increases in heart rate and some arrhythmias were slightly more frequent on days when the AQHI value was higher; suggesting that an effect of air pollution on heart rate and rhythm might be one way that air pollution is linked to heart disease and stroke. These data also suggest that AQHI may be a useful tool to estimate cardiovascular risks related to air pollution. Increasing our understanding of how the AQHI can be used to inform Canadians of health risks related to air pollution is part of Health Canada's mandate under the Clean Air Regulatory Agenda.

MISSION STATEMENT FOR PROJECT: The results of this study suggest that the AQHI may predict cardiovascular morbidity risks related to air pollution. Increasing our understanding of how the AQHI can be used to inform Canadians of health risks related to air pollution is part of Health Canada's mandate under the Clean Air Regulatory Agenda.

5.18 Metal Composition of Fine Particulate Air Pollution and Acute Changes in Cardiorespiratory Physiology

S. Cakmak[1], S. Weichenthal[2], L.M. Kauri[1], M. Mahmud[1], K. Van Ryswyk[2], R. Shutt[1], J. Vanos[1], L. Liu[1], P. Kumarathasan[1], E. Thomson[1], R. Vincent[1], and R. Dales[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Clean Air Regulatory Agenda, Health Canada is mandated to assess the health impacts of air pollution from industry, in support of developing industrial emissions regulations. It has long been understood that fine particulate matter has negative effects on health; however less is understood about how the composition of particulate matter contributes to these effects. In this study we compared the lung and circulatory system function of a group of healthy young adult volunteers when they spent five consecutive 8-hour days either at a site very close to a steel plant or at a site several kilometers removed from the plant.

We also measured levels of outdoor air pollution at both sites and collected samples of the fine particulate matter. Levels of different metals in the fine particulate matter were measured and compared between the two sites. The effects of these metals on lung and circulatory system function were then estimated. Based on these estimates, we were able to determine that seven of the metals found in higher concentrations in particulate matter from the steel plant site may have negative impacts on circulatory and lung health.

MISSION STATEMENT FOR PROJECT: Studying the physiologic effects of components of fine particulate matter ($PM_{2.5}$) could contribute to a better understanding of the toxicology of air pollution, and inform future regulation of specific components of $PM_{2.5}$.

5.19 The Air Quality Health Index: Science that Speaks to Canadians

AQHI Team

[1] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Air Quality Health Index (AQHI) is health management tool that provides information about air pollution levels in over 70 cities across Canada. Developed by Health Canada, Environment Canada and a number of stakeholders, the index communicates the local air pollution level on a scale of one to ten directly to Canadians through a number of public media. The higher the number, the greater the risk to health. The AQHI also incorporates two sets of health messages: one for the general population and one for the at-risk population (seniors, children, individuals with cardiac and respiratory disease, etc.). The AQHI exemplifies Health Canada's mandate to maintain and improve health by providing advice on how people can maintain a healthy, active lifestyle, and when to adjust their activity to protect their health when pollution levels pose a greater risk.

A key component to the AQHI program is promotion and outreach, to educate the public, particularly the at-risk population, about the tool. The AQHI is a key program under the Clean Air Regulatory Agenda. This abstract outlines the multiple partnerships, techniques and tools we have developed to promote the AQHI across the country.

MISSION STATEMENT FOR PROJECT: The AQHI is a health management tool developed for Canadians, by Canadians, providing information to maintain an active lifestyle, while avoiding the risks posed by elevated levels of air pollution.

5.20 Possible Indoor Air Health Effects of 21 Volatile Organic Compounds and Application of Indoor Air Reference Levels to Health Based Product Emission Standards

J. Wong[1], C. Khoury[1], P. Goegan[1], A. Wilson[1], D. Schoen[1], D. Won[2], and W. Yang[2]

[1] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON
[2] Building Services and Indoor Environment Program, National Research Council, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Volatile organic compounds (VOCs) are a diverse group of chemicals measured in both outdoor and indoor air. One source of VOCs indoors is off-gassing from building materials. Health Canada, in collaboration with the National Research Council (NRC), is identifying materials that emit VOCs of greatest health concern.

Health risk assessments for VOCs published by international organizations were evaluated to determine 21 Indoor Air Reference Levels (IARLs) – defined as air concentrations below which no appreciable health effects would be expected from long-term exposure. When the IARLs were compared to the VOC levels measured in Canadian homes, four VOCs – acrolein, acetaldehyde, benzene, and formaldehyde – were identified as potential health concerns.

In preliminary chamber testing, NRC measured VOC emissions from 52 materials (flooring, wood-based materials, insulation, coatings, adhesives, caulking, foam sealants). Indoor air concentrations were estimated assuming typical use of the materials. Among the tested materials, the greatest contributor of benzene was insulation, whereas paint was the biggest contributor for acetaldehyde, acrolein, and formaldehyde.

Combining health assessment with emissions testing can support the development of VOC emission standards. Products certified to a health-based VOC standard would emit lower levels of the chemicals of greatest concern and contribute to healthier indoor air.

MISSION STATEMENT FOR PROJECT: Health Canada's work will support the development of a health-based product emissions standard by an external standards organization. Although the eventual standard would be initially voluntary, its adoption by provincial agencies or in commercial applications would be an important step to improving indoor air quality for Canadians.

5.21 Air Health Indicator

H.S. Shin[1], M. Mahmud[1], W. Burr[1], M. Smith-Doiron[1], B. Jovic[1], D. Stieb[1], B. Jessiman[2], and R. Burnett[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation and Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: The Air Health Indicator (AHI) provides a measure of the impact of outdoor air pollution on Canadian public health, in particular cardiopulmonary (heart-lung) deaths. Heart-lung deaths do not result solely from air pollution exposure (e.g., ozone and fine particulate matter), but rather from the combination of a variety of causes. The AHI aims to identify the risk for heart-lung deaths related solely to exposure to air pollution.

The AHI shows a slight increasing trend between 1990 and 2007 for heart-lung deaths that can be attributed to the exposure to ground-level ozone. The measure also indicates that 5% of heart-lung deaths were due to ozone exposure overall at the national level, and 3-7% across regional levels. Among five regions across Canada, two regions (Southern Ontario and British Columbia) were also found to have an increasing trend.

Neither an increasing nor decreasing trend between 2001 and 2007 is observed in the heart-lung deaths related to fine particulate matter ($PM_{2.5}$) exposure, whether nationally or at the regional level. About 1% of heart-lung deaths can be due to $PM_{2.5}$ exposure at the national level and 0-2% across the regional levels.

MISSION STATEMENT FOR PROJECT: While other studies have examined geographic patterns in mortality risk due to air pollution, the AHI study is the first to have evaluated the change in risk over time. These results are important from a policy perspective because they provide evidence for the success of departmental programs aimed at reducing air pollution concentrations, that is, whether such reductions improve population health.

5.22 Drivers of Toxic Potency in Particulate Air Pollution Samples Collected in the Vicinity of Industrial Sources

E. Thomson[1], S. Karthikeyan[1], D. Breznan[1], P. Kumarathasan[1], C. MacKinnon-Roy[1], N.Q. Vuong[1], S. Cakmak[1], J. Brook[2], E. Dabek-Zlotorzynska[2], J.-P. Charland[2], and R. Vincent[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Air Quality Research Division, Science and Technology Branch, Environment Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Airborne particulate matter is linked to adverse health effects. Industrial emissions are important contributors to particulate air pollution, but it is not clear exactly which particle characteristics and components are important in driving the health effects. This information is critical for more effective regulation of pollution sources. In this study we collected particles from the air at locations close to industrial sites. We exposed cells to the particles and measured a variety of biological measures. We then used statistical approaches to compare the responses to the composition of the particles. We found that biological responses varied by site, and were associated with particle size, the content of water-soluble metals, or the amount of non-water-soluble metals.

The study indicates that industrial emissions contribute to the composition of airborne particles, which in turn impacts biological responses. By studying the link between particle composition and biological effects, we hope to gain a better understanding of the specific factors in particulate air pollution that contribute to health effects. This information can then be used to help guide regulatory action.

MISSION STATEMENT FOR PROJECT: Attribution of toxic potency to particle constituents will help guide regulatory efforts aimed at reducing the health burden due to particulate air pollution.

5.23 Using the Canadian Census Health and Environmental Cohort to Support Canadian Accountability Tools

D.L. Crouse[1], P.A. Peters[1], and R. Burnett[2]

[1] Health Analysis Division, Statistics Canada, Ottawa, ON
[2] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Clean Air Regulatory Agenda, Health Canada is mandated to assess the risks of air pollution to the health of Canadians. The majority of studies about health risks associated with air pollution are based in the United States. No previous studies have evaluated the risks to health associated with long-term exposures to pollution among residents in urban, rural, and remote locations across Canada. The purpose of this research program is to identify associations between air pollution and risk of mortality among Canadian adults.

The 1991 Canadian Census Health and Environmental Cohort is a sample of 2.7 million adults who completed the 1991 long-form questionnaire and who have been linked to the Canadian mortality database with follow-up to 2006. Subjects have also been linked to tax files, which include annual, residential postal codes. We assigned estimates of exposure to fine particulate matter to subjects all across Canada, and estimates of nitrogen dioxide to subjects in the 10 largest cities.

In models adjusted for many personal and contextual characteristics (e.g., income, education, city size), we found elevated risk for cardiovascular mortality associated with exposure to these pollutants. Risks were insensitive to further indirect adjustment for smoking habits and obesity. Our results were somewhat surprising given the relatively low concentrations of pollution across Canada.

MISSION STATEMENT FOR PROJECT: Previously, there have been no studies that could evaluate the risks to health associated with long-term exposures to pollution across Canada, including residents in urban, rural, and remote locations.

5.24 The Association between Heart Rate Variability and Air Pollution Levels in the Sault Ste Marie Crossover Study

S. Weichenthal[2], R. Shutt[1], L.M. Kauri[1], M. Mahmud[1], K. Van Ryswyk[2], L. Liu[1], P. Kumarathasan[1], E. Thomson[1], R. Vincent[1], N. Evans[1], and R. Dales[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Under the Clean Air Regulatory Agenda, Health Canada is mandated to assess the health impacts of air pollution from industry, in support of developing industrial emissions regulations. Studies have shown that as air pollution increases the risk of death from heart disease also increases. We wished to examine the effects of industrial air pollution on heart rate variability (HRV), a measure of subtle changes in heart rate and rhythm. Changes in HRV can be an early indicator of stress on the cardiovascular system or heart disease in otherwise healthy individuals.

Previous studies have shown an effect of air pollution on HRV in healthy volunteers who cycled in high traffic areas. In this study, healthy young adult volunteers spent five consecutive 8-hour days either at a site very close to a steel plant, at a site several kilometers from the plant, or at the site close to the plant but wearing a personal air filtration system. When comparing between the three different air pollution exposure scenarios, no difference in HRV was seen. More in-depth investigation of the effects of single pollutants on HRV showed that some measures of HRV may change in response to changes in levels of some pollutants. Distance from the steel plant alone did not change HRV in this study. However, when we looked at the relationships between single pollutants and HRV, we saw changes. These relationships between changes in air pollution and changes in HRV may be one of the links between air pollution and risk of death from heart disease.

MISSION STATEMENT FOR PROJECT: Under the Clean Air Regulatory Agenda, Health Canada is mandated to assess the health impacts of air pollution from industry, in support of developing industrial emissions regulations. A better understanding of subtle effects of air pollution on the cardiovascular system will enhance the regulatory process by broadening the knowledge base available for use in risk assessment.

5.25 Toxicity of Air Particles from Different Sources Assessed by High Throughput Screening of Protein Profiles in Exposed Murine Macrophage Cells

P. Kumarathasan[1], D. Das[1], S. Mohottalage[1], D. Breznan[1], S. Karthikeyan[1], and R. Vincent[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Epidemiological studies have shown correlations between exposure to ambient air particles and adverse human health outcomes such as cardio-respiratory diseases. Air particles are complex mixtures consisting of particles of different sizes, inorganics including metals and organic constituents, based on emission sources. It is well known that the diesel exhaust particles contribute significantly to the overall properties and toxicity of urban air pollution. Although *in vitro* cell culture models are useful in investigating particle toxicity, our previous work indicated that traditional target assays are not sufficient to understand toxicity mechanisms. Hence, in this work we used a mass spectrometry-based protein screening methodology to obtain high-content information on protein profile changes in mouse macrophage cells exposed to particles from different sources. Our results showed that source related changes in physicochemical properties can influence protein profiles in the exposed cells and thus toxicity pathways.

MISSION STATEMENT FOR PROJECT: Information generated from this project can be applied towards risk characterization and regulation of air pollution, mission of Health Canada.

5.26 Evaluation of Direct-Reading Instruments for Monitoring Exposures to Ultrafine Particles in Indoor Environments

J. Niu[1], P.E. Rasmussen[1], R. Magee[2], G. Nilsson[2], and L. Lavigne-Brunette[3]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Intelligent Building Operations, Construction, National Research Council of Canada, Ottawa, ON
[3] HPFB, Health Canada, Ottawa, ON (during HCAP assignment to HECS Branch)

PLAIN LANGUAGE SUMMARY: Under the Clean Air Regulatory Agenda (CARA), Health Canada is mandated to conduct scientific research that aims to improve indoor air quality. A major challenge in monitoring indoor exposures to ultrafine particles (<100 nanometres) is the selection and effective use of suitable instrumentation. Portability, response time, and reliability are important selection criteria in addition to reasonable cost. Also, the sampling strategy must be able to capture the spatial and temporal variability of ultrafine particles. In this study, Health Canada collaborated with National Research Council to conduct an instrument performance evaluation in a room-sized experimental chamber, with the goal of recommending a suite of instruments to provide particle number, surface area and mass concentrations as well as particle size distributions with an acceptable level of uncertainty.

The performance of newly available portable instruments compared well with large stationary instruments which are currently the industry standard. We concluded that a combination of instruments is required to fully characterize exposures to ultrafines, due to the fact that no one instrument can provide all the required information.

MISSION STATEMENT FOR PROJECT: Under the renewed Clean Air Regulatory Agenda (CARA), Health Canada is mandated to conduct scientific research in support of indoor air quality management. This research, which was conducted in collaboration with the Ventilation and Indoor Air Quality Group at the National Research Council, has increased Departmental capacity for monitoring exposures to indoor air pollution, with particular focus on ultrafine particles, and provides a basis for development of indoor exposure monitoring guidance.

5.27 Biological Changes Relevant to Air Pollution in the Vicinity of Steel Mill

P. Kumarathasan[1], S. Karthikeyan[1], E. Blais[1], A. Bilecki[1], K. Blank[1], E. Thomson[1], S. Cakmak[1], S. Weichenthal[2], L.M. Kauri[1], R. Shutt[1], L. Liu[1], R. Dales[1], and R. Vincent[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON

[2] Water and Air Quality Bureau, Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Elevation in ambient air pollution is correlated with increased cardiorespiratory health effects. Health Canada is mandated to investigate air pollution exposure-related adverse health impacts, and especially the Clean Air Regulatory Agenda (CARA) focuses on identifying source emission-related effects. The information that is lacking currently is the understanding of what drives the toxicity of these pollutant mixtures, and if and how the different sources contribute to air pollution. In order to achieve this, we have analysed biomarkers of effects in blood plasma and saliva of healthy volunteers who spent five consecutive days either at a site closer to a steel plant with a personal air filter system, or without it or at a site several kilometers away from the plant.

Our observations indicated that big endothelin a molecule both in saliva and blood plasma that can affect the health of blood vessels was correlated with air pollution exposure namely ozone and with blood pressure measurements. This can be an important pathway by which air pollution exerts negative cardiovascular effects. Such information is essential in terms filling the gaps in knowledge required for regulating (e.g., CARA) and in managing the risk associated with these pollutants by Health Canada.

MISSION STATEMENT FOR PROJECT: Mission statement: Information obtained from this study will be used to identify risk associated with source emissions and in turn will assist in the regulatory process.

5.28 Development of a Comprehensive Screening Strategy for the Toxicity of Airborne Particulate Matter in Support of the Clean Air Regulatory Agenda

D. Breznan[1], E. Thomson[1], S. Karthikeyan[1], P. Kumarathasan[2], C. MacKinnon-Roy[1], N.Q. Vuong[1], Y. Siddiqui[1], J. Crispo[1], A. Filiatreault[1], J. Brook[3], and R. Vincent[1]

[1] Hazard Identification Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Mechanistic Studies Division, Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[3] Atmospheric Environment Service, Environment Canada, Downsview, ON

PLAIN LANGUAGE SUMMARY: Exposure to air pollution has been linked to cardiovascular health effects. The understanding of the contributions of different industrial sources to toxicity of air pollution particles requires a combination of numerous methods that have to be developed and tested for reliability. We have created protocols for tracking particles and biological samples, separation of particles from filters on which they were collected, testing their toxicity in cells, quantifying particle potency (strength of the toxic effects), managing bacterial contamination in particles, handling large datasets, determining particle material properties, and developing methods for further testing in cells and animals.

Particles were collected on foam filters over several weeks using an instrument that can separate them based on size. We established methods for separation of particles from filters in liquids and for obtain their accurate weight. We developed miniaturised tests to study the effects of particles on several cell lines using several different measures of toxicity. Bacterial contamination was controlled by heating the particles and treating the cells with antibiotics. A spreadsheet for efficient experimental data management was designed. We created an approach to evaluate toxicity of air pollution particles from various industrial sources and determine which particle properties drive the toxic effects. This information will be useful for regulation of air pollution based on source-contribution.

MISSION STATEMENT FOR PROJECT: This project was intended to create an approach to evaluate the toxicity of air pollution particles from various industrial sources and determine which particle properties drive the toxic effects. This information will be useful for filling knowledge gaps on source-contribution, aiding in achieving air quality objectives.

5.29 Source, Size and Seasonal Differences in the Cytotoxicity of Ambient Urban Particulate Matter Collected at Three Different Locations across Canada

S. Karthikeyan[1], E. Thomson[1], D. Breznan[1], Y. Siddiqui[1], P. Goegan[1], P. Kumarathasan[1], J. Brook[2], M. Denison[3], and R. Vincent[1]

[1] Environmental Health Science and Research Bureau, Environmental and Radiation Health Sciences Directorate, HECSB, Health Canada, Ottawa, ON
[2] Processes Research Section, Air Quality Research Division, Atmospheric Science and Technology, Environment Canada, Toronto, ON
[3] Department of Environmental Toxicology, University of California, Davis, California, USA

PLAIN LANGUAGE SUMMARY: Exposure to particulate air pollution has been linked to adverse health effects. Observed population health effects vary depending on study location, season and the size of particles. Validation of these observations through laboratory studies, and identification of particle constituents responsible for toxicity is critical to our regulatory efforts. In this work, we assessed the toxicity of airborne particles collected during the summer and winter seasons from three different locations in Canada, Pitt Meadows (British Columbia), Downsview (Ontario) and Saint John (New Brunswick). The toxicity was assessed in cells using established laboratory tests.

Our results show that location and season has a large impact on the composition and toxicity of airborne particles. In particular, the composition of elements such as aluminum and copper were most related to the toxicity responses. We are further assessing the contribution of wind direction during particle sampling as a measure of contribution of specific local pollution sources versus distant pollution sources to observed toxicity responses. Such information will further support regulatory efforts.

MISSION STATEMENT FOR PROJECT: This work provides a better understanding of the impact of specific factors such as particle size, season and chemistry on the toxicity and potential health risks of ambient particulate matter, leading to a more informed regulation of the criteria air pollutant.

5.30 Differential Effects of the Soluble and Insoluable Fractions of Urban Particulate Matter Assessed by Proteomic and Genomic Analyses of Human Lung Epithelial Cells

N. Vuong[1], S. Karthikeyan[1], S. Mohottalage[2], A. Star[1], C. MacKinnon-Roy[1], D. Breznan[1], D. Vladisavljevic[1], E. Thomson[1], P. Kumarathasan[2], and R. Vincent[1]

[1] Inhalation Toxicology Laboratory, Hazard Identification Division, HECSB, Health Canada, Ottawa, ON

[2] Analytical Biochemistry and Proteomics Laboratory, Mechanistic Studies Division. HECSB, Health Canada, Ottawa, ON

PLAIN LANGUAGE SUMMARY: Ambient airborne particles are complex mixtures of metals, ions and organic species that can vary a thousand-fold in size. It is a challenge to identify the mechanisms of action of urban particles that may lead to adverse health effects. This study aimed to identify the molecular mechanisms of toxicity in human lung cells in response to Ottawa urban particles. The soluble chemicals from urban particles, as well as the insoluble material, were found to independently affect lung cells, and to interact, showing distinct patterns of changes in proteins and genes. The particles affect the mitochondria, the location in the cells where cellular energy is produced, and activate molecules that lead to cell death. The integrative proteomic and genomic approach will be useful for future studies of urban particle from different cities in Canada.

MISSION STATEMENT FOR PROJECT: This work provides a better understanding of the molecular mechanisms leading to the toxicity and potential health effects of ambient airborne particulate matter. The knowledge gained will be useful for informed regulation of air pollutants.

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