Book of Abstracts

2009 Health Canada Science Forum

Health Canada Science Plan - Implementing Health Canada's Science and Technology Strategy

Foreword

As the Department's Champion for Science, and as host of the 2009 Science Forum, it is my pleasure to thank you all for participating in the eighth annual Health Canada Science Forum, the most important science event on the department's calendar. I hope you will find this year's program and new venue exciting and find it a valuable opportunity to develop and strengthen collaborations in support of departmental priorities.

The overall theme for this year *"Health Canada Science Plan – Implementing Health Canada's Science and Technology Strategy"* is intended to respond to the Health Canada Science and Technology Strategy that was launched at the 2008 Forum, by introducing the Science Plan. The objectives of the Forum are to: 1) showcase the excellent work of Health Canada's science community; 2) identify and address gaps in the contribution of science to the implementation of Health Canada's mandate; 3) promote new collaborations within the department, portfolio and the broader Canadian and international health science community; and 4) contribute to a stronger science culture in Health Canada.

Presentations and discussions will be structured around three sub-themes: 1) Strengthening the Science, Policy and Regulatory Continuum; 2) Science Foresight: Surfing the Innovation Wave; and, 3) Interdisciplinary Networks to Integrate Science. The Organizing Committee has put much thought in identifying topics that will, I trust, generate interesting presentations and fruitful discussions.

I would like to express my appreciation by thanking the Organizing Committee and the Abstract Review Committee, as well as the staff in the Science Policy Directorate, for their dedication and outstanding work in planning this event.

Karen L. Dodds, Ph.D.
Assistant Deputy Minister
Strategic Policy Branch

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Jamie Nakai
Research Scientist, Research and Radiation Directorate, HECSB

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Anu Shukla
Laboratory Technician, Food Directorate, HPFB

Phil Shwed
Research Scientist, Research and Radiation Directorate, HECSB

Trevor J. Stocki
Research Scientist, Research and Radiation Directorate, HECSB

Azam Tayabali
Research Scientist, Research and Radiation Directorate, HECSB

Renaud Vincent
Head, Research and Radiation Directorate, HECSB

Mike Wade
Research Scientist, Research and Radiation Directorate, HECSB

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Strengthening the Science, Policy and Regulatory Continuum

Science Foresight:: Surfing the Innovation Wave

Interdisciplinary Networks to Integrate Science

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

FNIHB: First Nations and Inuit Health Branch
HECSB: Healthy Environments and Consumer Safety Branch
HPFB: Health Products and Food Branch
SPB: Strategic Policy Branch
RPB: Regions and Programs Branch
PACCB: Public Affairs, Consultation and Communications Branch
CSB: Corporate Services Branch

Other Acronyms:

PMRA: Pest Management Regulatory Agency
PHAC: Public Health Agency of Canada
CIHR: Canadian Institutes of Health Research

1.01 Lead in Indoor Dust From a 60-Year Old Home: A Novel Method of Linking its Origins to Old Paint

S. Beauchemin, PhD[1], P.E. Rasmussen, PhD[2,3], and L. Maclean, PhD[1,2]

[1] Natural Resources Canada, CANMET-MMSL, Ottawa, ON
[2] Exposures and Biomonitoring Division, HECSB, Health Canada, Ottawa, ON
[3] Earth Sciences Department, University of Ottawa, Ottawa, ON

SUMMARY: This study demontrates that the X-ray absorption near-edge structure (XANES) spectra of lead in old paints were identical to those of the indoor dust samples collected from a 60-year old house, indicating that old paint was the dominant source of lead in the household dust.

BACKGROUND/OBJECTIVES: Organic and inorganic lead (Pb) compounds have been used in the manufacture of paint since the 19th century. Prior to the 1960s, the Pb content of paint was as high as 50% weight. Therefore, lead-rich paint in houses built during those years may remain a significant source of indoor Pb contamination. The objective of this study was to assess whether Pb in paint significantly contributed to the Pb signature of the settled, indoor dust from a 60-year old house located in an urban residential area.

METHOD: Prior to any renovations, settled dust samples were collected from individual rooms using the high volume small surface sampler (HVS3). A composite dust sample was obtained by homogenizing the contents of householder vacuum bags collected over a one-year period. XANES spectroscopy was performed on both types of dust samples, and on old paint layers collected during a renovation, to determine the Pb speciation. The Pb concentration in the household dust samples varied from 200 to 1000 mg kg^{-1}, while paint samples contained from 380 to 2 920 mg Pb kg^{-1}.

RESULTS: All dust samples exhibited a Pb XANES signature identical to that of Pb found in the paints, whether the dust samples were a composite sample of the whole house or representative of individual rooms. According to the fitting results, either Pb citrate on its own or a mixture of $PbSO_4$, $PbCrO_4$ and PbO gave a very close fit to the measured spectra of the paint.

CONCLUSIONS: This study underscores the importance of guidance to Canadians to minimize their exposures to Pb in housedust, especially during renovation activities. XANES analyses unequivocally identified subsurface layers of leaded paint to be the dominant source of Pb in settled dust. Precise identification of the Pb compounds used in the paint will require additional micro-spectroscopic and infra-red analyses.

1.02 Glycosylation of Interferon Alpha 2a Alters the Dynamics of the Protein Backbone

P. Belcourt[1], S. Sauvé[2], D. Brochu[2], M. Gilbert[3], and Y. Aubin[3]

[1] Department of Biology, Carleton University, Ottawa, ON
[2] National Research Council Canada, Institute for Biological Sciences, Ottawa, ON
[3] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

SUMMARY: After synthesis in human cells, many proteins are modified by the addition of saccharides (sugars) by a process called glycosylation. These saccharides modulate the biophysical properties of the protein such as structure, stability and bioactivity. This paper describes the effects of one sugar unit on the structure of interferon alpha 2a. The latter is a member of the type I interferons (IFN) which are among the most widely used human recombinant protein therapeutics for the treatment of several cancers and viral infections.

OBJECTIVES/BACKGROUND/ISSUE(S): Study the effects of glycosylation on the structure of interferon alpha 2a using nuclear magnetic resonance spectroscopy.

DESIGN/METHOD/DESCRIPTION: A sample of the glycosylated IFN alpha-2a is prepared by adding the GalNAc moiety with *in-vitro* synthesis techniques on carbon-13 and nitrogen-15 labelled IFN alpha-2a prepared by recombinant techniques in *E.coli*. The structure and dynamics of the resulting glycoprotein was then studied by the application of a number of nuclear magnetic resonance (NMR) experiments.

OUTPUT/RESULTS: Analysis of the NMR data first confirmed that threonine 106 was the site of glycosylation. In addition, measurements of the heteronuclear nuclear overhauser enhancement (NOE) of nitrogen-15 show that the presence of a single sugar unit, significantly rigidifies the protein backbone at the glycosylation site. Calculation of the three-dimensional structure is underway.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Recombinant protein therapeutics are produced by a variety of biotechnologies. For many products such as interferons, glycosylation is not required for biological activity but it modulates important quality attributes such as solubility and long-term stability of the product. In addition to providing a better characterisation of a glycosylated protein, this study is the first step toward developing NMR-based methods for the analysis of these health products.

While successful hybridoma production experiments consistently yield 80% IgM and 20% IgG monoclonal antibodies (MAb), routine immunoassay-based target protein quantitative studies on vulnerable populations extensively rely on IgG MAbs only with no standard protocols available for IgM. The size and complex pentameric structure of IgM (Mr 1000kDa) is generally speculated, by many investigators, to contribute towards steric hindrance, that may, potentially nullify immunoassay results. There are no reports to confirm whether this speculation is a real occurrence or not.

1.03 Copper Transporter 1 Plays a Major Role in the Uptake of Silver in Mammalian Cells

J. Bertinato, PhD[1], L.J. Plouffe[1], L. Cheung[1], and R. Hoque[1]

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

SUMMARY: Silver is a nonessential toxic metal found in foods and used in a variety of applications. Currently, it is not known how silver enters into mammalian cells. Here we show that an enzyme required for importing copper into cells is also involved in the uptake of silver.

OBJECTIVE: Silver is a nonessential metal that is toxic to humans. Although exposure to high levels of silver is rare, the presence of silver in certain foods and use in a variety of applications as an antibacterial agent (e.g., topical gels, washing machines) can lead to exposures causing toxic effects. Despite its widespread use, the mechanism(s) by which silver enters into mammalian cells is presently unknown. Studies have shown that silver can block copper transport into cells by copper transporter 1 (Ctr1) suggesting that silver may be imported into cells by Ctr1. In this study we investigated the role of Ctr1 in the uptake of silver into mammalian cells.

METHODS: Human Ctr1 (hCtr1) and a hCtr1 variant containing amino acid substitutions M150L, M154L known to abrogate copper transport were transiently over-expressed in COS-7 African green monkey kidney cells as green fluorescent protein (GFP) fusion proteins. Transfected cells and Ctr1-deficient mouse embryonic fibroblast ($MEF^{-/-}$) and isogenic wild-type ($MEF^{+/+}$) cells were incubated in medium supplemented with 10 uM $CuSO_4$ or $AgNO_3$ for 5 h prior to measuring cellular copper or silver content, respectively.

RESULTS: Cells over-expressing hCtr1-GFP hyper-accumulated both copper (>10-fold increase) and silver (>3-fold increase) compared to control cells transfected to express GFP alone. Copper and silver content in $hCtr1_{M150L,M154L}$-GFP expressing cells was similar to control cells indicating complete abrogation of copper and silver transport by the M150L, M154L substitutions. $MEF^{-/-}$ cells accumulated approximately 2-fold less silver compared to $MEF^{+/+}$ cells.

CONCLUSIONS/IMPLICATIONS: These data indicate that Ctr1 can transport both copper and silver and suggest that Ctr1 plays a major role in the uptake of silver into mammalian cells. This is the first demonstration of a mechanism for silver import into mammalian cells and provides valuable information for future assessment of the health risks associated with exposure to silver.

1.04 Prescription Opioid Use Among Convicted Drinking Drivers

B. Brands[1,2,3], R. Flam Zalcman[2], R.E. Mann[2,3], G. Stoduto[2] , and R.K. Thomas[2]

[1] Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON
[2] Centre for Addiction and Mental Health, Ottawa, ON
[3] University of Toronto, Toronto, ON

SUMMARY: Study examines self-reported prescription opioid use among convicted drinking drivers in Ontario. Data based on completion of Ontario remedial program "Back on Track" (2000 - April 30, 2005). Prevalence of use within 90 days preceding assessment was 7.6%. Further research on use of prescription opioids in this population is warranted.

AIMS: Relatively little evidence exists on the prevalence of use of prescription opioids among high risk groups such as convicted drinking drivers who are known to be at elevated risk of collision involvement. In this study we examine self-reported use of prescription opioids among convicted drinking drivers.

METHODS: Data are based on 22 277 convicted drinking drivers (88% males, mean age=44years) who completed Ontario's remedial program 'Back on Track' (BOT), including assessment and 6 month follow-up, between 2000 and April 30, 2005. Measures examined included numbers of days using alcohol and other drugs, average number of drinks per drinking occasion, number of substance-related problems experienced and number of users of each substance in the 90 days prior to the assessment and follow-up interviews. The substances examined were alcohol, cocaine, amphetamines, cannabis, benzodiazepines, barbiturates, prescription opioids and tobacco. Substance-related problems were measured by the Research Institute on Addictions Self Inventory, Alcohol Dependence Scale and the Drug Abuse Screening Test.

RESULTS: The prevalence of prescription opioid use in the 90 days preceding assessment was 7.6%. Among drivers who reported use of only one prescription drug, the largest number reported using prescription opioids (1156), compared to 261 who reported using benzodiazepines. Drivers who reported using alcohol and prescription opioids but no other drugs had similar scores on problem measures to those who reported using alcohol alone, or alcohol and drugs other than prescription opioids. However, drivers who reported using alcohol, prescription opioids, and other drugs had significantly higher scores on all problem measures, suggesting that this group is at particularly high risk for subsequent problems.

CONCLUSION: Further research on the use of prescription opioids in this population is warranted. As we start our discussions to define a new drug strategy post National Anti-Drug Strategy (NADS), data such as this will be useful in priority considerations.

1.05 Bisphenol A in Bottled Water Products

X.-L. Cao, PhD[1], and J. Corriveau[1]

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

SUMMARY: Levels of bisphenol A in bottled water products sold in Canada were determined in order to provide data for exposure assessment.

OBJECTIVES: To determine levels of bisphenol A (BPA) in bottled water products sold in Canada and to provide data for human exposure assessment.

DESIGN/METHOD/DESCRIPTION: The main source for BPA contamination of the aquatic environment and water supply is from the discharge of BPA manufacturing or processing plants. For polycarbonate (PC) bottled water products, the additional source of BPA is from the migration of the residual BPA in PC containers. Higher BPA levels could be observed in some PC bottled water products due to accidental or careless exposure to heat for extended periods of time during storage and transportation. In this study, levels of BPA in 56 bottled water products sold in Canada packaged in PC and non-PC containers were determined using a method based on isotope dilution headspace solid-phase microextraction and gas chromatography-mass spectrometry.

OUTPUT/RESULTS: Levels of BPA in samples of all 51 non-polycarbonate bottled water products were lower than the method detection limit (0.50 µg/L). Levels of BPA in most of bottled water products in PC carboys were low, ranging from < 0.50 to 1.4 µg/L with an average of 0.75 µg/L. However, BPA was detected at levels of 8.8 and 6.5 µg/L in two samples of the same brand bottled water products in PC carboys, likely due to accidental or careless exposure of the products to heat during storage and/or transportation for extended periods of time.

IMPACT/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Since PC is a clear, strong, and rigid thermoplastic, PC carboys are still the convenient containers for storage of large volumes of water. While levels of BPA in water bottled in PC carboys stored under normal conditions (at or below room temperature) are low, care should be taken to avoid accidental and careless exposure of the PC bottled water products to heat (e.g., under the sun) during storage and/or transportation.

1.06 Bisphenol A in Canned Soft Drink Products

X.-L. Cao, PhD[1], J. Corriveau[1], and S. Popovic[1]

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

SUMMARY: Levels of bisphenol A in various canned soft drink products sold in Canada were determined to provide data for exposure assessment under government of Canada's chemicals management plan.

OBJECTIVES: To determine levels of bisphenol A (BPA) in canned soft drink products sold in Canada and to provide data for human exposure assessment.

DESIGN/METHOD/DESCRIPTION: BPA is used in the production of epoxy phenolic resins, which are used in the internal coating for food and beverage cans to protect food and beverage from direct contact with metal. Residual BPA in can coatings could migrate into foods, especially at elevated temperatures. As part of the evaluation process for BPA under the Government of Canada's chemical management plan, exposure data from various canned food products are needed to conduct human exposure assessment. In this study, levels of BPA in 72 canned soft drink products were determined using a method based on solid phase extraction and gas chromatography-mass spectrometry.

OUTPUT/RESULTS: Except for three products from which BPA-d16 could not be recovered at all due to product composition interferences (e.g., quinine hydrochloride in tonic water), BPA was detected in all of the other products at levels ranging from 0.032 to 4.5 mg/L. About 75% of the products had BPA levels less than 0.5 mg/L, and 85% of the products had BPA levels less than 1 mg/L.

IMPACT/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Compared to the BPA levels in other canned food products, BPA levels in canned soft drink products are much lower. Thus exposure to BPA through consumption of canned soft drink products will be low. If an adult (60 kg body weight) consumes one canned drink (355 mL) per day, the dietary intake of BPA will be 0.0034 µg/kg body weight/day based on the average BPA level in soft drinks (0.57 µg/L) or 0.027 µg/kg body weight/day based on the highest BPA level (4.5 µg/L) in one of the drinks, much lower than the provisional TDI of 25 µg/kg body weight/day established by Health Canada.

1.07 Biological Effects of Radon Gas Exposure

V. Chauhan, PhD[1], M. Howland[1], S. O'Hara[1], B. Kutzner[1], C. Ferrarotto[1], J. McNamee, PhD[1], P. Bellier, MSc[1], T.J. Stocki, PhD[1], L.A. Beaton, MSc[2], and R.C. Wilkins, PhD[1]

[1] Research and Radiation Directorate, Product Safety Program, HECSB, Health Canada, Ottawa, ON
[2] Department of Physics, Carleton University, Ottawa, ON

SUMMARY: Approximately half of the exposure to natural radiation is through alpha (α)-particles from radon (^{222}Rn) gas. Epidemiological studies have found a positive correlation between ^{222}Rn gas exposure and lung cancer. An understanding of the mechanistic basis for these effects remains limited. The aim of this study was to determine the biological effects of ^{222}Rn gas exposure.

OBJECTIVE: Experiments were designed to investigate the induction and repair of DNA double strand breaks (DSBs) and the release of pro-inflammatory chemokines from human peripheral blood cells (THP-1) exposed to α -radiation.

METHODS: THP-1 cells were exposed to Americium (^{241}Am) electroplated discs and analyzed for biological endpoints. As it is well known that DNA is a critical target for the biological effects of radiation, experiments were designed to quantitatively determine the presence of DNA DSB repair foci following α-particle exposure in cells using a standard technique that monitors the presence of phosphorylated H2AX foci (γ-H2AX). The alkaline comet assay was employed to measure the amount of primary DNA damage in relation to the dose of radiation received. In addition, cell culture supernatants were tested for the expression of pro-inflammatory chemokines known to be involved in tumour genesis.

RESULTS: Cells irradiated with α-particles showed statistically significant, dose-dependant increases in γ-H2AX formation. The alkaline comet assay showed no evidence of DNA damage following cell irradiation at low doses relative to the control cells, potentially due to rapid repair. A linear dose-dependant increase in the chemokines (IL-8, RANTES and CXC-IP10) involved in tumour formation was observed relative to untreated cells.

CONCLUSION: These results suggest that α-particle radiation causes DNA damage but at low dose rates of exposure this damage is efficiently repaired. The release of pro-inflammatory chemokines involved in tumour formation suggests a possible mechanistic basis for the association of ^{222}Rn gas to lung carcinogenesis. Future studies will examine similar biological endpoints using an *in vivo* model.

1.08 Dietary Wheat Bran and Fructooligosaccharide Elicit Different Gene Expression Responses in Colon Epithelial Cells of Fisher 344 Rats

Q. Chen, PhD[1], E. Swist[1], J. Beckstead[1], J. Kwan, BSc[1], F. Matias, MSc[1], J. Roberts, BSc[2], C. Qiao, MSc[3], J. Raju, PhD[2], S.P.J. Brooks, PhD[1], and K.A. Scoggan, PhD[1,4]

[1] Nutrition Research Division, HPFB, Health Canada, Ottawa, ON
[2] Toxicology Research Division, HPFB, Health Canada, Ottawa, ON
[3] Bureau of Food Policy and Science Integration, HPFB, Health Canada, Ottawa, ON
[4] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

SUMMARY: Information on the gene response pattern elicited by dietary fibre is required for Health Canada to understand potential differences between the physiological action of diverse dietary fibres and fermented materials. Our preliminary data indicate that differentially fermented dietary fibres elicit different gene responses in colon epithelial cells in Fischer rats.

OBJECTIVES/BACKGROUND/ISSUE(S): To investigate the gene expression profile in colon epithelia in response to incompletely fermented dietary fibre and completely fermented carbohydrate in Fisher (F344) inbred rats in order to determine the importance of fermentation in eliciting cell responses to dietary fibre feeding.

DESIGN/METHOD/DESCRIPTION: Male F344 rats (10/group) were fed for six weeks on either a control diet (containing 10% alphacel; poorly fermented wood cellulose); or a diet containing 2, 5, or 10% (g/g) wheat bran (incompletely fermented dietary fibre); or a diet containing 2, 5 or 8% fructooligosaccharide (completely fermented but not accepted as dietary fibre in Canada). Total RNA was extracted from the colon epithelial layer of each rat. Real-time quantitative PCR and/or hybridization to rat gene 1.0 ST arrays were used to assess the mRNA expression of 28826 colon epithelial genes.

OUTPUTS/RESULTS: Microarray analyses identified 111 genes that were differentially expressed by 10% wheat bran feeding compared to the control diet ($q < 0.05$). Two of these genes were up-regulated (>2 fold) and two were down-regulated (>2 fold). All four genes demonstrated a dose-dependent fold change. A total of 3364 genes showed detectable changes in their expression by 8% fructooligo-saccharide feeding ($q < 0.05$). Of these, 47 genes were up-regulated (> 2 fold), and 41 genes were down-regulated (>2 fold). Real-time quantitative PCR confirmed that, compared to control diet, a diet containing wheat bran did not alter the expression of cell cycle related genes: cyclin D, cyclin A2, cyclin E1, cyclin dependent kinase 2, p21, p27, p53, and retinoblastoma 1. 10% wheat bran up-regulated (fold change = 1.35) mRNA levels of monocarboxylate transporter 1 (MCT1). Diets containing 5% and 8% fructooligosaccharide increased cecum weight and cecum content as well as up-regulated mRNA levels of MCT1 (fold change = 1.85) and cyclin D (fold change = 1.28).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Our results demonstrated that wheat bran and fructooligosaccharide elicit different gene responses in colonic epithelial cells. Contrary to published results in cultured cells, our *in vivo* data suggest fermentation has little effect on cell cycle related genes.

1.09 Iron Bioavailability Estimates of Canadian Women 19-50 Years of Age with High and Low Intakes of Total Dietary Iron

M. Cooper, PhD, RD[1], I. Rondeau, BSc, RD[1], M. Villeneuve, BSc, RD[1], and M. Vigneault, MSc[1]

[1] Nutrition Research Division, HPFB, Health Canada, Ottawa, ON

SUMMARY: The recommendations for iron was based on an assumption that overall iron bioavailability in the mixed North American diet is 18 percent. This research demonstrated that iiron n a sub-group of women from the Canadian Community Health Survey (CCHS 2.2) that iron bioavailability was estimated to be lower than originally assumed.

OBJECTIVES/BACKGROUND/ISSUE(S): The current recommended dietary allowance (RDA) for iron was based on an assumption that overall iron bioavailability in the mixed North American diet is 18 percent. Requirements for bioavailable dietary iron (BDI) in adult women are influenced by menstruation, pregnancy, and lactation, with an RDA of 18 mg/day. Published research suggests that iron bioavailability across different population groups may be <10%. There is little published data related to the iron bioavailability of the diets of women in the 19-50 age range. The objective of this work is to estimate and compare BDI of the lowest and highest decile of total iron intake of women between 19-50 years from CCHS 2.2 – Nutrition.

DESIGN/METHOD/DESCRIPTION: Utilizing a modified Monsen model (1978) the calculations of BDI per meal included: total iron intake for each food consumed, calculated heme/non-heme iron, level of enhancing factors for non-heme absorption [vitamin C, amount of meat, fish, poultry (MFP)], and an assumption that women have iron stores that approximate 250 mg. Available iron and percent iron bioavailability were estimated using 954 - 24-hour dietary recalls of women 19-50 years of age from CCHS 2.2. Recent research has suggested that the heme content of MFP is not consistent for all categories of foods as was originally proposed at 40%. We have used more accurate literature values to calculate BDI.

RESULTS: The mean iron intake for the lowest decile was 4.1 +/- 1.2 mg/d and 26.1 +/- 6.7 mg/d for the highest decile. The mean available iron was 0.31 +/- 0.17 mg/d and 2.46 +/- 1.16 mg/d, representing an iron bioavailability of 3.9-17.1% [Mean=7.5%] and 3.9-20.5% [Mean=9.4%], respectively for the lowest and highest deciles. The estimate of iron bioavailability is much lower than the assumed 18%, and is greatly affected by enhancing factors of non-heme iron absorption.

IMPACTS/CONCLUSIONS: Lower iron bioavailability could impact dietary iron recommendations by increasing the need for higher intakes. This could also affect diet-based calculations of iron adequacy. The impact of a low iron bioavailability will be best explained with updated information on the iron status of Canadians.

1.10 Identify Barhl1 as a Novel Biomarker of Exposure to Thyroid Hormone Disruptors

H. Dong[1], C.L. Yauk[2], and M. Wade[1]

[1] Hazard Identification Division, EHSRB, HECSB, Health Canada, Ottawa, ON
Mechanistic Studies Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: Numerous chemicals in our environment can alter thyroid hormone physiology and, consequently, impact neurodevelopment. Using novel methods to investigate thyroid hormone receptor action, we have identified Barhl1 as a potential novel biomarker of thyroid hormone action in the developing cerebellum. The data provide insight into risk evaluation of thyroid disrupting chemicals.

BACKGROUND/OBJECTIVES: Maternal thyroid hormone (TH) insufficiency retards brain development in childhood. Environmental contaminants such as PCBs and dioxins have measurable adverse effects on neuro-development that may be mediated by disruption of TH homeostasis. BarHl1 is a transcription factor that regulates sensorineural development. The phenotype of Barhl1 null mice is similar to that of developmental hypothyroidism. The objective of this research is to identify whether Barhl1 could be used as a biomarker of exposure to TH disruptors that affect brain development.

METHOD: Chromatin Immunoprecipitation (ChIP) combined with custom promoter microarrays (ChIP-chip) was used to identify TH response element (TRE) in the promoter region of Barhl1 in developing brain. ChIP-PCR was used to confirm the TRE in Barhl1. The transcriptional activity of the potential TRE was measured using luciferase reporter assays. The gene expression of Barhl1 in cerebellum was examined in TH aberrant animal models, as well as following exposure to polychlorinated biphenyls (PCB) or Benzo[a]pyrene. Protein expression of Barhl1 under different conditions was also evaluated.

RESULTS: The candidate TRE in the promoter region of Barhl1was confirmed with ChIP-chip, ChIP-PCR and reporter assay. Barhl1 gene expression was negatively regulated by TH in various TH aberrant animal models. The effects of PCB and Benzo[a]pyrene (known to disrupt TH response) exposure on the expression of Barhl1 is under investigation.

CONCLUSION: We propose that Barhl1 can be used as a novel biomarker of thyroid hormone-dependant brain development in studies of developmental toxicity. Ongoing validation exercises will confirm its utility as a tool for risk assessment and provide insight into the mechanisms of TH insufficiency-induced neurodevelopmental impairment.

1.11 Isolation and Detection of Verotoxigenic *Escherichia coli* from Foods

A. Gill, PhD[1], A. Martinez-Perez, MSc[2], and B. Blais, PhD[2]

[1] Microbiology Research Division, Bureau of Microbiological Hazards, HPFB, Health Canada, Ottawa, ON
[2] Research and Development Section, Canadian Food Inspection Agency, Ottawa, ON

SUMMARY: The verotoxigenic *Escherichia coli* (VTEC) serogroup O157 is an established public health threat. However, risk assessment and response to other VTEC serogroups has been inhibited by the absence of a standard protocol for VTEC isolation and detection. We present here such a protocol, developed collaboratively by HC, CFIA and PHAC.

BACKGROUND: Verotoxigenic *Escherichia coli* (VTEC), including *E. coli* O157 are significant foodborne pathogens in Canada. Currently, there is no standard protocol available for the detection of all VTEC serogroups. The aim of this project was to develop a standard protocol for the detection and isolation of VTEC, as part of a major joint interdepartmental initiative between HC, AAFC, PHAC and CFIA.

METHOD: Strains of five different VTEC serogroups (O157:H7, O26:H11, O103:H2, O111:NM, O145:NM) were inoculated individually into ground beef. 25 g samples of ground beef were prepared in triplicate and incubated in 225 ml of enrichment broth for 16-24 hours. The enrichment broths were screened by PCR for the genes of verotoxin 1 and verotoxin 2. Dilutions of the enrichment broth were plated on agar medium and incubated for 24 hours. Colonies from enrichment broths, which tested positive for verotoxin genes were screened to isolate VTEC. Presumptive VTEC isolates were confirmed by a cloth hybridisation assay which simultaneously identifies the presence of the virulence factors verotoxin 1 and 2, intimin, enterohemolysin and identifies the serotypes O157, O26, O103, O111, O145. The same protocol was also applied to the isolation *E. coli* O157 from spinach, lettuce and cider.

RESULTS: *E. coli* O157 were detected and isolated from 25g samples of ground beef, lettuce, spinach and cider when present at concentrations of 0.5 to 0.9 CFU/g. The other four serogroups were detected and isolated from ground beef at concentrations of 0.4 to 1.2 CFU/g.

CONCLUSIONS: The protocol is currently undergoing inter-laboratory validation for inclusion in the Health Canada compendium of methods. With validation, the protocol will be available to Canadian regulatory and public health agencies and industry as a standard method for the detection of VTEC in foods. A modified protocol will also be validated for application to clinical and environmental samples.

1.12 Inflammatory Responses to a High Resistant Starch Diet and Energy Restriction in Rats with Diet-Induced Obesity

B. Goulet[1], J. Roberts, BSc[2], L. Kenney, MSc[1], J. Raju, PhD[2], and A. Aziz, PhD[1]

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

[2] Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: The effects of a diet high in indigestible starch and of energy restriction on inflammation markers were examined in selected tissues of obese male rats. Preliminary data support the hypothesis that inflammatory responses are lowered by the indigestible starch diet and/or energy restriction.

OBJECTIVES/BACKGROUND/ISSUES: Inflammation is a common biological process in many chronic diseases. The aim of this study is to investigate whether inflammation markers associated with obesity and colon cancer are reduced by a high resistant starch (RS) diet and energy restriction (ER) in target tissues of male rats with diet-induced obesity (DIO).

DESIGN/METHOD/DESCRIPTION: Male Sprague-Dawley rats (n=10-12/group) with established DIO were fed for 4 weeks one of the following ad libitum (ad lib) or ER diets: low RS amylopectin (LRS) and high RS amylose (HRS). ER rats received the diets at 70% of the energy intake of an age-matched, non-obese group fed the AIN-93G diet. At the end of the study, overnight-fasted rats were euthanized, and blood and tissues were collected for gene expression analyses at the transcriptional and post-translational level.

OUTPUTS/RESULTS: When fed ad lib, rats on the LRS diet gained more weight, had higher energy intake and higher fat pad mass ($P<0.01$) than rats on the HRS. However, ER resulted in similar weight loss, fat mass and energy intake between LRS and HRS fed rats. To date, gene expression analyses revealed lower mRNA levels of COX-1 and 2, CPLA2, TNF-a and its two receptor subtypes 1 and 2 ($P<0.05$), as well as IL-1í by HRS and/or ER in the colon. Additional analyses of inflammation markers by RT-PCR and Western Blotting are currently underway in the colon, adipose tissue and liver.

IMPACTS/OUTCOMES/CONCLUSION: Our preliminary data show that inflammation markers associated with obesity and colon cancer are lowered by a diet high in RS and/or ER in a diet-induced obesity rat model. The results of this study could contribute to the development of dietary guidelines aimed at preventing obesity and colon cancer, and the evaluation of potential future health claims related to RS or other indigestible and fermentable carbohydrates.

1.13 Who is Most Likely to Gain Weight? Relationships Between Body Mass Index and Occupation

J. Grose, BSc, BA[1], and T. Messele, MSc[1]

[1] Applied Research and Analysis Directorate, Strategic Policy Branch, Health Canada, Ottawa, ON

SUMMARY: Trends in body mass index (BMI) in the Canadian population and their relationships to socioeconomic, demographic and, for those in the workforce, occupational data were studied. Obesity rates by occupational groups were followed, with some increasing more than others. Intervention should focus on occupational groups most at risk of obesity.

OBJECTIVE: Examine trends in body mass index (BMI) in the Canadian population, and their relationships to socio-demographic and, for those in the workforce, occupational data.

DESIGN/METHODS: Socio-demographic and BMI data was extracted from the Canadian Community Health Survey (CCHS). Correlational analysis revealed which variables were significantly associated with BMI. Socio-demographic, obesity and occupational data on the Canadian workforce was extracted from the National Population Health Survey (NPHS). Logistic regression revealed which variables were significantly associated with changes in obesity rates over time.

OUTPUT/RESULTS: Impacts of socioeconomic status and demographic variables on BMI showed age, physical activity and gender were significantly associated with BMI, with those who were older, less physically active, or male tending towards higher BMI.

Our longitudinal analysis revealed that the prevalence of obesity for all occupational groups almost doubled from 1994/95 to 2006/07, but that obesity rates and growth varied by occupational group, with some showing much higher increases than others. Those in occupations involving more physical activity are less likely to gain weight than those confined to more sedentary work. The prevalence of obesity increased by more than 500% among workers in construction, transportation, and related occupations.

IMPACTS/OUTCOMES/CONCLUSIONS: Canada is in the midst of an obesity epidemic. While obesity-related absenteeism may directly cost employers and employees loss of productivity and income, respectively, it may also indirectly result in labour replacement costs and poor quality of life, respectively. The direct and indirect costs of obesity to government are lost tax revenue and treatment costs, respectively. While socioeconomic factors play a significant role in the weight gain of workers of all occupations, the type of occupation is also an important contributor to obesity. Given scarce government resources, any intervention should focus on those workers in occupational groups identified as being most at risk of obesity.

1.14 Saliva as a Surrogate Matrix for Plasma in Monitoring Endothelin Cardiovascular Peptides

R. Gurusankar, PhD[1], P. Kumarathasan, PhD[1], E. Thomson, PhD[1], A. Saravanamathu, PhD[1], A. Filiatreault[1], and R. Vincent, PhD[1]

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

SUMMARY: We aim to validate the use of saliva as surrogate to plasma for the analysis of critical biomarkers of cardiovascular effects from exposure to air pollutants. Others have reported a significant correlation between plasma and salivary endothelin (ET)-1 levels with disease progression in congestive heart failure patients. Here we show that all three ET isoforms, ET-1, ET-2 and ET-3 are positively correlated in plasma and saliva of healthy subjects.

BACKGROUND AND OBJECTIVE: The value of endothelin peptides in blood as biomarkers of effects from exposure to urban contaminants has been established through animal and human experimental work as well as epidemiological investigations. Endothelin (ET)-1, the most potent vasoconstrictor in circulation, has been well studied in relation to its role in the pathophysiology of cardiovascular disease. For example, elevation of ET-1 in plasma is predictive of cardiac death in congestive heart failure patients, while decrease of ET-1 levels is associated with improvement of symptoms and survival. Recently, salivary ET-1 has been shown to correlate with disease severity in chronic heart failure patients. Our objective here was to study the relationship between the different circulating endothelin isoforms, bigET-1, ET-1, ET-2, ET-3 in saliva and plasma of healthy human subjects in order to validate a non-invasive biomonitoring approach for investigation of cardiovascular health impacts of air pollutants.

METHOD: Matched plasma and saliva samples (n=30) from healthy adults were obtained from a commercial supplier. Proteins were precipitated in acid acetone, peptides were recovered by 30 kDa molecular filtration and reconstituted in acetonitrile for HPLC-fluorescence analysis. Levels of endothelins (bigET-1, ET-1, ET-2, ET-3) were compared between saliva and plasma.

RESULTS: Our results show a statistically significant positive correlation for all endothelin isoforms between saliva and plasma. The ratio of saliva levels to plasma levels for bigET-1 (average 2.1 vs 3.4 pmoles/ml, slope=0.62, p=0.045), ET-1 (2.1 vs 3.5 pmoles/ml, slope=0.58, p=0.002), ET-2 (0.8 vs 1.6 pmoles/ml, slope=0.49, p=0.013) and ET-3 (1.5 vs 2.3 pmoles/ml, slope=0.60, p=<0.0001) was consistently 0.5-0.6, despite a five-fold range of mean ET concentrations within both compartments between subjects, suggesting diffusion of the peptides from plasma to saliva.

CONCLUSION: Our analyses confirm the correlation of plasma and saliva endothelin levels. In contrast to blood sampling, the non-invasive collection of saliva should reduce anxiety and discomfort and simplify the procurement of repeated samples. This should increase the power of air pollutant health effects investigations by allowing correlation with other physiological measurement time-series.

1.15 A Proteomic Approach for Identification of Sensitive Biomarkers of Exposure to Mutagenic Carcinogens in Complex Environmental Matrices

M. Hapsatou, PhD[1], P. Mineau, BSc[1], N. Osika, BSc[1], A. Williams, MSc[1], I.B. Lambert, PhD[1], R. Vincent, PhD[1], P. Kumarathasan, PhD[1], C.L. Yauk, PhD[1], G.R. Douglas, PhD[1], and P.A. White, PhD[1]

[1] Mechanistic Studies Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Occupational settings are often associated with exposures to complex mixtures however; biomarkers indicating exposure are generally only identified for single chemicals. This project investigated secretome expression profiles, which were elicited in response to coal tar, with the aim of identifying candidate biomarkers of exposure to complex environmental mixtures.

OBJECTIVES: To illustrate that *in vitro* secretome expression profiles can be used to identify precise biomarkers of exposure associated with mutagenic carcinogens in complex environmental matrices (coal tar).

DESIGN: Murine lung epithelial cells were exposed *in vitro* to a complex mixture of carcinogenic polycyclic aromatic hydrocarbons. After 6 hours exposure, the serum-free media were collected and secreted proteins purified. Two-dimensional gel electrophoresis was used to separate the protein spots and visualized by silver staining. Image acquisition and spots analysis were performed using PDQuest Software. The resulting protein spots displaying a minimum 2-fold change in expression levels between control and treatment were excised from the gel and identified by MALDI-TOF mass spectrometry and database searching (MS-Fit/SwissProt). Subsequent bioinformatics analysis (SignalP, SecretomeP and Gene ontology) were used to refine the list of putative secreted proteins.

OUTPUT/RESULTS: Two-dimensional gel analysis resulted in the identification of over 250 protein spots. Sixty-five proteins changed expression levels significantly across treatment and were identified by MALDI-TOF MS/Database searching. The results of putative secreted proteins were subjected to bioinformatics analysis, yielding a list of 16 secreted proteins (candidate biomarkers), including SPARC precursor, interleukin-11, thrombopoeitin, apolipoprotein A-V precursor, and WNT4. Validation of findings via Western blot is ongoing.

IMPACTS/CONCLUSIONS: This proteomic approach using 2D-gel electrophoresis, mass spectrometry, and bioinformatics tools identified several candidate biomarkers of exposure to complex mixtures. Our findings could potentially assist in biomonitoring exposure to carcinogens and improve exposure and risk assessment. Results from this *in vitro* project are promising, and indicate that the research strategy employed can be used in an *in vivo* setting.

1.16 Integration of Policy and Science for the Viral Safety of Canadian Shellfish

J. Harlow[1], A. Hughes[1], D. Oudit[1], and K. Mattison[1]

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

SUMMARY: Shellfish are an important cause of foodborne viral illness. We aim to understand and mitigate the risk of infection by: (1) surveying viral contamination in Canadian wastewater treatment plants and ocean water, (2) comparing human enteric viruses and male-specific coliphage, a proposed indicator, (3) producing consumer-friendly cooking recommendations for shellfish.

OBJECTIVES/BACKGROUND/ISSUES: Shellfish are filter feeders that concentrate viral particles from their environment. A low level of contamination in shellfish growing waters can pose a consumer safety risk. The presence and behaviour of human enteric viruses in wastewater and in the environment has not been well studied. We have participated in three projects in collaboration with regulators to quantify and reduce the risk of viral infection form shellfish.

DESIGN/METHOD/DESCRIPTION: Wastewater and water from the surrounding area were tested from Ladysmith, BC, Digby, Yarmouth, Cornwallis, NS, and Bouctouche, Richibucto, NB for human enteric viruses using an adsorption/elution method with molecular detection published in the Health Canada Compendium of Analytical Methods. To test for male-specific coliphage, we used a plaque count protocol provided by the Canadian Shellfish Sanitation Program. These results were compared to the data for human enteric viruses. For cooking guidelines, the hepatitis A virus was injected into mussels, which were subjected to different domestic steaming techniques before virus was extracted and enumerated by plaque assay.

OUTPUT/RESULTS: Norovirus and hepatitis A virus were occasionally discharged into the surrounding environment, but were not detected in approved harvest areas. There was no apparent correlation between the proposed indicators and norovirus or hepatitis A virus. Steaming for 90 seconds efficiently reduces the hepatitis A virus titre by 5 orders of magnitude, so long as the product is in close proximity (20 cm or less) from the steaming water.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The current Canadian Shellfish Sanitation guidelines for approved harvest areas should be sufficient to ensure no routine viral contamination. However, the current indicator testing may not detect accidents or overflow events that temporarily increase contaminants. Consumers could follow guidelines for cooking palatable shellfish that would decrease their risk of contracting illness if viruses were present.

1.17 Biomarkers of Radon Exposure: Genomic Profiling

M. Howland[1], S. O'Hara[1], M. Malowany[1], A. Williams, MSc[1], J. McNamee, PhD[1], S. Qutob, PhD[1], T.J. Stocki, PhD[1], L.A. Beaton, MSc[2], R. Wilkins, PhD[1], and V. Chauhan, PhD[1]

[1] Research and Radiation Directorate, Product Safety Program, HECSB, Health Canada, Ottawa, ON
[2] Department of Physics, Carleton University, Ottawa, ON

SUMMARY: Radon (^{222}Rn) gas produces decay progeny that emit high-energy alpha (α)-particles. Epidemiological studies have shown that exposure to ^{222}Rn gas is associated with an elevated risk of developing lung cancer.

OBJECTIVE: The aim of this study was to mine for potential biomarkers of α-particle exposure and to identify genes responding to low and moderate doses of α-particle radiation in a dose-and time-dependent manner, as they would potentially represent reliable α-particle radiation responsive genes.

METHODS: Human lung epithelial cells (A549) were exposed to various doses of α-radiation from an americium (^{241}Am) source. In addition, 2 Gy of gamma (γ)-radiation from a cesium (Cs^{137}) source was employed as a positive control. RNA was extracted from α- and γ-exposed cell cultures 4 h and 24 h after exposure. Microarray analysis was then employed to determine transcript expression levels.

RESULTS: Sixteen genes were identified that exhibited time- and dose-dependant properties. The majority of these genes were involved in cell cycle regulation. One gene, *CY1F2*, was also shown to be radiation-type specific as it was only expressed in the α-particle exposed sample treatment groups and not in the γ-exposed samples. Five other genes of undetermined function, unique to α-particle exposed samples displayed dose-but not time-dependant effects.

CONCLUSION: Using whole genome microarray analysis, we have identified a vast array of genes that have been shown to significantly change following α-particle irradiation. Some of these genes are known radiation-response genes however; unique α-particle radiation specific genes were also identified with unknown functions. These transcriptional responses warrant further investigation as they may prove to be candidates for biomarkers for α-particle exposure.

1.18 The Possible Structure-Activity Relationship (SAR) of Hydrazine and Related Substances on Systemic Toxicology

J. Jiao[1], L. Gorham[2], and R. Bose[1]

[1] New Chemical Substances 2 Section, New Substances Assessment and Control Bureau, HECSB, Health canada, Ottawa, ON

[2] Interdisciplinary Program, Department of Biomedical Sciences, Ontario Veterinary College, University of Guelph, Guelph, ON

SUMMARY: We have collected and assessed toxicity data for over 69 hydrazine and related substances to investigate the possible structure-activity relationship. We found substances with two particular substractures that were consistently of high concern for systemic toxicity and tumorigenicity. The chemical nature of the hydrazine sub-groups significantly affect the toxicity potency.

OBJECTIVES: Substances of similar structures often exhibit similar toxicity potentials. It is possible to find the trend on how the specific sub-structures influence the toxicity potentials. Hydrazine and its derivatives are a class of chemicals of wide-spread industrial applications. However, the toxicity data received under the new substance notification program often are inadequate to assess long term hazards; hence the need for a SAR-based approach.

METHOD: We have collected both published and internal data on hydrazine and related substances. We have collected data on 69 substances, of which, 25 have genotoxicity test results, 11 with tumorgenicity, and 13 with repeated dose or subchronic toxicity data. The SAR correlations will be analysed by grouping together substances with similar subgroups and for each toxicity endpoint. Factors such as site of toxicity, size of derivation group in relation to and structure distance from functional group, as well as molecular wight will be studied to find possible clues of SAR.

CONCLUSION AND DISCUSSION: We have identified two substructures with toxicological importance. Substances with these two substructures are likely to exhibit high acute and subchronic toxicity and to be tumorgenic. In addition, although many substances of this category induced tumours in local tissues, tumours at diverse tissues were also reported. The outcomes of this study will help the assessment of furture new hydrazine and related substance.

1.19 *In Vivo* and *In Vitro* Effects of Methylmercury on Markers of Metabolic and Cardiovascular Diseases

X. Jin, PhD[1], M.Coughlan[1], J. Yan, PhD[1], K. Kapal[1], M. Taylor[1], H.M.Chan, PhD[2], and R. Mehta, PhD[1]

[1] Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Community Health Program, University of Northern British Columbia, Prince George, BC

SUMMARY: Effects of Methylmercury on oxidative stress, inflammatory response, and endothelial function were examined in rats and cultured human coronary artery endothelial cells. Findings from these *in vivo* and *in vitro* studies suggested a potential role of methylmercury in the pathogenesis of metabolic and cardiovascular diseases.

OBJECTIVES/BACKGROUND/ISSUE(S): Along with the elevated concentrations of methylmercury (MeHg) and other contaminants in the Artic biota and humans, an increased rate of metabolic and cardiovascular disorders have been observed in the Northern populations. Rapid changes in lifestyle and moving away from traditional diets have been considered as important contributing factors. However, it remains unclear if chronic exposure to contaminants such as MeHg also plays a role. We therefore examined the effects of MeHg on oxidative stress, inflammation, endothelial function, and energy metabolism using both an animal model and cultured human coronary artery endothelial cells (HCAEC).

DESIGN/METHOD/DESCRIPTION: Spraque-Dawley rats were treated with 0 or 3 mg/kg BW MeHg for 14 days. Urine and serum samples were collected and analyzed for markers of oxidative stress, inflammation, endothelial function, and energy metabolism. HCAEC were cultured and dosed with 0, 0.5, 2, or 5 µM MeHg for 24h. Supernatants and cell lysates were analysed for reactive oxygen species (ROS), antioxidant enzymes, and endothelial functional markers.

OUTPUTS/RESULTS: In dosed aminals, MeHg significantly increased urinary isoprostane and 8-hydroxydeoxyguanosine levels, monocyte counts, and serum oxidized-LDL, monocyte chemotactic protein-1, lipase activity, and total cholesterol levels, and decreased serum paraoxonase-1 and amylase activities and insulin levels. In dosed HCAEC, MeHg increased production of ROS, endothelin-1, and plasminogen activator inhibitor-1, altered cytoskeleton structure, increased paraoxonase-2 and tubulin protein expression, and caused nuclear translocation of thioredoxin reductase-1 and cytoplasmic translocation of glutathione peroxidase-1.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: These results suggest that exposure to MeHg may increase the risk of metabolic and cardiovascular diseases by increasing systemic oxidative stress and circulating cholesterol levels leading to increased formation of oxidized-LDL, which activates monocytes and causes systemic inflammation, resulting in endothelial dysfunction; altering the redox state of the endothelial cells leading to disruption of the cytoskeleton and endothelial dysfunction; and/or decreasing circulating insulin levels leading to decreased production of vasodilator(s) and/or increased release of vasoconstrictor(s) and pro-thrombotic factor(s) from endothelial cells, resulting in hypertension and hypofibrinolysis. These findings are of significance for the Canadian Government and Northern communities to implement more effective

science-based strategies in contaminant control and human health promotion in the Canadian North.

1.20 O-Linked Glycosylation Leads to Decreased Thermal Stability of Interferon Alpha 2b as Measured by Two Independent Techniques

M.J.W. Johnston, PhD[1], S. Smith[1], and M.A. Hefford, PhD[1]

[1] Centre for Biologics Research, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Thermal stability is considered an indication of protein fold and stability. Here we investigate the influence of glycosylation on the thermal stability of interferon alpha 2b. We demonstrate that O-linked glycosylation decreases the thermal stability of interferon alpha 2b compared to a non-glycosylated variant of the protein.

BACKGROUND: Glycosylation is important for therapeutic proteins as the carbohydrate can influence molecular stability, solubility, activity and circulation lifetimes. Interferon alpha is naturally an O-linked glycosylated protein, however many therapeutic formulations are not glycosylated due to their manufacturing process. Here we use two techniques to investigate the role of glycosylation on the thermal stability of interferon alpha 2b. Thermal stability of proteins is considered indication of correct folded conformation overall stability.

METHODS: Far ultraviolet light circular dichroism spectroscopy (UV CD) and differential scanning calorimetery (DSC) were used to assess the thermal stability of EDQM interferon alpha 2b (INF a-2b) references standards as well as an O-linked glycosylated interferon alpha 2b (INF a-2bG) produced in human embryonic kidney cells. The carbohydrate was removed from the glycosylated interferon enzymatically and the thermal stability of the deglycosylated sample was subsequently assessed with far UV CD and DSC.

RESULTS: Assessment of thermal stability of INF a-2b and INF a-2bG by DSC revealed that non-glycosylated interferon (temperature of melting, tm = 65.6C) was more thermally stable than the glycosylated variant (tm = 63.4C). These observations were confirmed with far UV CD (tm INF a-2b = 65.3C, tm INF a-2bG = 63.6C). Enzymatic deglycosylation of INF a-2bG resulted in improved thermally stability when assessed with far UV CD (tm=64.8C).

CONCLUSION: Thermal stability of proteins is considered an indication of correct folded conformation (3 dimensional shape) and overall stability. It is generally believed that glycosylation leads to increased protein stability; however this was not the case for this particular interferon as determined by two separate orthogonal techniques. These observations may have implications for production methods and storage conditions.

1.21 Impact of Biodiesel Blends on the Toxicity of Automotive Emissions

S. Karthikeyan, PhD[1], Y. Siddiqui, MSc[1], E. Thomson, PhD[1], P. Kumarathasan, PhD[1], D. Rosenblatt, MSc[2], G. Rideout, MSc[2], and R. Vincent, PhD[1]

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

[2] Emission Research and Measurements Section, Air Quality Research Division, Science and Technology Branch, Environment Canada, Ottawa, ON

SUMMARY: We compared the cytotoxicity of 30 diesel emission particle (DEP) samples from engines operated with different biodiesel fuels, run cycles and emission treatment technologies. Canola based biodiesel blend (B20) showed higher cytotoxic potency than soy or animal tallow biodiesel blends or ultralow sulfur diesel. Emission treatment reduced this cytotoxicity.

OBJECTIVES: The objective of the study was to assess the impact of biodiesel blending and feedstock on the toxicity of emissions and the impact of selected emission reduction technologies in modifying the toxicity.

METHODS: Emissions were generated using a heavy-duty diesel engine, Caterpillar C11 (2004 emission standard) operated on conventional ultra-low sulphur diesel (ULSD) and 20% (v/v) blends of canola, soy and animal tallow biodiesels in ULSD on three different steady-state loads (50, 75 and 100%). Engines were run with or without emission after-treatment consisting of diesel oxidation catalyst (DOC) or a combination of DOC and selective catalytic reduction technologies (SCR). The emission particles were collected on Teflon® filters and extracted for analysis of cytotoxic potency using a panel of validated *in vitro* assays for cellular energy metabolism, DNA synthesis and membrane integrity in human lung epithelial cells (A549).

RESULTS: The biodiesel feedstock impacted the toxicity of DEP. Among the fuels compared, canola derived biodiesel (B20 canola) was the most cytotoxic, with a cytotoxicity ranking of B20 Canola > ULSD > B20 soy > B20 animal tallow. Higher engine loads in general also resulted in higher toxicity of generated emissions for both the base fuel and biodiesels. The toxicity of canola-based biodiesel was reduced by emission after-treatment (either by DOC alone or by a combination of DOC and SCR).

CONCLUSIONS: These data show that sources of fuels, conditions of combustion, and after-treatment impact the potency of particulate emissions. Therefore, this opens up the possibility of using high throughput *in vitro* screening tools to guide alteration of fuels, emission reduction technologies and combustion conditions towards the reduction of toxic potency and potential adverse health impacts, in addition to reduction of mass of emissions.

1.22 Source, Size and Seasonal Differences in the Cytotoxicity of Ambient Urban Particulate Matter Collected at Three Different Locations Across Canada

S. Karthikeyan, PhD[1], E. Thomson, PhD[1], Y. Siddiqui, MSc[1], J. Brook, PhD[2], and R. Vincent, PhD[1]

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

[2] Air Quality Research Division, Atmospheric Science and Technology, Science and Technology Branch, Environment Canada, Ottawa, ON

SUMMARY: Ambient particulate matter (PM) collected at three different locations across Canada showed location-, size- and season-dependent differences in cytotoxic potency. The large observed differences in the toxicity points to a need to identify specific chemical constituents responsible for potency and the emission sources for regulation of ambient PM.

OBJECTIVES: The objectives of this study were to assess whether ambient particulate matter collected at different locations and seasons from across Canada show differences in cytotoxic potency and to identify underlying determinants of any observed differences in their biological effects.

METHOD: PM10 and PM2.5 samples were collected from Downsview (Ontario), Saint John, (New Brunswick), and Pitt Meadows (British Columbia) during summer and winter seasons. Samples were analyzed for cytotoxicity in lung epithelial (A549) and macrophage (J774) cell lines using *in vitro* assays for cellular energy metabolism, DNA synthesis and membrane integrity. Cytotoxic potency (í) was determined from Fold-effect = $(\text{Dose} + 1)^{í}$.

RESULTS: The cytotoxic potency of the particles was determined by the geographical location of sample, season, and particle size. Three way ANOVA analysis of cytotoxic potency in J774 cell line with location, season and particle size as factors showed significant ($p<0.05$) two way interactions between location and particle size, and between location and season. For example, PM2.5 samples were more potent than PM10 in Downsview and Saint John, whereas the PM10 samples were more potent than PM2.5 in Pitt Meadows. The ranking of average potencies in A549 were generally consistent with rankings in J774.

CONCLUSIONS: The results show that particle potencies are impacted by the interaction of a number of factors, including the location, season of collection, sources, and particle size. These findings suggest that identification of the underlying contributors of toxicity is critical for a more informed regulation of ambient PM. We are currently analyzing data on particle chemistry and wind patterns during sampling in order to identify determinants and point sources (local or distant) of toxicity.

1.23 Changes in the Toxic Potency of Urban Particulate Matter during Atmospheric Transport of Particles Across the Great Lakes Basin

S. Karthikeyan[1], E. Thomson[1], Y. Siddiqui[1], J. Brook[2], and R. Vincent[1]

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

[2] Air Quality Research Division, Atmospheric Science and Technology, Science and Technology Branch, Environment Canada, Ottawa, ON

SUMMARY: Large differences were noted in the toxic potencies of fine particles (PM2.5; particulate matter with 2.5µm size cut-off) collected from ambient air on multiple days from six different locations in the Great Lakes Basin along the corridor between Michigan and Ontario. Trajectory analysis suggests that the observed potency contrasts are determined mainly from local atmospheric events and emission sources.

OBJECTIVE: This study is aimed at understanding the impact of atmospheric transport of ambient particles in modulating toxic potencies and at identifying specific determinants of toxicity.

METHOD: PM 2.5 samples were collected from ambient air at six sites across the Great Lakes Basin chosen based on their location along the path of predominant north-easterly wind: Vermillion (Ohio), Ann Arbor, Sanillac (Michigan), Tiverton, Egbert, Dorset (Ontario). Particles were analyzed for elemental and polyaromatic hydrocarbon composition, and acidity. The cytotoxic potencies were assessed, by using human epithelial (A549) cell lines. For each location and sampling period, backward wind trajectories were calculated in order to assess the contribution of sources along the wind path to particle composition and potency.

RESULTS: Cytotoxicity analyses showed large variations in the toxic potency of particles collected at different sites, and within those collected on the same site on different days. Six out of the 9 particle samples collected on different dates at Egbert, Ontario ranked the most toxic among all particles (40) tested. In general, the direction of wind trajectories varied for different locations and days. On days when the air mass moved north-easterly across the Great Lakes Basin over the multiple sampling sites, no consistent increases in acidity or potency were noted.

CONCLUSIONS: The absence of effects on potency attributable to air mass transport across the Great Lakes Basin suggests that the observed particle potencies are largely impacted by local atmospheric factors and emission sources. Regression of cytotoxic potencies on particle chemistry, and correlation of particle chemistry to wind trajectory directions and potential sources along the trajectory should enable quantitation of contribution of local events and sources versus atmospheric transport to modification of particle toxic potencies.

1.24 The NAFTA Groundwater Modelling Project

I. Kennedy[1], D. Young[2], L. Avon[1], G. Malis[1], and E. Behl[2]

[1] Environmental Assessment Directorate, PMRA, Health Canada, Ottawa, ON
[2] Environmental Fate and Effects Division, OPP, EPA, Washington D.C., United States

SUMMARY: Under the North American Free Trade Agreement (NAFTA), Canada and the US are collaborating to develop common modelling procedures for estimating pesticide concentrations in groundwater in support of the federal registration process for pesticides.

BACKGROUND AND OBJECTIVES: Canada's Pest Management Regulatory Agency and the US EPA Office of Pesticide Programs conduct human health and enviromental risk assessments, which include the need to estimate concentrations of pesticides in groundwater. Currently the two agencies use different methods to estimate potential pesticides concentrations in groundwater. Harmonized methods would lead to more consistency between estimated groundwater pesticide concentrations and improve joint reviews. The major objective of this project is to standardize how leaching of pesticides is modelled in the US and Canada for federal registration of pesticides.

DESIGN AND DESCRIPTION: The project has three major steps: 1) reach agreement on a conceptual model; 2) choose a computer model to implement the conceptual model; and 3) write guidance on use of the model to estimate pesticide concentrations. The NAFTA group has completed step 1 after agreeing on the conceptual model, which includes a one dimensional soil profile and reports an average concentration in the top 1 m of the water table. The group is currently completing step 2 and has reviewed 23 models based on criteria including the ability to simulate pesticide flow and transformation, ease-of-use, and availability of source code. Three models were chosen for further evaluation (PRZM, LEACHM, and PEARL). To test the three candidate models, simulations were compared to field data from four prospective groundwater studies conducted in the US. In these studies, bromide and pesticide concentrations were available at 3 to 4 vadose zone depths and at about 8 spatially dispersed locations on about 1 acre plots.

RESULTS: Preliminary results show how the three models simulate movement of both a nonreactive tracer (bromide) and pesticides. The field concentration data exhibited large spatial variability, which made it difficult for any of the models to provide good simulation at all points. No model appears to distinguish itself as a superior predictor at this time in the analysis. All models appear to be adequately conservative in comparison to field data.

CONCLUSIONS AND NEXT STEPS: The next steps are to finalize the choice of a NAFTA pesticide-leaching model and to prepare guidance for how to use the selected model for use in federal registration of pesticides.

1.25 Sampling and Nutrient Analysis Program of Canada: Granola Bars

R. Klutka[1], J. Deeks[1], M. Munro[1], and M.F. Verreault[1]

[1] Nutrition Survey Section, Nutrition Research Division, Bureau of Nutritional Sciences, HPFB, Heath Canada, Ottawa, ON

SUMMARY: Granola bars were collected, processed into composites and analyzed for nutrient content through the Sampling and Nutrient Analysis Program of Canada (SNAP-CAN). The results will be published in the Canadian Nutrient File (CNF).

BACKGROUND: SNAP-CAN was initiated in 2008 to improve the ability of the CNF to provide Canadians with access to current and relevant food composition data. Granola bars were selected as a priority food because available data from the United States standard reference food composition database were dated and did not reflect the Canadian market for this commonly consumed snack food.

METHOD: An initial sampling plan was developed using 2005 AC Nielsen data. The resulting list was verified and supplemented through store visits in Ontario and Quebec to confirm the availability of varieties and capture new products. All varieties available for selected brands were included in the sampling plan. Samples were collected mainly for convenience from the Toronto region; however, brands specific to certain regions were also collected to ensure national representation. Sources of variation were determined to be solely due to batch production, therefore three different lot numbers were sampled for each variety.

Bars were divided into 13 subtypes based on common ingredients and texture (i.e., chewy chocolate coated, crunchy plain). Limited funding prevented individual analysis of each variety, therefore composites were formed in which all varieties for each brand within a subtype were combined into one composite for analysis. A total of 116 varieties formed 95 composites.

All bars were processed according to instructions for processing, packaged into subsamples and transported to Health Canada Regional Laboratories for designated nutrient analysis. Nutrients were analyzed according to internationally accredited methods.

OUTPUTS: Analytical results were reported in a standardized format. Data will be compiled and aggregated according to established criteria into 13 granola bar profiles containing proximate, mineral, vitamin, fatty acid, amino acid and sugar data.

IMPLICATIONS: The data will be available in the next release of the Canadian Nutrient File (CNF) providing Canadians with access to improved nutrient data on granola bars.

1.26 Determination of Phthalates in Cosmetic and Personal Care Products Sold on Canadian Market: Implications for Dermal Exposure

D. Koniecki, MSc[2], R. Wang, PhD[1], R.P. Moody, PhD[1], and J. Zhu, PhD[1]

[1] Exposure and Biomonitoring Division, HECSB, Health Canada, Ottawa, ON
[2] Cosmetics Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Phthalates are multifunctional chemicals and can be used in a variety of cosmetic and consumer products. Some phthalates have been associated with reproductive or endocrine-disrupting effects. This is the first national survey, which addresses the contribution of cosmetic and personal care products to the overall body burden of phthalates.

OBJECTIVES: This study is aimed at predicting possible exposure of Canadians to cosmetic and personal care products to support the Department's efforts in assessing and regulating these chemicals to ensure products acceptability to consumers.

DESIGN: 252 cosmetic and personal use products were collected throughout Canada by the Consumer Product Safety Directorate (CPSD). Phthalates were determined by gas chromatography-mass spectrometry (GC/MS). Several exposure scenarios have been proposed.

RESULTS: Of the investigated compounds, five phthalates were detected with the following frequency order: diethyl phthalate (DEP, 104/252) > di-n-butyl phthalate (DnBP, 15/252) > diisobutyl phthalate (DiBP, 9/252) > bis (2-ethylhexyl) phthalate (DEHP, 8/252) > dimethyl phthalate (DMP, 1/252). Both DEP and DnBP were present in the products in concentrations (up to 2.5%). The levels of other phthalates were low. DEP was found in a variety of cosmetic and personal are products especially fragrances, while DnBP use was limited to nail polish. The estimated upper bound dermal exposure (µg/kg bw/d) to phthalates through the use of cosmetic and personal care products for female adults (body weight: 60 kg) is 78 for DEP. It is much lower for DMP (0.03), DnBP (0.34) and DEHP (0.79). Toddlers (0.5-4 years) and infants (0- 6 months) are exposed to DEP only in this case with upper bound values of 20 and 42, respectively.

CONCLUSIONS AND FUTURE RESEARCH: Our in market survey of 252 products including baby products showed that DEP is the predominant phthalate used in cosmetic and personal care products. The use of DnBP may have declined and it is unlikely that DEHP is intentionally added to the products. Due to the potential human health risk from cumulative effect of the overall exposure from several phthalates, we will continue our investigation on the emission rate to determine if indirect exposure via inhalation can be an important contribution to the global exposure of phthalates from cosmetics.

1.27 Effect of Physicochemical Properties on Relative Potencies of Carbon Nanotubes

P. Kumarathasan[1], M.A. Salam[2], D. Das[1], S. Mohottalage[1], Y. Siddiqui[1], N. de Silva[3], B. Simard[4], and R. Vincent[1]

[1] Safe Environments Programme, HECSB, Health Canada, Ottawa, ON
[2] King Abdelaziz University, Jeddah
[3] University of Ottawa, Ottawa, ON
[4] NRC Steacie Institute of Molecular Sciences, Ottawa, ON

SUMMARY: Four variants of carbon nanotubes (CNTs) were tested for cytotoxicity *in vitro*. Physicochemical properties were well characterized and associated with observed biological changes. Our observations indicate the influence of specific physicochemical characteristics of CNTs on cytotoxic potency.

BACKGROUND&OBJECTIVES: Carbon nanotubes are a class of emerging engineered nanomaterials that have potential applications in advanced engineering, medical technologies, as well as in consumer products due to their attractive physical and chemical properties. The same properties that make them unique also lead to concerns on their toxicity characteristics and associated health risks. Currently, there are very few studies of the toxicity of these materials, with conflicting findings, and essentially no detailed comparative studies. Our objective was to validate and conduct an *in vitro* cellular toxicological assessment of well-characterized CNTs to understand the impact of physicochemical properties on cytotoxic potency.

METHODS: Human lung epithelial cells (A549) and murine monocytes (J774) were exposed *in vitro* to four variants of CNTs. The CNT variants were pristine (P-) and oxidized (O-) single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). Cytotoxicity of all four CNT variants, were evaluated using classical bioassays (MTS, Alamar Blue, BrdU and ATP). Physico-chemical properties of CNTs were determined and correlated with the cytotoxicity results. Finally, shotgun differential proteomic profiling was conducted on the cell lysates.

OUTPUTS/RESULTS: Our observations revealed that surface-polarity was predominantly driving the cytotoxic responses irrespective of the cell type (O-CNTs > P- CNTs). Within the non-polar P-CNTs, surface area influenced cytoxicity, particularly in epithelial cells. In macrophages, cytotoxicity appeared to be dictated by the metal content of the P-CNTs. Proteomic profiles clearly indicated that cellular responses to carbon nanotubes (P-SWCNT, O-SWCNT, P-MWCNT, O-MWCNT) could be discriminated based on alteration in levels of candidate peptide/protein markers.

IMPACTS/OUTCOMES/CONCLUSIONS: Our data provide new insights into the biological effects of nanomaterials and their relative potencies, in association with variation in structure and functionalities. Screening assays should provide an insight into the relationship between physicochemical properties of carbon nanotubes, their behaviour in biological systems and primary toxicity mechanisms, supporting risk management of these emerging nanomaterials, and help formulate safer nanomaterials for application especially in the field of medicine.

1.28 Global Genomic Profiling Reveals Species-Specific Responses to Altered Thyroid Hormone Balance

B. Kuo[1], P. Panchal[2], A. Williams[1], M. Wade[1], H. Dong[1], B. K. Padhi[1], G. Pelletier[1], and C.L. Yauk[1]

[1] Environmental Health Science and Research Bureau, Research and Radiation Directorate, HECSB, Health Canada, Ottawa, ON
[2] UCL Genomcis, The Wolfson Institute for Biomedical Research, University College, London, ON

SUMMARY: To investigate potential cross-species differences in response to endocrine disrupting chemicals, we compared global gene expression in cerebella of hypothyroid mouse and rat models relative to euthyroid controls. The two species exhibited vastly different responses, with only 5.6% and 2.6% of orthologous and differentially expressed genes of mice and rats, respectively, in common.

BACKGROUND: Animal models are essential for determining the chemical toxicity and potential risk to human health. Thus, risk assessment requires extrapolation of animal data to humans and generally assumes similarity between model organisms. To investigate this assumption, we used DNA microarrays to characterize gene expression profiles in rats and mice rendered hypothyroid at matched stages of development.

METHOD: Pregnant dams were treated with 0. 01% and 0.04% 6-propyl1-2-thiouracil (PTU), a hypothyroidism inducing agent, for rats and mice respectively (resulting in similar decreases in serum T4 levels), from gestation day 6 to post-natal day 11 in mice and post-natal day 14 in rats (matched developmental stages for cerebellum). RNA from cerebella of 5 males and females from the treated and untreated groups was collected and hybridized to Agilent whole genome microarrays. Data were normalized and differentially expressed genes were identified with MAANOVA, which is a microarray statistical analysis package. Using data downloaded from publicly available databases, genes on the microarrays were comprehensively annotated. Queries were performed to investigate the differentially expressed genes found common to mouse and rat, and their functional information.

RESULTS: Of the 21,513 and 19,902 genes annotated on the mouse and rat arrays respectively, 13,866 were orthologous. Approximately 4% (mouse) and 9% (rat) of genes were differentially expressed (false discovery corrected p-value < 0.05). Thirty-one (approximately 5.6% in mouse and 2.6% in rat) of the genes were differentially expressed in both species. Of these, Gstm1 is known to play a role in thyroid cancer and Camkk2 is known to be involved in memory development.

CONCLUSION: Our results indicated that a very small percentage of genes in mouse and rat cerebella respond similarly to hypothyroidism. These data are concerning and indicate that much more work is needed to determine what animal models are relevant for human health exposures to chemicals that affect thyroid hormone concentrations. Analyses will be expanded to compare changes in functionally related genes in hypothyroid models.

1.29

WITHDRAWN

1.30 Toxicokinetic modelling of pyrethroids for dose reconstruction in the Canadian population

C. Lapointe, MEng[1], M. Bouchard, PhD[1] and G. Carrier, PhD in biomedical engineering[1]

[1] Safe Environments Programme, HECSB, Health Canada, Longueuil, QC

SUMMARY: Health Canada, Quebec Region, has joined a biological monitoring project at the Université de Montréal in which toxicokinetic models of permethrin and cypermethrin will be developed in order to reconstruct daily absorbed doses from urinary metabolites measured in the population.

GOALS: The aim of this study is to develop new toxicokinetic models for the pyrethroids detected most frequently in the environment. First, the researchers will try to develop human toxicokinetic models for permethrin and cypermethrin that link absorption doses to exposure biomarkers (cis-DCCA, trans-DCCA and 3-PBA) on the basis of the route of exposure and temporal scenarios. Second, the development of these models will make it possible to estimate the doses absorbed in the general population using biological monitoring data published in Quebec.

METHODS: *Development of toxicokinetic models.* A toxicokinetic model will be developed for each pyrethroid (permethrin and cypermethrin) with temporal profile data from the literature on exposure in humans. The first step will involve estimating the parametric values of models adjusted to published human data. The data will be derived from the literature on the metabolism of permethrin and cypermethrin and on temporal data for pyrethroids and their metabolites *in vivo* in volunteers exposed to these substances orally and dermally under controlled conditions. The model design will also be supported by animal data on the fecal, urinary and tissue kinetics of permethrin, cypermethrin and their metabolites, as well as the results of the mass balance following the administration of marked compounds. The second step consists of examining interindividual variations in the parametric values.

Next, the model will be validated with various sets of experimental human data. For permethrin, the data will come from van der Rhee et al. (1989), Asakawa et al. (1996) and Tomalik-Scharte et al. (2005), which are not being used to develop the models. For cypermethrin, the data will come from Eadsforth and Baldwin (1983), Eadsforth et al. (1988), Wilkes et al. (1993) and Khün et al. (1999). Sensitivity analyses will be systematically conducted to determine the key parameters for which a detailed characterization of uncertainty may be useful.

Once the parameters of the internal dynamics of permethrin and cypermethrin are determined on the basis of time and conditions of exposure in humans, the models will be used to predict the temporal regression of permethrin and cypermethrin and their metabolites following various exposure scenarios (one-time or repeated exposure, intermittent or continuous exposure through inhalation, dermal contact or ingestion). Simulations of various temporal exposure scenarios will be conducted by introducing input data that varies over time and by individual. This will produce an approximation of the parameter distribution in the population.

Reconstruction of absorbed doses. Daily absorbed doses of permethrin and cypermethrin will be reconstructed from biomarker data from two Quebec populations using the new toxicokinetic models. The absorbed doses will be

reconstructed for each individual from the total quantity of urinary metabolites excreted over given time periods. A distribution of absorbed doses will thus be established for each population in the study.

Two methods of dose reconstruction will be tested. One involves an analytical solution of the differential equation system, which will lead directly to the daily doses of the parent molecule absorbed (or bodily loads at all times) in association with the excretion of metabolites, measured in moles. The other involves the numerical determination of absorbed doses through successive iterations by means of a differential equation system (the Runge-Kutta method, for example).

ANTICIPATED RESULTS: The results of this two-year project will establish a link between human exposure to pyrethroids and the toxicokinetic models for the interpretation of the biomarker data. In addition, the daily absorbed doses, reconstructed using the models, can be compared to the acceptable daily doses or oral reference doses in order to interpret the data in relation to the health risks. The models can also determine the urinary biomarker concentrations corresponding to the normal or guideline exposure values (acceptable daily dose, for example) and thereby establish biological reference values that government authorities can use to draw better conclusions about the health risks, basing themselves on the biological monitoring data rather than external concentrations. The biological monitoring data will be more useful overall and easier to interpret for public health.

ANTICIPATED RESULTS FOR FALL 2009: Conceptual and functional representation of the toxicokinetic models for permethrin and cypermethrin.

1.31 Producing BLT Mice in Canada: A Pilot-Study

C. Lavigne[1], M. Navarro[2], W. Lezama[2], and P. Sandstrom[1]

[1] National HIV and Retrovirology Laboratories, National Microbiology Laboratory, IDEP, Public Health Agency of Canada, Ottawa, ON
[2] Scientific Services Division, HPFB, Health Canada, Ottawa, ON

SUMMARY: A collaborative research project was established between the Public Health Agency of Canada and Health Canada to produce the most advanced humanized mouse model developed for HIV/AIDS research, the BLT (Bone marrow, Liver, Thymus) mice, not yet available in Canada.

BACKGROUND: BLT mice are generated by implanting human fetal liver and thymus under the kidney capsule of a non-obese diabetic (NOD)/ severe combined immunodefecient (SCID) mouse followed by transplantation of autologous human fetal liver CD34+ hematopoietic stem cells. The BLT mouse model is unique among the humanized mouse models available as it generates a robust and extensive complete human immune cells reconstitution in blood and in different tissues including humanization of the gut mucosa. The BLT system is not available commercially and not yet produced in Canada.

OBJECTIVES: The objectives of this pilot study were: 1) To establish and determine how to house these special NOD/SCID mice at the HC animal facility. 2) To develop and adapt the different procedures required to produce BLT mice to our research facilities. 3) To perform successfully, the surgery and all the procedures to produce the humanized BLT mouse model.

DESIGN: The whole surgical procedures, which include tissue implant, irradiation, and bone marrow transplant (will be) first evaluated in NOD non-SCID mice. The non-SCID mice (will be) kept in a sterilized environment to practice our handling and housing procedures in a sterilized environment.

RESULTS: In October 2008, training at the University of Texas allowed us to obtain key information to produce BLT mice in our facilities. In order to meet the specific needs to house the immunodeficient BLT mice we purchased a Biolevel 3 Isolation Caging System that will maintain a negative air pressure within the cages and avoid exposures to microbes from ambient laboratory air. The proposal for this pilot-study was filed and approved in May 2009 by the Animal Care Committee of HC. Consent form and proposal for human fetal tissue collection has been submitted for approval to the Ottawa Hospital Research Ethics Board. Creating BLT mice is challenging because it is considered an invasive procedure. We developed surgical procedures to perform all pre, peri, and post-operative manipulations under sterile conditions. Trials have begun.

IMPACTS: This pilot study was to establish the requirements and obtain the skill to produce BLT mice in Canada to offer this new promising humanization strategy to Canadian HIV researchers. The availability of this innovative technology in Canada will facilitate collaboration and multidisciplinary research projects in the field of preclinical evaluation of novel therapeutic approaches and prevention strategies as the development of vaccines and microbicides.

1.32 Bacterial Enumeration Method for Seawater-Based Health Products

J. Bellemare,[1] H. Boucher,[1] I. Disnard,[1] G. Gouin,[1] K. Lebel,[1] C. Coignaud,[1] and J. Gagnon[1]

[1] Longueuil Laboratory, Microbiology Section, HPFB Inspectorate Laboratory Programme, RPB, Health Canada, Longueuil, QC

SUMMARY: In order to determine whether seawater-based health products are in compliance with established standards, the performance of conventional culture media was compared to that of media adapted to marine bacteria and the testing method was modified through the substitution of culture media.

INTRODUCTION: Quality control of health products is generally performed using Pharmacopoeia methods that, among others, make it possible to determine whether the number of microorganisms in a given product is in compliance with established safety standards. The culture media used in the vast majority of testing laboratories are those suggested in the Pharmacopoeias. However, since marine bacteria have unique nutritional needs, the appropriateness of using conventional culture media to test seawater-based products has been called into question.

METHOD: In order to determine that the count obtained is representative of the microbiological content of seawater-based products, the culture media suggested in the European Pharmacopoeia under 2.6.12 “Microbiological Examination of Non-Sterile Products: Total Viable Aerobic Count” (buffered sodium chloride-peptone solution and Tryptic Soy Agar, TSA) were compared with media that simulate the composition of seawater (Marine Broth and Marine Agar, DIFCO).

RESULTS AND DISCUSSION: In the four tests carried out, the number of bacteria per gram of product was 1.6 to 39.2 times higher with Marine Broth and Marine Agar than with conventional media. Variations between tests can be explained by the provenance and manufacturing/sterilization process of the different products. If examined with conventional media, some of these products would have been determined to be in compliance with specifications and would have been left on the market even though the degree of contamination exceeded allowable bacterial counts and represented a health hazard.

CONCLUSIONS: In order to adequately monitor the quality and safety of seawater-based health products, conventional culture media should be replaced with media adapted to marine bacterial flora, such as Marine Broth and Marine Agar. These results represent an interesting avenue to explore the next time official methods are reviewed.

1.33 An Efficient Method for Analysis of Chloroform in Blood Samples with Headspace Solid Phase Microextraction

F. Wu[1], and N. Li[1]

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

SUMMARY: Chloroform is a widely used industry and laboratory solvent and a major by-product of water chlorination disinfection. A method with headspace solid phase micro-extraction (SPME) and gas chromatography (GC) was developed for analysis of chloroform in blood samples. The method was found to be simple and efficient.

OBJECTIVE: To develop a sensitive and efficient method for analysis of chloroform in serum or other blood samples. The method is applicable to environmental survey, epidemiological, toxicological, or other health effect study of the chemical.

DESIGN: Headspace SPME and GC with electron capture detection (GC-ECD) was the apparatus used. 1,2-Dichloroethane (1,2-DCE) was chosen as internal standard for quantification. Chromatographic separation was conducted with a Supelco VOCOL capillary column (60m*0.25mm ID*1.50m). Headspace SPME with 75μm Carboxen-PDMS fibre was chosen for extraction of the analytes. The conditions of SPME were established and optimized. Because a blank serum without contamination of chloroform is difficult to obtain, a solution of colloidal cetyltrimethylammonium bromide (CTAB, a surfactant) was studied instead of blank serum for analysis calibration. The method was validated.

OUTPUTS: With stirring, the extraction equilibrium at 25°C could be reached within 10 min for chloroform and 1,2-DCE. The temperature and time for desorption were optimized and chosen as 250°C and 1.0 min respectively. Because of association of the analyte with protein, the SPME equilibrium concentration with serum was significantly lower than that with pure water. For SPME analysis calibration, when a colloidal CTAB was used instead of blank serum, good linearity was obtained with a concentration range of standard from 0.02 to 20 ng/mL and with internal standard. Satisfactory recoveries and relative standard deviation were obtained with replicate analyses of spiked blood samples of three different sources and with a spiking level of 0.2 and 2.0 ng/mL each. The detection limit was estimated to be 0.05 ng/mL. Finally, the approach for analysis quality assurance was studied.

CONCLUSIONS: Headspace SPME was demonstrated to be an efficient method for analysis of chloroform in serum. Comparing with the traditional headspace, the method is much more sensitive. Comparing with the currently widely used purge-and-trap, SPME is much simpler. The potential of use of a colloidal CTAB solution instead of blank serum for analysis calibration was demonstrated, which is significant for a relative analytical method like SPME.

1.34 Develop a New Method for Analysis of a Mixture of Polychlorinated Biphenyls and Organochlorine Pesticides in Rat Adipose Sample with Thermal Extraction and Gas Chromatography

N. Li[1], S.-Y. Lee[1,2], W.J. Bowers[1], I. Chu[1,3], and F. Wu[1]

[1] Hazard Identification Division, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] COOP Student from Ottawa University, Ottawa, ON
[3] Scientist Emeritus, Health Canada, Ottawa, ON

SUMMARY: A new method is developed and validated for analysis of a mixture of polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) in rat adispose samples. The method makes use of thermal extraction instead of conventional organic solvent extraction, and is simple, fast, and cost-saving.

OBJECTIVES: To improve the efficiency of method of chemical residue analysis in animal tissues to save cost and time. The method is validated and applied to analysis of samples from toxicological study.

DESIGN: Adipose sample is heated at given temperature for a length of time. The lipid (oil) is released from the tissue and the sample is then extracted with a small amount of organic solvent before it is cleaned and applied for gas chromatography (GC) analysis. The thermal stability of the PCBs and OCPs during heating is evaluated, and the conditions for thermal extraction (time and temperature) are studied. The new method is validated and compared to the conventional solvent extraction method for the method blank, recovery of the analyte, relative standard deviation of replicate analyses, and detection limit. A number of rat adipose samples from previous toxicological studies were collected and analyzed with both the new method and previous method. Analysis results obtained with the two methods were compared.

OUTPUTS: The lipid is easy to be released from the adipose at a high temperature. The lipid extracted by heating at 100°C for 2 hours is compatible to that obtained with the conventional method of solvent extraction following homogenization, as tested with 13 rat adipose of different age and storage time. All the PCBs and OCPs show excellent thermal stability after heating the sample at 100°C for 4 hours, even for the *p,p'*-DDT, which is found to be labile at high injection temperature with GC. Good recoveries (generally over 90%) are obtained for all the PCBs and OCPs. Moreover, thermal extraction is simple, and involves use of much less solvent and glassware. Therefore a low sample blank and lower detection limits can be obtained for most of the components.

CONCLUSIONS: The thermal extraction is an efficient method for analysis of PCBs and OCPs in adipose samples. With this new method, nearly 50% time, 50% solvent and 50% cost can be saved. The application of this method can also be extended to other environmental chemicals or adipose samples of other biological and environmental sources.

1.35 Inhibitory Effect of Cree Anti-Diabetes Plants Extract on Cytochrome P450 (CYP) 3A4

R. Liu, BSc[1,2]; T.W. Tam, MSc[1,2]; P.S. Haddad, PhD[2,3]; J.T. Arnason, PhD[1,2]; and B.C. Foster, PhD[1,2,4]

[1] Centre for Research in Biopharmaceuticals and Biotechnology, University of Ottawa, Ottawa, ON
[2] CIHR Team in Aboriginal Anti-Diabetic Medicines
[3] Department of Pharmacology, University of Montreal, Montreal, QC
[4] Therapeutic Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Seventeen Cree traditional medicines have been examined for their effect on cytochrome P450-mediated metabolism. The results of this study found that most of these medicines have a competitive inhibitory effect; some have a mechanism-based inhibitory effect suggesting that many can affect the safety and efficacy of other therapeutic products.

OBJECTIVE: The Cree Nation of Eeyou Istchee (CEI) of Northern Quebec has a high prevalence of Type II diabetes and uses a number of herbal medicines to treat the symptoms of diabetes. The anti-diabetic activity of several of these botanicals has been established through *in vitro* bioassays, however, their metabolism profiles and capability to interact with conventional therapeutic products are not known. As these Cree medicines will be used as both alternative and complementary medicines it is critical to determine their capacity to affect drug metabolism, potentially affecting the efficacy and safety of drugs or other herbal medicines. The purpose of this study is to examine the inhibition effect of these Cree products on cytochrome P450 (CYP) 3A4 and to identify the mechanism of inhibition (MBI) effects.

METHODS: Ethanol extracts were made from 17 botanicals: AD01, AD02, AD03, AD06, AD07, AD08, AD09, AD11, AD12, AD13, W1, W2, W3, W4, W5, W6, W7, W8, and W9, then dissolved in methanol (10 mg/ml) and examined for their effect on CYP3A4 activity by using fluorometric microtitre plate assay and testosterone hydroxylation assay.

RESULTS: The methanolic extracts of all 17 Cree products showed inhibition ranging from low (0-35%) to high (70-99%). None of the plant extracts showed significant MBI; however in the testosterone hydroxylation assay AD08, AD09, and W6 showed a significant MBI while AD02, AD06, AD11, W1, W2, and AD12 showed features of MBI, which were not statistically significant.

CONCLUSIONS: Some of the Cree medicines exhibited a strong inhibitory effect on CYP3A4-meidated metabolism and some also had MBI. This suggests that they may have the potential capacity to affect the safety and efficacy of drugs and other health products, and may also have the potential capacity to interfere with the metabolism of some endogenous substrates. Further studies are warranted to identify the *in vivo* inhibitory effects of Cree anti-diabetes medicines.

1.36 Exposures to Metals in Urban Homes Assessed Using Wipe Sampling Methodologies

L. McDonald[1], P.E. Rasmussen[12], M. Chénier[2], and C. Levesque[2]

[1] Department of Earth Sciences, University of Ottawa, Ottawa ON
[2] Environmental Health Science Research Bureau, Safe Environments Program, HECSB, Health Canada, Ottawa, ON

SUMMARY: Dust is a matrix of particles consisting of a variety of organic and inorganic substances, including metals derived from both indoor and outdoor environments. This research will provide baseline information about residential exposures to metals assessed using the wipe methodology. Information about metal loadings inside the home is critical to assess childhood exposures caused by ingestion of dust.

OBJECTIVES: This study seeks to obtain baseline values for arsenic, cadmium, chromium, copper, lead, and nickel in urban homes located in contrasting geological settings. Yttrium is included in the analysis due to its recommended use as a soil tracer.

METHODS: Following protocols implemented by the United States Environmental Protection Agency and Department of Housing and Urban Development, 1372 samples were collected with Ghost Wipes™ from 222 homes. Wipe samples were taken from a central location in rooms with non-carpeted floors. For quality control and quality assurance, one field blank and one duplicate sample were collected in each home. Samples were digested using the standard hotplate protocol, modified by adding hydrofluoric acid to increase extraction efficiency, and analyzed using ICP-MS.

OUTPUTS: Results show that the metal composition of house dust varies widely amongst different rooms in a home. Generally, higher metal loadings are observed in the entryway of homes as compared to interior rooms. This observation suggests that tracking in dirt from outside by residents and their pets, influences metal loadings in the indoor environment. However, indoor sources from crafts and hobbies, old paint, and products, also contribute to metal loadings.

IMPACTS: This research will generate the first multi-element wipe sampling database in Canada. The information obtained in this study regarding the quality of indoor residential environments will assist Health Canada in quantifying typical urban residential exposures. These data will also assist Health Canada to develop guidance to Canadians about ways to reduce exposures to metals in their homes.

1.37 Folic Acid Supplementation is Associated with Increased Tumor Load and Progression in a Model of Colitis-Mediated Colon Cancer

A.J. MacFarlane, PhD[1], N. Lukenbill, BSc[1], and D. Caldwell, PhD[2]

[1] Nutrition Research Division, HPFB, Health Canada, Ottawa, ON
[2] Science Services Division, HPFB, Health Canada, Ottawa, ON

SUMMARY: Folic acid (FA) containing diets were associated with increased incidence of high tumor load and development of adenocarcinomas in inflammation-driven colorectal cancer (CRC). FA intake correlated with the production of IL-6, a cytokine required for the development of inflammation-mediated CRC, suggesting that FA alters CRC by modifying the immune response.

OBJECTIVES: Folic acid (FA), a water soluble B-vitamin, is involved in the maintenance of genomic stability and gene expression. FA deficiency is associated with increased colon cancer (CRC) risk. However, excessive FA supplementation is implicated in the progression of established CRC. This study determined the effect of FA deficiency and supplementation on tumorigenesis in colitis-mediated CRC.

METHOD: Inbred male C57BL6 mice were fed diets containing 0, 2 or 8 mg FA/kg diet. Mice were assigned to either a control, colitis (DSS) or colitis-mediated CRC (AOM-DSS) treatment. Colitis was induced by feeding mice dextran sodium sulphate (DSS) in drinking water for three cycles of 4, 3 and 2 days each, separated by two weeks of normal drinking water. Mice in the CRC group were injected once with azoxymethane (AOM) prior to DSS treatment.

RESULTS: FA at adequate or supplemental levels was associated with an increased incidence of high tumor load and the development of adenocarcinomas in AOM-DSS mice. Adenocarcinomas were not observed in FA deficient mice. Tumors were not observed in FA deficient DSS mice; however, mice fed FA adequate or supplemented diets demonstrated a low tumor incidence. Colons cultured *ex vivo* from mice fed a diet containing FA expressed increased IL-6 in comparison with FA deficient mice. No differences were observed for TNFα, IL-1α, IL-4, IFNγ or IL-10.

CONCLUSIONS: FA containing diets were associated with increased incidence of high tumor load and the development of more agressive tumors in inflammation-driven CRC. FA intake correlated with the production of the inflammatory cytokine IL-6, which is required for the development of inflammation-mediated CRC by its promotion of tumor cell survival and progression. Future studies will focus on the mechanism by which FA promotes the expression of IL-6. These studies will impact policies and guidelines for FA fortification and supplement use.

1.38 A Synchrotron Radiation-Based Approach to Determining Pb Speciation in Household Dusts

L.C.W. MacLean[1], S. Beauchemin[2], and P.E. Rasmussen[1,3]

[1] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] Natural Resources Canada, CANMET, Ottawa, ON
[3] University of Ottawa, Earth Sciences Department, Ottawa, ON

SUMMARY: This study demonstrates that synchrotron-based X-ray techniques can differentiate various lead species in household dust. Our results suggest that paint is still an ubiquitous source of Pb in housedust. This study also identifies additional sources of Pb in newer buildings.

OBJECTIVES: Knowledge of metal speciation is needed to: a) understand the oral bioaccessibility of the metal compounds in the host matrix; b) identify their chemical form (e.g., carbonates, oxides, alloys, sulfides, organometallics); and c) determine their probable sources (e.g., consumer products, such as paint, or external industrial pollution sources). This study investigates Pb compounds in dust, which vary widely in bioaccessibility (e.g., Pb in a carbonate form is more bioaccessible than Pb in an oxide form).

METHOD: In this paper we used molecular-scale chemical probes (X-ray absorption fine structure spectroscopy (EXAFS), micro X-ray fluorescence spectroscopy (micro-XRF) and micro X-ray diffraction (micro-XRD) to determine the speciation of lead (Pb) present at elevated concentrations (>1000 mg kg^{-1}) in settled house dust.

RESULTS: The results of this study demonstrate that these molecular-scale probes are capable of identifying Pb species in house dust. Linear combination fitting of the spectra shows that Pb is bound in a variety of molecular environments, associated with both the inorganic and organic fractions of the dust samples. The inorganic species of lead identified were: Pb metal, Pb carbonate, nanocrystalline Pb hydroxyl carbonate, Pb sulphate and Pb oxide. Pb citrate was the only organic species identified.

CONCLUSIONS: Information about the chemical form of Pb in house dust assists Health Canada develop guidance for minimizing residential exposures. Synchrotron-based radiation studies have the potential to provide a fingerprint for various sources of Pb in houses (outdoor vs. indoor) and may help to determine any transformation processes that Pb may undergo inside a building.

1.39 Validation of the Cytokinesis-Block Micronucleus (CBMN) Assay for Use as a Triage Biological Dosimetry Tool

J.P. McNamee[1], F.N. Flegal[2], H. Boulay Greene[3], L. Marro[4], and R.C. Wilkins[1]

[1] Consumer and Clinical Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON
[2] Radiological Protection Research and Instrumentation Branch, Atomic Energy of Canada Limited, Chalk River Laboratories, Chalk River, ON
[3] Capabilities for Asymetric and Radiological Defence and Simulation, Defence R&D Canada, Ottawa, ON
[4] Biostatistics and Epidemiology Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: This study has demonstrated that a triage version of the cytokinesis-block micronucleus assay, where only 200 binucleated cells are scored per sample, provides a sensitive and reliable technique for identifying individuals that have received clinically-relevant radiation exposures. This assay may provide a useful screening tool in a large-scale radiological emergency.

OBJECTIVES/BACKGROUND/ISSUE(S): Biological dosimetry is a method that provides dose estimates for individuals exposed to ionizing radiation by examining damage to chromosomes. Traditionally, the dicentric chromosome (DCA) assay has been used to derive biological dose estimates for unknown radiological exposures. While very sensitive, this assay requires highly-trained evaluators and is extremely time-consuming. The cytokinesis-block micronucleus (CBMN) assay has been suggested as an alternative to the DCA since it is faster to evaluate samples and requires less technical expertise. Thus, the CBMN assay may be more appropriate for deployment as an initial screening tool in a wide-scale biodosimetry network. This study evaluated the CBMN assay for use in triage radiation biodosimetry.

DESIGN/METHOD/DESCRIPTION: In order to validate the CBMN assay for triage biodosimetry, dose response curves were generated by exposing blood from 6 donors to 8 different doses of γ-radiation (0, 0.1, 0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 Gy). Each sample was evaluated in a blinded fashion by 12 individuals, among 3 different laboratories, using a common protocol and scoring criteria. The incidence of micronuclei was determined after counting 50, 100, 200, 300, 400 or 500 binucleated cells (BNC) per sample.

OUTPUTS/RESULTS: This study has demonstrated that a triage version of the CBMN assay, where only 200 BN cells are scored per sample, provides a sensitive and reliable technique for rapidly identifying individuals that have received clinically-relevant radiation doses (> 1 Gy).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The results indicate that the CBMN assay would provide a rapid initial screening technique for emergency situations that would quickly prioritize samples for DCA analysis. Ongoing efforts in our laboratory are focused on further evaluating this technique for use in a radiation mass casualty scenario. The effects of dose-rate, partial-body irradiation and different radiation energies on the CBMN response need further evaluation.

1.40 A Dynamic Data Fusion Based Based Investigation and Analysis Model for Collaborative Computational Toxicology and Health Risk Analysis

A. Mohapatra, MSc, MPhil (pre-doctoral), EMC, Risk, Cert. (Harvard)[1]

[1] Safe Environments Directorate, RAPB, Health Canada, Calgary, AB

SUMMARY: A Collaborative Risk Analysis Framework is proposed by means of computational tools to integrate toxicology and human health risk analysis data so that the health risk assessment protocols and methodologies become more efficient, effective and robust and ultimately strengthen the scientific and regulatory policy community through intra and inter-agency collaborations.

OBJECTIVES: The objective of a front end toxicological and risk analysis datasets integration via a dynamic knowledgebase and data fusion modelling framework would proactively detect patterns in toxicological and human health datasets by computational and informatics tools and therefore prevent environmental and human health consequences and protect public health.

DESIGN: The research is aimed at formulating a fusion based modified JDL (Joint Director Laboratories) modelling framework that can address various types of datasets and can effectively facilitate collaborative toxicological and health risk data integration and analysis. This model is built around a set of algorithms in various levels of fusion, which can be executed continuously and autonomously in its environment and able to carry out activities in a flexible and intelligent manner while being responsive to changes in its environment. This poster highlights emerging toxicological and health risk assessment datasets integration in light of critical evaluation and issues in computational toxicology approaches discussed and reviewed in the “Toxicity Testing for the 21st Century” projects from the National Academy of Sciences.

OUTPUT EXAMPLES: Result 1: A collaborative toxicological informatics book project was initiated in 2007 in the areas of emerging information resources in toxicology highlighting toxicological databases, environmental and human health risk related resources, emerging analytical approaches and collaborative technologies. A new edition of the book entitled, “Information Resources in Toxicology was published by Elsevier in 2009.

Result 2: In December 2008, formulation of a collaborative platform based on the emerging web 3.0 (Semantic Web) technologies was carried out. A Semantic Web Informatics Facilitated Tools -Dynamic Analysis of Risk Tools (SWIFT-DART): A Knowledgebase framework concept was created in the context of effective public health risk analysis reviews of chemicals and contaminated sites.

Result 3: In July 2009, the proposed data fusion methodologies was presented and published in the context of its application in computer forensics and web based database security analysis. This specific component of the research project showed that the data fusion based digital investigation model can be used as an effective forensic tool in the risk assessment and management of cyber security systems.

FUTURE WORK: I propose to extend the proposed data fusion methodologies in the context of public health risk analysis, toxicology and Health Care and Life

Sciences data fusion and develop specific sets of algorithms for various levels and degrees of environmental, human health, chemical, toxicological, genomics and disease database integration, mash-ups and fusion and use them in a collaborative health risk analysis platform facilitated by semantic web informatics.

IMPACTS: Application of these data fusion and data mash up technologies facilitated by a semantic web informatics framework can increase the efficiency of dynamic data integration and environmental health risk analysis. These investigative collaborative tools and frameworks can be used in health based evaluations of global climate change, nanotechnologies, global food crisis and Chemical, Biological, Radiological and Nuclear (CBRN) risks by integrating environmental, ecological, ecosystem based, clinical and public health toxicology databases integration, mash-ups and fusion. It would facilitate both intra- and inter-agency collaboration to assess, manage and communicate environmental and human health risks that would ultimately strengthen the scientific and regulatory policy community.

1.41 Radon Chamber at the Radiation Protection Bureau, Health Canada

N. Mahbub Rahman[1], B.L. Tracy[1], R. Falcomer[1], B. Walker[1], and J. Whyte[1]

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

SUMMARY: The Radiation Protection Bureau is currently using a radon chamber for testing radon detection techniques. The chamber is semi-rectangular and made of steel and Plexiglas with a volume of 0.50 m3 and with controls for environmental parameters. The internal sources are now producing radon at a constant concentration of 1.4X103 Bq/m^3.

OBJECTIVES/BACKGROUND/ISSUE: Radon chambers serve to produce consistent radon levels under specific ambient conditions to test the performance of radon monitoring equipment and to carryout research on radon and radon progeny. This chamber was set up to support on-going projects of radon monitoring and research, including the modeling of various indoor conditions contributing to the health effects of radon.

DESIGN/METHOD/DESCRIPTION: A sealed glove box was converted into a radon chamber. The box consisted of a gas-tight enclosure with a window, a pair of gloves and a transfer chamber to allow the introduction of equipment into the chamber with minimum compromise of the internal atmosphere. The temperature, pressure and relative humidity inside the box are all monitored. The stainless steel back wall was cut to add a panel for electrical connections and a sampling port. A mixing fan was installed to maintain proper distribution of the radon gas inside the chamber. Experiments were performed to measure the build-up of radon in the chamber and to test for radon homogeneity the chamber.

OUTPUTS/RESULTS: Four different types of techniques were used to measure various levels of radon concentrations inside the chamber. All techniques showed very similar concentrations with an average bias of only ±7% compared to the calculated values. A performance test on commercially available detectors for home-use showed very small differences with one another with a bias of -10.9% to 5.9% compared to calculated activity concentrations.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The radon chamber was established to expedite various QA and QC functions and to support research and inter-comparison studies. In the future aerosols will be introduced into the chamber to study complex radon-aerosol interactions.

1.42 Discerning Household and Outdoor Ambient Air Pollution in Personal Exposure to Volatile Organic Compounds

S. Cakmak, PhD[1], R.B. Mills, PhD[1], S.L. Martin, PhD[1], A.J. Wheeler, PhD[1], and R. Dales, MD[1]

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

SUMMARY: We developed a method of source attribution for personal exposure to volatile organic compounds (VOCs). This method successfully identified a sample's microenvironment of origin in every case for samples collected in both the summer and winter. Furthermore, we have identified several distinct emission sources in Windsor, ON, based on chemical signature and evaluated the influence of each source on personal exposure.

BACKGROUND: Many volatile organic compounds have been listed under Schedule 1 of the Canadian Environmental Protection Act (CEPA) as toxic due to their carcinogenic and respiratory health impact. Regulation and control of VOC emissions requires that the source of compounds of concern are known; however, source attribution poses a serious challenge due to the presence of emissions from multiple sources.

OBJECTIVE: Our objective is to develop a method to attribute VOCs to specific sources such as traffic related pollution, industrial pollution, and household pollution using fuzzy cluster and factor analysis.

METHODS: We studied 48 homes by placing Summa™ stainless steel canisters indoors, outdoors, and on personal backpacks to analyze 188 volatile organic compounds. VOCs were measured using cryogenic pre-concentration followed by high-resolution gas chromatography and mass spectrometry. Each home was sampled for 24 hr intervals, over five consecutive days in the winter and in the summer. Weighted factor analysis based upon a fuzzy algorithm was used to partition samples by source based upon the composition of VOCs and similarity between constituents identified as primarily indoor and outdoor.

RESULTS: Fuzzy cluster analysis explained 73.2% of the variance in indoor and outdoor VOC concentrations collected in the summer and 72.9% of the variance in the samples collected in the the winter. By performing the factor analysis on the weighted concentrations derived from the fuzzy cluster analysis, we were able to explain an additional 9 % variance in personal samples compared to un-weighted data (63.1% vs. 72.4% respectively). Factor analysis identified eight factors, which explained personal exposure to VOCs. Vehicle emissions were the most important factor contributing to personal exposure with outdoor and an indoor factors totalling 19.3% of the variation. VOCs from trees and the natural environment were the second most important factor for personal exposure, while industrial emissions and long distance transport corresponded to the third and fourth most important factors. Indoors, carpets, cooking and the use of consumer products including acrolein, a –pinene, styrene and acetone was the most important indoor factor and VOCs that are released by humans and by consumer products namely, methyl ethyl ketone, toluene and m,p-xylene dominated the final two and least explanatory indoor factors.

CONCLUSION/IMPLICATIONS: Volatile organic compounds have known carcinogenic effects and personal exposure to several compounds is sufficient to cause detrimental respiratory health effects. We demonstrated that fuzzy cluster analysis can facilitate identification of VOCs sources. This method will help policy makers prioritize emission sources for control or regulation to mitigate health effects.

1.43 Sampling and Nutrient Analysis Project: Flour

J. Deeks[1], R. Klutka[1], M. Munro[1], M.F. Verreault[1], and M. Villeneuve[1]

[1] Nutrition Survey Section, Nutrition Research Division, Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON

SUMMARY: Comprehensive nutrient data profiles for five retail types of Canadian milled flour were generated utilizing Food Directorate's Sampling and Nutrient Analysis Program (SNAP-CAN) for inclusion in the Canadian Nutrient File (CNF).

BACKGROUND / OBJECTIVES: SNAP-CAN was initiated in 2008 to enable the collection, processing and nutrient analysis of Canadian food samples with the goal of improving access to quality nutrient data. Flour is a Canadian staple sold as a household commodity or incorporated into bakery products. It is a major contributor of nutrients in the Canadian diet as well as an important fortification vehicle for iron, thiamin, niacin, riboflavin, and folic acid. Despite its significant contribution within Canadian food products, no complete nutrient data profiles of Canadian flour samples currently exist. There is evidence that the classes of wheat grown in Canada result in a flour of higher protein content and lower mineral content than in the US, and that milling practices in the US are quite different, resulting in a product with a different nutrient profile. Health Canada is presently studying the options of redefining the standard regulations for the definition of whole wheat and whole grain flour as well as revising the fortification regulations for nutrients in flour. Thus, flour became the top priority food in 2008/9 for generation of a nutrient profile to better reflect the Canadian product.

METHOD: Funds were allocated for sample costs, processing and transport of materials. A sampling plan was developed to reflect all major sources of variations such as season, regions and brand names; and instructions were developed for the formation of composites. Sample collection was arranged and materials were processed and delivered to the appropriate labs for analysis. All Health Canada regional laboratories collaborated to run internationally approved methods and report their findings to the Nutrition Research Division.

RESULTS: There is a complete set of nutrient data for five types of flour that includes proximates, minerals, vitamins, amino acids, fatty acids, sugars and other nutrients. It was also noted that nutrients exhibited a wider than expected variation in levels of fortification, which warrants closer scrutiny.

OUTCOMES: This work provided the necessary analytical nutrient profiles for Canadian flours and also strengthened a science based decision-making process for a number of groups at Heath Canada for policy development.

1.44 The Food Virology Reference Centre and ViroNet Canada

O. Mykytczuk[1], E. Grudeski[2], S. Bidawid[1], T.F. Booth[2], and K. Mattison[1]

[1] Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] National Microbiology Laboratory, PHAC, Winnipeg, MB

SUMMARY: Human enteric viruses are transmitted through food and water to cause gastroenteritis and more serious disease. The Food Virology Reference Centre has launched ViroNet Canada for communication in real time about norovirus outbreaks. This tool can be expanded for molecular analysis of other viruses of public health concern.

OBJECTIVES/BACKGROUND/ISSUES: Monitoring viral outbreaks and sequences is important to understand how disease is spread in the Canadian population. We have formed a Food Virology Reference Centre for Canada. Surveillance information can identify and link common source outbreaks to guide prevention efforts. It can also be used to predict circulating strains for vaccine development and disease burden estimates. ViroNet Canada provides the means to track any viral sequences across Canada. We have also harmonized the norovirus genotyping and detection methods to facilitate communication via the “Norovirus” module of ViroNet.

DESIGN/METHOD/DESCRIPTION: ViroNet is a Bionumerics database. It was launched as a parallel database in close collaboration with the US-CDC and CaliciNet USA. It provides a national repository and communications hub for provincial public health professionals analyzing viral sequence information. For the norovirus genotyping harmonization, 9 laboratories tested 96 samples each by two typing protocols. For the detection methods, 20 laboratories tested 25 samples each and methods were assessed for sensitivity, specificity and detection limit.

OUTPUT/RESULTS: ViroNet is located at the National Microbiology Laboratory server in Winnipeg and is ready for provincial laboratories to upload samples. The recommended genotyping method for submission to ViroNet is the region C protocol, which amplifies the conserved shell layer of the capsid protein. Additional typing may provide more detailed analysis for strain variants. Multiple detection methods are useful for norovirus typing, we have selected one recommended real-time RT-PCR protocol for labs that require assistance with this technique.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The ViroNet database presents a major advance in viral sequence analysis and communications across Canada. Our next steps will be to provide training in Bionumerics and ViroNet to the participating laboratories. We will then provide both data and samples to laboratories for processing. Once successful with these test samples, users will be certified to use the ViroNet system.

1.45 UV Photo-Oxidation Studies of Airborne 1-Methylnaphthalene

J. Prokash Nandy[1], J. Zhu[1], and Y.-L. Feng[1]

[1] Exposure and Biomonitoring Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Photo-oxidation of a series of potential indoor air contaminants have been studied under different doses and durations of exposures of these materials to UV radiation, using a sunlight simulator. Attempts are also made to identify the products of such UV incitement on these materials.

OBJECTIVES/BACKGROUND/ISSUE(S): With Canadians spending about 90% of their time in the indoor environment, its potential effects on health have become the subject of increasing research attention. Contaminations in indoor environment including volatile and semi-volatile organic compounds are causing long term or immediate sickness to many. Some of them have been identified as the top priorities in the CMP program and the Government of Canada is obligated to assess all of these substances within a three-year timeframe. The environmental fate of these chemicals in air, after interaction between themselves co-existing in the environment and with other environmental parameters such as UV, ozone and PMs has not been well understood. Photo-oxidation under UV radiation is one of the potential ways these materials can follow to transform into their secondary pollutants. The present study has been undertaken to check the fate of some of the common indoor air organic pollutants under UV irradiation and its impact with the possible secondary pollutants.

DESIGN/METHOD/DESCRIPTION: 1-methylnapthalene (a representative example from the series chemicals studied), was injected into a sealed quartz chamber, and allowed to sit for 30 min to let the chemical in the chamber evaporate and reach the equilibrium. Then the chamber was exposed to a beam of UV light with certain energy, for certain time (various doses). The residues of the chemicals in the chamber was then extracted with hexanes and analyzed by Agilent GC/MS for the degradation information. The possible secondary products from the extractions were further identified by LC/MS/MS.

OUTPUTS/RESULTS: The photo-oxidised degradation of airborne 1-methylnapthalene under UV irradiation has been confirmed by this study, which is similar to the results of photo-oxidation of this chemical in seawater with UV light. The influence of various doses of UV exposure and various exposure times of low energy of UV has been investigated. Our initial studies indicate that the major secondary products from the UV photo-oxidation are the methylisobenzofuranones whose toxicity and impact on the air quality need to be further investigated.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This study provides important information that the airborne CMP chemicals can be easily photo-oxidised by UV light, and the exposure dose and the exposure time will definitely affect the formation of secondary pollutants. The results here will be very helpful to assess the impact of fate of airborne contaminants under environmental conditions on the air quality, and be useful in toxicity study and risk assessment of those chemicals.

1.46 Influence of Bovine Serum Albumin on the Secondary Structure of Interferon Alpha-2b as Determined by Far U/V Circular Dichroism Spectropolarimetry

K. Nemr[1], M.A. Hefford, PhD[2], and M.J.W. Johnston, PhD[2]

[1] Department of Biochemistry, University of Ottawa, Ottawa ON
[2] Centre for Biologics Research, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa ON

SUMMARY: The correct structure of a therapeutic biologic is critical for its safety/efficacy and can be dramatically influenced by formulation excipients. Here we present a simple method, using far U/V circular dichroism spectropolarimetry, to assess the influence of bovine serum albumin (BSA) on the secondary structure of interferon alpha-2b.

BACKGROUND: Many therapeutic biologics are formulated with excipients, including the protein excipient human serum albumin (HSA), to increase stability and prevent protein aggregation and adsorption onto glass vials. One biologic formulated with HSA, interferon alpha-2b (INF-2b), was used for these studies. As is the case with other therapeutic biologics, the increased structural complexity of INF -2b compared to a small molecule drug requires that both the correct chemical structure (amino acid sequence) and also the correct secondary and tertiary structure (3 dimensional fold) be verified to assure safety and efficacy. Although numerous techniques are available to assess a biologic's primary, secondary and tertiary structures, difficulties arise when assessing higher order structure in the presence of protein excipients. In these studies far U/V circular dichroism spectropolarimetry (far U/V-CD) was used to determine the secondary structure of INF-2b in the presence of a protein excipient.

METHODS: Far U/V-CD was investigated as a potential technique to assess the influence of BSA on the secondary structure of the EDQM INF-2b reference standard and other proteins (RNAaseA/Lysozyme) at a variety of protein concentrations and BSA/protein ratios.

RESULTS: We demonstrated that the secondary structure of INF-2b remains mostly unchanged at a variety of BSA to INF-2b protein ratios. A slight, but significant, increase in beta sheet content was noted when the BSA to INF-2b ratio was 5:1 (wt/wt) suggesting a potential conformational change in INF-2b secondary structure when BSA is in molar excess.

CONCLUSION: Far U/V-CD is a suitable technique to assess the secondary structure of therapeutic biologics in the presence of protein excipients. As many manufacturers currently offer the same biologic with variations in formulation, this technique may be of importance in current and future assessments of similar biologics with varying formulations from the same or different manufacturers.

1.47 Cadmium Telluride Quantum Dot Nanoparticles Cause Sub-Cellular Toxicity Suggesting Oxidative Stress and Apoptosis in Mammalian Cells

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

[1] Biotech Lab, Mechanistic studies, EHSRB, HECSB, Health Canada, Ottawa, ON
[2] The University of Ottawa Heart Institute, Ottawa, ON

SUMMARY: The mechanisms of toxicity caused by Cadmium Telluride quantum dots (CdTe-QDs) in mammalian cells were investigated in this study. For this purpose, mouse macrophage and human epithelial cells were exposed to the nanoparticles. Microscopic and enzymatic-based assays revealed that QDs induce oxidative stress leading to cell death in exposed cells.

OBJECTIVES: Currently, there is a lack of data related to toxicity potential of nanoparticles. Our previous studies found that CdTe-QDs caused cytotoxicity in mammalian cells. To understand the mechanisms of toxic effects of CdTe-QDs to cells, here we investigate whether QDs cause oxidative stress and apoptosis in mammalian cells.

DESIGN: Murine J774A.1 macrophages and human HT29 epithelial cells were exposed to CdTe-QD nanoparticles (10^{-7}- 10^{1}ug/ml) for 4hr and 24hr. After treatment, cells were fixed and processed for confocal microscopy and transmission electron microscopy (TEM) to detect apoptosis. In a parallel set of experiments, cell lysates were screened for total glutathione (GSH) and superoxide dismutase (SOD) using colorimetric/ enzymatic assays. Phophoprotein levels were measured using multiplex bead-based assays.

OUTPUTS/RESULTS: TEM results showed changes in sub-cellular architecture and enlargement of mitochondria in CdTe-QD-treated cells. A 2-fold decrease in total GSH level and a 2 to 8-fold increase in SOD activity in CdTe-QD-treated cells were observed, suggesting that cells were undergoing oxidative stress. Confocal microscopy showed apoptotic cells from CdTe-QD treatment. CdTe-QDs also caused increase in phosphorylation of selected proteins such as JNK, Erk-MAP kinase, CREB, and p38 and caused a decrease in IkBa and p70 S6 kinase levels.

IMPACTS/OUTCOMES/CONCLUSIONS: The results show that CdTe QDs affect different signal transduction pathways that are related to metabolic activity of cells. The results also reveal mitochondrial dysfunction in cells caused by CdTe-QD treatment. This study suggests that CdTe-QDs cause cytotoxicity to mammalian cells by inducing oxidative stress and apoptosis. This study provides much needed mechanistic details for understanding toxicity endpoints that might be important for nanoparticle risk screening by Health Canada evaluators and the scientific community at large.

1.48 Effects of Functional Foods on Human Health and Wellness: Antimicrobial and P450 Inhibitory Properties of Common Food Plants

S. Nguyen, BSc[1]; H. Huang, BSc[1,2]; T.W. Tam, MSc[1]; T. Xing, PhD[2]; M.L. Smith, PhD[2]; J.T. Arnason, PhD[1]; H. Akhtar, PhD[3]; and B.C. Foster, PhD[1,4]

[1] Centre for Research in Biopharmaceuticals and Biotechnology, University of Ottawa, Ottawa, ON
[2] Carleton University, Ottawa, ON
[3] Agriculture and Agri-Food Canada, Guelph, ON
[4] Therapeutic Products Directorate, Health Canada, Ottawa, ON

SUMMARY: We investigated potential risk posed by common pulses, herbs and spices on the cytochrome P450-mediated drug metabolism and the gut microflora. Compromising these two systems may lead to adverse drug reactions due to CYP inhibition and disruption of the microflora by phytochemicals in these food plants.

OBJECTIVE: The demand for functional foods have increased in recent years as consumers are seeking ways to control their own health through diet. This study was undertaken to determine the capacity of pulses, herbs and spices on human cytochrome P450 (CYP)-mediated metabolism and the gut bacterial microflora to delineate the potential affect on therapeutic product metabolism, and ultimately affect human health and wellness.

DESIGN: This study examined a variety of products from the *Apiaceae, Fabaceae,* and *Lamiaceae* families for their inhibitory potential on CYP 2D6-, 3A4-, 3A5-, and 3A7-mediated metabolism. Plant extracts were analyzed via high throughput fluorometric microtitre cytochrome P450 inhibition assays. The antimicrobial effects of these samples are also investigated to determine potential affects on the gut microflora. Extracts were tested against *Acenobacter calcoaceticus, Bacillus subtilis, Enterococcus faecalis, Escherichia coli, Listeria innocua, Providencia stuartii* and *Pseudomonas putida*using the Kirby-Bauer disc diffusion assay.

RESULTS: The highest CYP inhibitory activities were observed from samples belonging to the *Apiaceae* and *Lamiaceae* families, such as celery seed, cumin, fennel seed, basil, oregano, and rosemary. The strongest antimicrobial activities were also observed in the *Apiaceae* and *Lamiaceae*. No significant antimicrobial and CYP inhibition was observed in the *Fabaceae*extracts.

IMPACT: Results demonstrated the possible risk of food-drug interactions from the spice and herb families, and also the potential effect on the composition of the bacterial gut microflora, which may further affect drug disposition. These food plants possess phytochemicals, which may influence drug metabolism directly by inhibiting CYP enzymes or by creating a higher drug load on the host by affecting the gut flora. Furthermore, these food plants may affect these two systems individually or synergistically. Complications such as adverse drug reactions and drug resistance may be a result of diet, thus more focus is needed on patient diet when assessing drug metabolism complications.

1.49 Sources of Trace Metal Contamination in the Lab: Acid Dispensers

J. Niu, PhD[1] and P.E. Rasmussen, PhD[1,2]

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

SUMMARY: Sources of metal contamination in our laboratory have been identified and eliminated to improve the accuracy and precision of trace metal analyses required for exposure assessments. Commonly used acid dispensers were investigated in this study, and some were found to contribute unacceptable levels of contamination.

OBJECTIVES: To identify laboratory sources of contamination and recommend appropriate contamination-free equipment for accurate measurement of metals in samples of airborne particulate matter.

DESIGN: Four commonly used hydrofluoric acid (HF) bottle-top acid dispensers, SeaStar (SS), OptiFix (OF), Labmax (LM), and BrandTech (BT), were selected to assess contamination levels of more than twenty elements. Samples from HF dispensers were collected by direct dispensing from a freshly opened HF bottle and from an HF bottle, which had been in use for several months, and diluting appropriately with 2% nitrogen acid solution. Elemental concentrations were determined using inductively-coupled plasma mass spectrometry (ICP-MS). Reagent blanks (prepared without using the dispenser) and Certified Reference Materials (TM28.3, NIST 1640, and TMDA 64) were used for quantification of background and quality control.

RESULTS: The test results indicate that three of the HF dispensers (BT, OF, and LM) contribute unacceptable levels of contamination of certain key elements. Al, Ti, and Fe were found to be the top three contaminants contributed by BT (36 ng ml^{-1} to 980 ng ml^{-1}), OF (68 ng ml^{-1} to 115 ng ml^{-1}), and LM (20 ng ml^{-1} to 103 ng ml^{-1}), respectively. The SS HF dispenser contributes insignificant levels of these and other elements. Dispensers also cause significant contamination (from 9 ng ml^{-1} to 36 ng ml^{-1}) for other elements including Cr, Ni, As, Zn, and Ba, depending on the brand.

CONCLUSIONS: Results indicate that the selection of HF dispenser is important, as this may be a significant source of contamination in an ICP-MS lab. The contamination is both element- and dispenser-dependent.

1.50 Assessing Factors Contributing to Infant Internal Exposure to Persistent Organic Chemicals in Northern Population with Bayesian PBPK Modeling

A. Nong[1], M.-A. Verner[2], and S. Haddad[2]

[1] Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] Sciences biologiques, TOXEN, Université du Québec à Montréal, Montréal, QC

SUMMARY: In a collaborative effort to develop health assessment tools of environmental substances, our intention is to identify factors leading to persistent organic pollutants found in infants of northern population. Unique biological values for this subpopulation were estimated using a statistical physiological model describing the kinetics in mothers and infants.

OBJECTIVES: A previously published physiologically-based pharmacokinetic PBPK model for mothers was modified to assess mother-infant transfer of persistent organic pollutants (POPs) from an Inuit population. The purpose of this research is to investigate these subpopulations physiological and metabolic factors with the model contributing to internal levels of these pollutants. No such work has been published related to the pharmacokinetic disposition of any Northern populations.

METHODS: The model development involved incorporating into the model: population tissue data (plasma, breast milk and cord blood concentration) and prior distribution of physiological values for infants and mothers (body weights and height). Bayesian statistical modeling using a Markov Chain Monte Carlo (MCMC) approach of the PCB dataset generated specific posterior physiological and metabolic distributions for this population. The MCMC simulations were implemented in acslX (Aegis Technologies) on a cluster computer and statistical analysis were computed with a Bayesian Output Analysis program (University of Iowa).

RESULTS: Preliminary results indicate that prior values for the North American adult and infant population differed by more than a standard deviation with the estimated posterior distributions from the simulations for this infant subpopulation. Uncertain distributions of infant adipose tissue lipid composition were as sensitive as milk volume or lipid content in affecting internal level predictions.

OUTCOMES/NEXT STEPS: Future work is progressing at examining several forms POPs (e.g., DDT or DDE) and validating the estimated posterior physiological parameters with the model. Combination of statistical calculations and biological models are applied to determine the population sensitivity of the kinetic components and confidence interval of internal dose metrics. The biological models from all this study will provide as essential tools for the support of sensitive subpopulation health risk assessment to environmental contaminants.

1.51 Thermal Inactivation Studies of *Vibrio parahaemolyticus* Strain NY477 for Policy Development on Safe Preparation of Molluscan Shellfish

D. Oudit, MSc[1], L. Bakouche, BSc[2], and S. Banerjee, PhD[2]

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

[2] Microbiology Research Division, Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Adequate cooking temperatures and times are important steps in food processing for both safety and sensorial aspects. Minimum thermal processes required to assure food safety will help to mitigate illness due to *Vibrio parahaemolyticus* among consumers of seafoods, some of which are eaten raw or minimally cooked.

OBJECTIVES: The aim of the study was to determine thermal inactivation characteristics of *V. parahaemolyticus* (Vp) strain NY477 (via D value, time at a set temperature to kill 90% of microorganisms and z value, number of temperature degrees to change *D* by factor of 10), for calculation of science-based time-temperature combinations to be used in safe preparation of molluscan shellfish, particularly oysters, for human consumption.

DESIGN: Vp strain NY477 was grown overnight at 35°C to the stationary phase (7-8 log/mL), centrifuged, washed in artificial seawater (ASW) and concentrated in ASW. One millilitre of the suspension was added to 99 mL of ASW equilibrated at a pre-determined temperature. Aliquots (1 mL) were withdrawn at regular intervals, diluted and plated for determining the surviving fraction. Thermal inactivation graphs were drawn using the surviving fractions to derive *D*- and *z*-values using five temperatures between 46°C and 54°C.

OUTPUTS/RESULTS: Five temperature settings between 46°C and 54°C at intervals of 2°C, yielding five survivor curves and five *D*-values, were used to determine the *z*-value. *D* values at 54°C was 14 seconds to achieve one log reduction of Vp, and *D* at 46°C was 20 minutes to achieve one log reduction of Vp. The calculated *z*-value was 4.24°C.

IMPACTS/OUTCOMES/NEXT STEPS: The widespread occurrence of Vp in molluscs from Canadian coastal waters indicate that aquacultural and feral molluscs present a potential human health risk if consumed raw. However, minimum thermal processing can reduce the risk of exposure to Vp by several factors based on the time-temperature combinations derivable from this study. Follow up studies will include (i) determining the *D*- and *z*-values when seafood matrix such as mollusc homogenate is used, and (ii) inclusion of other environmental strains of Vp for checking variability in resistance patterns.

1.52 Radon Exhalation from Various Household Tiles and Dry Walls

J. Chen, PhD[1], and N. Rahman, PhD[1]

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

SUMMARY: Radon exhalation rates were determined for 17 different types of tile and dry wall commonly used in home construction. The radon exhalation rates ranged from nondetectable to 45Bq/m-2/d . Analysis showed that indoor radon from various tile and dry wall materials is negligibly small even for a completely sealed home.

OBJECTIVES/BACKGROUND/ISSUE: Long-term exposure to radon increases the risk of lung cancer. There is considerable public concern about radon exhalation from building materials. To address this concern, radon exhalation rates were determined for 17 different types of tile and dry wall commonly used in home construction.

DESIGN/METHOD/DESCRIPTION: Building materials for interior use were chosen randomly from two hardware outlets in Ottawa. These included 4 types of dry wall, 4 types of porcelain tile, 4 types of marble tile, 3 types of ceramic tile, and 2 types of slate tile. The surfaces of these materials were covered with containers to collect radon exhaled from the surfaces. Radon concentrations inside the containers were recorded by the continuous-flow technique with AB-5 radon monitors. For each type of tile or dry wall, repeat measurements were performed. Radon exhalation rates in unit of Bq m^{-2} d^{-1} were determined from the slopes of the radon growth curves.

OUTPUTS/RESULTS: The radon exhalation rates ranged from nondetectable to 45 Bq m^{-2} d^{-1} with higher values occurring for slate tiles. Even if a house had its entire floor installed with tiles of the highest radon exhalation rate measured in this study, the maximum radon concentration due to radon exhalation from the floor would be only 2 Bq m^{-3}in a completely sealed home. Normal ventilation would further reduce the radon concentration significantly.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This study demonstrated that building materials, such as tile and dry wall, contribute very little to indoor radon concentrations.

1.53 High Doses of Dietary Acrylamide Do Not Augment Azoxymethane-Induced Colon Aberrant Crypt Foci Formation in Male F344 Rats

J. Raju[1], C. Sondagar[1], J. Roberts[1], A. Bielecki[2], D. Caldwell[3], and R. Mehta[1]

[1] Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Safe Environment Programme, HECSB, Health Canada, Ottawa, ON
[3] Bureau of Chemical Safety, Food Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: The effect of dietary acrylamide to modulate the growth of chemically-induced rat colon pre-cancerous lesions was studied. High doses of dietary acrylamide did not augment the growth of colon pre-cancerous lesions but on the contrary reduced them.

OBJECTIVES/BACKGROUND/ISSUE(S): Acrylamide is a known rodent carcinogen, and has been classified as a “probable human carcinogen” by the International Agency for Research on Cancer. Public health concern about acrylamide escalated after it was found to be spontaneously formed in fried and baked foods. While further research continues to fill the toxicology data gaps, Health Canada has implemented various risk management strategies to reduce exposure to dietary acrylamide. In the present study, we aimed to understand the role of dietary acrylamide in modulating the early stages of colon carcinogenesis and to assess if dietary fat level was critical in altering the effects of acrylamide.

DESIGN/METHOD/DESCRIPTION: Six weeks-old male F344 rats were acclimatised for 2 weeks and then received two weekly s.c. injections of azoxymethane (AOM) at a dose of 15 mg/Kg body wt. Simultaneously, rats (n = 8/group) were randomized into 8 dietary groups. Diets were based on AIN-93G semi-synthetic formula modified to contain either low fat (7% corn oil) or high fat (23.9% corn oil) and acrylamide at 0 (Control), 5 (low), 10 (medium) or 50 (high) mg/Kg diet (wt/wt). All rats were on the experimental diets *ad libitum* for 8 weeks, after which they were killed and their colons assessed for aberrant crypt foci (ACF), putative precancerous lesions.

OUTPUTS/RESULTS: A 100% incidence of colon ACF was observed in rats of all dietary groups. Irrespective of dietary fat level, rats with the highest tested dose of acrylamide (50 mg/Kg diet) had significantly lower total ACF ($p<0.05$) and lower large ACF (those with 4 or more crypts/focus; $p<0.001$) compared with their respective Controls (0 mg/Kg diet). In addition, a significantly lower number of large ACF ($p=0.046$) was noted in rats treated with 10 mg/Kg diet acrylamide exclusively in the high fat group, compared to the high fat Control. There were no differences in either total or large ACF in rats treated with 5 mg/Kg diet of acrylamide in either the low or high fat diet groups, compared to their respective Controls.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: To our knowledge, this is the first experimental study designed to address the health effects of acrylamide when administered in the diet. Results suggest that dietary acrylamide does not augment the early stages of azoxymethane-induced colon carcinogenesis in F344 rats. On the contrary, dietary acrylamide decreased the total number of ACF in either low or high fat settings. These results suggest that acrylamide, when administered through the diet at doses earlier known to cause rat tumors, does not

increase the risk of developing precancerous lesions of the colon in rats. To address if these results would mirror the modulation of colon tumor outcomes by dietary acrylamide, a long term colon tumor bioassay is warranted. The cancer modulating effects of doses of acrylamide in the diet comparable to those at higher levels found in Canadian foods is elusive, and hence, needs further scrutiny. Future studies aimed to understand the health risks of acrylamide would facilitate more options for risk management.

1.54 Pesticide Residues in the Canadian Total Diet Study; 2003 and 2005 Results

T. Halldorson[1], V. Roscoe[1], G.A. Lombaert[1], and D.F.K. Rawn[2]

[1] Food Program Laboratory, Regions and Programs Branch, Health Canada, Winnipeg, MB
[2] Bureau of Chemical Safety, Food Research Division, Health Canada, Ottawa, ON

SUMMARY: An existing method for the analyses of a broad spectrum of pesticides in foods was adopted and validated for samples from the 2003 and 2005 sampling years of the Canadian Total Diet Study (CTDS). Concentration levels were found to be low relative to established maximum residue limits (MRLs).

OBJECTIVES/BACKGROUND: Total diet studies are recommended by the World Health Organization (WHO) to accurately determine dietary exposures of populations to contaminants. The CTDS involves the retail purchase, preparation and combination into composites of foods representing an average Canadian diet. Composites are analysed to determine contaminant concentrations from which dietary intakes can be estimated and compared to international and national guidelines as a direct measure of food supply safety.

DESIGN/METHOD: An existing method was adopted and validated for the analyses of a broad spectrum of pesticide residues in foods. In short, samples were solvent extracted and cleaned-up prior to analysis employing a gas chromatograph coupled to a high-resolution mass spectrometer (GC/HRMS). Method detection limits were generally determined to low pg g^{-1} levels. Two sampling years of the CTDS consisting of approximately 100 samples per year were analysed.

OUTPUTS/RESULTS: Pesticide residues have been detected in all food samples analysed for the 2003 and 2005 CTDS sampling years. Concentration levels were generally low relative to the MRLs established in the *Canadian Food and Drug Regulations*.

IMPACTS/NEXT STEPS: Concentration results will be compared with past CTDS surveys and converted to dietary intake estimates for both ongoing risk assessment and as a measure of the safety of the Canadian food supply. Next steps include the ongoing processing of CTDS sampling years as well as further method development and validation to include the analysis of a broader spectrum of pesticide residues in foods.

1.55 Investigation of Induced and Persistent Genetic Instability in Mice Exposed to Particulate Air Pollutants *In Utero*

C.E. Ritz[1], W. Ruminski[2], U. Vogel[2,3], H. Wallin[2], K. Hougaard[2], L. Berndt-Weis[1], A. Rowan-Carroll[1], and C.L. Yauk[1]

[1] Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] National Research Centre for the Working Environment, Copenhagen, Denmark
[3] National Food Institute, Technical University of Denmark, Soborg, Denmark and Institute of Science, Systems and Models, University of Roskilde, Roskilde, Denmark

SUMMARY: This project investigates genetic instability (elevated background mutation rates) following exposure to inhaled diesel exhaust particles (DEP) in utero. Analysis of tandem-repeat DNA mutation in sperm showed that descendents of males exposed *in utero* to DEP did not exhibit genetic instability. More work is needed to confirm this finding.

OBJECTIVES/BACKGROUND: Particulate Air Pollutants (PAPs) are widespread. Previous work has shown that PAPs from industrial environments cause germline mutations in mature male mice. It is unclear how PAP exposure will impact the developing germline during critical periods of gametogenesis. This work investigates transgenerational effects arising following exposure of males to DEP *in utero* during critical stages of gametogenesis. In mice, expanded simple tandem repeat (ESTR) loci exhibit the highest rates of mutation measured to date, and provide valuable tools for studying inherited mutation and genomic instability. Mutations are measured directly in germ cells, but also persist in unexposed descendents of exposed males, a phenomenon known as transgenerational genetic instability. The objective of this study was to quantify rates of induced ESTR mutation in sperm of the descendants of male mice exposed to DEP *in utero*.

METHOD/DESCRIPTION: C57Bl mice were exposed *in utero* to 20mg/m^3 NIST 2975 (a diesel exhaust particle [DEP]) for 1 hour daily from gestational day 7 until birth, alongside sham controls. Male offspring were collected and mated with unexposed mates. F2 males were sacrificed at maturity and DNA extracted from sperm. ESTR mutation frequencies for 6 exposed and control males was determined using single molecule PCR (SM-PCR), described previously (1).

RESULTS: No increase in mutation frequency was found in the descendents of exposed male mice (p=0.5521).

CONCLUSIONS/NEXT STEPS: The findings suggest that exposure *in utero* to 20mg/m3 NIST 2975 (DEP) does not cause transgenerational mutation mediated via the male germline in the F2 generation. However, a larger sample size, exposure through the female lineage, and different doses should all be examined.

1.56 Effects of Excess Dietary Iodine on Thyroid Gene Expression in Resistant and Thyroiditis-Prone BB Rats

E. Swist[1], C. Qiao, MSc[3], D. Caldwell, DVM[2], H. Gruber, MSc[1], and K.A. Scoggan, PhD[1,4]

[1] Nutrition Research Division, HPFB, Health Canada, Ottawa, ON
[2] Toxicology Research Division, HPFB, Health Canada, Ottawa, ON
[3] Bureau of Food Policy and Science Integration, HPFB, Health Canada, Ottawa, ON
[4] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

SUMMARY: The molecular mechanisms that lead to iodine-induced thyroiditis remain to be determined. We found that high intakes of iodine increased the incidence of autoimmune thyroiditis in thyroiditis-prone BioBreeding (BBdp) rats and that up-regulation of fatty acid-binding proteins may contribute to the disease process.

OBJECTIVES/BACKGROUND/ISSUE(S): To investigate the effects of excess dietary iodine on thyroid function and thyroid gene expression in thyroiditis-prone (BBdp) and -resistant (BBc) rats in order to identify genes specifically involved in the susceptibility to iodine-induced autoimmune thyroiditis.

DESIGN/METHOD/DESCRIPTION: Female BBdp and BBc rats (15/group) were fed purified diets of either the recommended (0.2 mg/kg) or high (50 mg/kg) levels of iodine for 8 weeks. Subsequently rats were killed and the incidence and severity of thyroiditis was determined by histopathology. Thyroid function was determined by measuring serum thyroid hormone levels. The expression of several thyroid genes was assessed using microarrays, real-time quantitative PCR and Western blot analyses.

OUTPUTS/RESULTS: Histological analysis of thyroids found no thyroiditis in BBc rats, whereas, 7.1% (1/14) and 33.3% (5/15) of BBdp rats on the recommended or high iodine dose had thyroiditis, respectively. Serum hormone levels of free triiodothyronine (T3) and thyroxine (T4) were lower in BBdp rats compared to BBc rats whereas serum thyroid stimulating hormone (TSH) levels were higher in BBdp rats than BBc rats, $p<0.05$. Excess dietary iodine decreased serum free T4 levels and increased serum TSH levels in both rat strains. Serum total T3 and T4 hormone levels were not different between the groups. High levels of dietary iodine up-regulated Cidec, Slc36a2, Plin, and Fabp4 mRNA and protein levels in thyroiditis-prone rats but not in thyroiditis-resistant control rats.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Our results indicate that high iodine intake increases the incidence of autoimmune thyroiditis in BBdp rats and that up-regulation of fatty acid-binding proteins may contribute to the disease process. This project contributes to Health Canada regulatory and policy activities to evaluate iodine fortification levels in food. These results also warrant future studies to determine if similar genes are involved in human populations susceptible to iodine-induced thyroiditis.

1.57 Substance Abuse in a National Population of Children Involved with the Child Welfare System

V.-A. Singh, MPH[1], L. Tonmyr, MSW, PhD[2], and T. Thornton, MSW[3]

[1] Health Information, Analysis and Research Division, Strategic Policy, Planning and Analysis Directorate, FNIHB, Health Canada, Ottawa, ON
[2] Injury and Child Maltreatment Section, Health Surveillance and Epidemiology Division, Public Health Agency of Canada, Ottawa, ON
[3] Office of Drugs and Alcohol Research and Surveillance, Controlled Substances and Tobacco Directorate, HECSB, Health Canada, Ottawa, ON

SUMMARY: Thirteen percent of a national sample of 10-15 year olds who had experienced maltreatment abused substances. Older age, aboriginal status, neglect, physical harm, child behaviours (running away, negative peer involvement, irregular school attendance) were associated with substance abuse. These findings can help inform social worker interventions.

OBJECTIVE: To describe the substance abuse patterns and identify the risk and protective factors associated with alcohol, drug and solvent abuse in a national sample of children involved with the child welfare system.

METHODS: Univariate analyses and logistic regression were conducted on a sample of children aged 10-15 years old from the Canadian Incidence Study of Reported Child Abuse and Neglect - 2003 (CIS-2003). The CIS-2003 is a randomly selected representative sample of child maltreatment investigations in 63 child welfare service areas across Canada (except Quebec). Analyses were conducted on all investigations in the sample and on a subset of investigations found to be substantiated for child abuse or neglect. A case is considered substantiated if the balance of evidence indicates that abuse or neglect has occurred after an investigation by child protection worker. The following factors were analyzed: age, sex, aboriginal status, substantiated neglect, substantiated maltreatment other than neglect, two or more forms of substantiated maltreatment, physical harm, caregiver substance abuse, negative peer involvement, running away from home, irregular school attendance, and conduct problems.

RESULTS: The CIS data demonstrates that substance abuse problems are prevalent among children investigated by child protection services (10.73% among all investigated cases). The prevalence is even higher among substantiated cases where almost 13% of children in this age group have a confirmed or suspected substance abuse problem. At this time, no comparable studies have been conducted in this age group on substance abuse in Canada; therefore, a comparison to the general population is not possible.

In assessing factors associated with substance abuse, age, aboriginal status, substantiated investigations of neglect, physical harm, certain child behaviours (e.g., running away, negative peer involvement, irregular school attendance) were found to be associated with substance abuse in all investigated cases. The same factors were also found to be associated with substance abuse in substantiated investigations of abuse and neglect.

CONCLUSIONS: The early identification of children involved in child welfare who were at-risk of or using substances is a critical need. Once identified, these children can receive the services required to deter their substance use and potential abuse.

The identified factors in this analysis could be a starting point to help in the early identification of children who may become substance abusers.

1.58 Soil Vapour Intrusion Investigation at a Site in Northern Manitoba and Implications for Health Canada's Guidance on Vapour Intrusion Assessment at Contaminated Sites

L. Smith, MSc[1], I. Hers, PhD[2], and A. Wagenaar, MSc[2]

[1] Contaminated Sites, Safe Environments, RAPB, Health Canada, Winnipeg, MB
[2] Golder Associates, Winnipeg, MB

SUMMARY: A study of subsurface and indoor vapours at an impacted site in the north to assure current guidance and models protect human health. Temperatures under the building were conducive to vapour formation. Further study is needed, but initial results suggest model can make useful predictions for conditions in the north.

BACKGROUND: Many federal contaminated sites are located in the subarctic and arctic, where conditions may be outside the default parameters of the Johnson and Ettinger (J&E) model, used to develop attenuation factors to predict vapour transport from the subsurface into buildings. In conjunction with INAC a provincial School Division, Brochet School, in Northern Manitoba, was selected to study vapour intrusion in the subarctic.

METHODS: Soil gas, groundwater, crawlspace and indoor air were sampled and analyzed for petroleum hydrocarbon vapours. Measured results were compared with results predicted from the Johnson and Ettinger model.

RESULTS: Temperatures (9°C to 18°C) under the school are warm enough to allow for the formation and transport of vapours even in winter. Likely contributing to elevated soil temperatures was a heated crawlspace. Soil vapour concentrations under the building ranged from 0.57 mg/m^3 to 1,900 mg/m^3 for CCME F1 petroleum fraction and 0.67 mg/m^3 to 315 mg/m^3 for the F2 petroleum fraction. The attenuation of soil vapour with decreasing depth, observed at some multi-depth probe locations, along with oxygen concentrations of at least 18%, suggest that aerobic biodegradation of hydrocarbon vapours is occurring. Surface staining from fuel line leaks and indoor sources of VOC's confounded the calculation of site-specific attenuation factors.

OUTCOME: Further research is needed before it can be determined how widely Health Canada's guidance can be applied to sites in the arctic and subarctic, but this first detailed study suggests it can have utility as a screening tool.

1.59 An Inter-Comparison of Radiation Dose Measurement Techniques with Potential Applications for Interventional Radiological Procedures

P. Steadman[1, 2], D. Gillis[1], K. Sears[1], and N. Martel[1]

[1] Medical X-ray and Mammography Division, Consumer and Clinical Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON
[2] McMaster University, Hamilton, ON

SUMMARY: Presently, there is no single skin dose X-ray measurement method in interventional procedures. Several radiation dose measurement methodologies were compared for potential use based on practicality, accuracy and reproducibility. The methodologies varied in capabilities with thermoluminescent dosimetry being the most flexible. Further research is underway to establish improved protocols.

OBJECTIVES/BACKGROUND/ISSUE(S): Currently a debate exists for the most effective way to measure complex interventional radiological procedure doses. This work attempts to determine precise and practical record methods by comparison of three different measurement techniques; Metal-oxide Semiconductor Field-Effect Transistors (MOSFETs), Optically Stimulated Luminescence of Al_2O_3 (OSL), and Thermoluminescent Dosimeters, LiF:Mg,Cu,P (TLD-100H). Dosimetry methods were chosen based on literature and availability.

DESIGN/METHOD/DESCRIPTION: MOSFETs, OSL, and TLD-100H were calibrated using a standard 30cc ionization chamber with electrometer placed on top of an ISO-4037 water phantom to simulate entrance skin doses. The instruments were calibrated and tested using a diagnostic x-ray generator at energies between 60 and 120 kVp. Dosimetric accuracy was performed by comparing the standard and dosimetry method measurements. An inter-comparison of the dosimeters was used for reproducibility, energy response, angular dependence and minimum detectable dose.

OUTPUTS/RESULTS: Accuracy varied amongst the three techniques when using practical calibration methods. The TLD-100H accuracy was 5% for doses above 1 mGy while the OSL yielded 3% over 0.5-10 mGy range. For reproducibility, the MOSFETs varied the most (stdev.= 25%), while the OSLs and TLD-100Hs varied similar amounts (stdev.= 5%).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The results from these experiments reveal a plausible dosimetry method for varying study designs, thus forming the foundation for future work. The TLD-100H appears to be the best method in means of practicality, performance and reliability. When dose is required to be known immediately after irradiation and few measurements are required, the use of the OSLs is recommended, as they are the most precise and accurate. The MOSFETs perform well as a real time measurement device but lack the accuracy and reproducibility to be effective. These results will allow for better instrumentation protocols and their dosimetric use in studies.

1.60 Activation of Proteolytic Pathways in the Lungs of Mice with Constitutive Expression of the Inflammatory Cytokine Tumour Necrosis Factor-α

E. Thomson[1], A. Williams[2], C.L. Yauk[3], and R. Vincent, PhD[1]

[1] Inhalation Toxicology Laboratory, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] Biostatistics and Epidemiology Division, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[3] Genomics Laboratory, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON

SUMMARY: Increased production of a protein called tumour necrosis factor (TNF)-α in the lungs causes inflammation and destruction of lung membranes. We examined whether TNF-α expression is associated with increased production of proteins called matrix metalloproteinases (MMPs) that are involved in the breakdown of connective tissue.

BACKGROUND: Elevated levels of the proinflammatory cytokine TNF-α have been implicated in the pathogenesis of a number of inflammatory lung disorders, including emphysema, fibrosis, chronic obstructive pulmonary disease, and connective tissue breakdown associated with cigarette smoking. Surfactant protein (SP)-C/TNF-α transgenic mice constitutively express a TNF-α transgene under transcriptional control of the SP-C promoter in type II alveolar epithelial cells, and consequently develop pronounced inflammation and airspace enlargement. We examined how overexpression of TNF-α altered the lung transcriptome and expression of matrix metalloproteinases (MMPs) and their inhibitors.

METHOD: Global transcriptional differences between 4-month old wildtype and TNF mice were assessed by microarray (n=5/genotype). Real-time polymerase chain reaction (PCR) was used to further characterise expression of genes implicated in inflammation and MMP regulation.

RESULTS: Analysis of microarray data identified altered expression of 2332 probes (false-discovery rate-adjusted $p<0.05$). Functional analysis of differentially expressed genes revealed enrichment of genes involved in inflammation and protease-antiprotease activities, consistent with the pronounced inflammation and airspace enlargement. Real-time PCR confirmed higher mRNA levels of TNF-α and the inflammatory caspases -1 and -4 ($p<0.001$). TNF mice had increased mRNA levels of MMP-2 (gelatinase A), MMP-9 (gelatinase B), MMP-12 (macrophage elastase), and MMP-14 (membrane type 1-MMP) ($p<0.05$). In contrast, expression of the MMP inhibitors RECK, TIMP-3, and procollagen C-proteinase enhancer protein 2 were all significantly decreased ($p<0.001$). Gelatin zymography confirmed increased proMMP-2 and proMMP-9 levels in bronchoalveolar lavage fluid, in line with the changes in gene expression.

CONCLUSIONS: Chronic overexpression of TNF-α resulted in pronounced inflammation and altered expression of genes implicated in basement membrane remodelling. The imbalance of MMPs and their inhibitors in the TNF model may be relevant to the pathogenesis of emphysema-like changes in inflammatory lung disease.

1.61 Contrasting Toxic Potency of Size-Fractionated Particulate Matter Collected at Sites in Windsor, Ontario

E. Thomson[1], S. Karthikeyan[1], Y. Siddiqui[1], N. Vuong[1], J. Brook[2], and R. Vincent, PhD[1]

[1] Inhalation Toxicology Laboratory, Environmental Health Science and Research Bureau, Healthy Environments and Consumer Safety Branch, Health Canada, Ottawa, ON

[2] Air Quality Research Division, Atmospheric Science and Technology Branch, Environment Canada, Ottawa, ON

SUMMARY: Health effects of ambient particulate matter may be due to complex interactions between chemical constituents (organic, metals) and physical properties (size) that differ from location to location and over time. We show that particle size fractions collected at various sites and times in Windsor, Ontario display a range of cytotoxic potencies, reinforcing the need for investigation of source-specific toxicity.

BACKGROUND: Canadian citizens are exposed to broad concentrations of ambient particulate matter contributed by local industrial point sources, commercial and residential area sources, transportation sources, and long-range transport. Characterisation of particle potency at specific locations is important to identify priority sources for regulatory action. To address the need for source-specific toxicity data, we evaluated the cytotoxic potencies of airborne particles collected at sites with contrasting emission sources within Windsor predominantly influenced by the Detroit urban area, steel mills, or local transportation (including diesel heavy-duty engines).

METHOD: Simultaneous $PM_{0\text{-}1}$, $PM_{1\text{-}2.5}$, and $PM_{2.5\text{-}10}$ size fractions were collected at selected sites over several weeks and recovered from filters by aqueous extraction and sonication followed by vacuum-evaporation. The cytotoxic potency of particulate matter samples was determined in human lung epithelial cells (A549) using bioassays for energy metabolism, cell proliferation, and membrane integrity. Potency (β) was determined from Fold-effect = $(Dose+1)^{\beta}$. Expression of genes representing inflammation, oxidative stress, heat shock, and xenobiotic metabolism pathways were studied by RT-PCR in cells exposed to a subset of samples with contrasting potencies.

RESULTS: Particle potency was impacted by location, day of sampling, and size range. The average cytotoxicity ranking was $PM_{1\text{-}2.5} > PM_{2.5\text{-}10} > PM_{0\text{-}1}$. Transcriptional activity of biological pathways revealed site- and size-specific differences in potency, with pronounced differences in the activation of inflammatory genes (TNF-a, IL-6, IL-8; $p<0.05$). Risk of toxicity expressed as the product of ambient concentration and particle potency revealed that days with relatively low levels of airborne particulate matter but with high potency still exhibited relatively high toxicity.

CONCLUSIONS: The data show that the relative potency of particles collected within a small geographical area such as Windsor can differ widely in cytotoxic potency, in relation to prevailing wind patterns and source contributions. The data underline the need for continued investigation of source-specific toxicity to inform regulatory efforts.

1.62 Perturbation of Biological Pathways in the Lungs by Mixtures of Ozone and Particulate Matter: Evidence of Pollutant Interactions

E. Thomson[1], R. Vincent[1], and P. Kumarathasan[2]

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

[2] Proteomics Laboratory, Environmental Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON

SUMMARY: A significant challenge in environmental health research is to understand the relationship between the composition of pollutant mixtures and their health hazard. This study shows that biological effects of inhaled pollutant mixtures may differ from the sum of effects of the individual constituents.

BACKGROUND: Air pollution is a complex mixture of gaseous and particulate constituents associated with cardiopulmonary morbidity and mortality. Despite exposures invariably occurring as mixtures, pollutants are generally studied and regulated as individual agents. As a consequence, we lack insight into the significance of multi-pollutant interactions on health. In the present study we examined effects of co-exposure to two criteria pollutants, particulate matter and ozone, on activation of biological pathways in the lungs.

METHOD: A factorial design was used to evaluate the effect of exposure to urban particulate matter (0, 5, 50 mg/m^3 EHC-93), ozone (0, 0.4, 0.8 ppm), or combinations of particles and ozone. Fisher-344 rats were exposed by inhalation for 4 h and euthanized immediately or 24 h post-exposure. Expression of genes involved in a number of relevant biological pathways (inflammation, oxidative stress, metal-response, xenobiotic metabolism, chemotactic factors, adhesion factors, vasoconstriction, vasodilation) was assessed by RT-PCR in cells recovered by bronchoalveolar lavage and in lung tissue homogenates.

RESULTS: Compared with effects of individual pollutants, effects of co-exposure in bronchoalveolar lavage cells were either additive (metallothionein-II, macrophage inflammatory protein-2, endothelin-1, heme oxygenase-1, intercellular adhesion molecule-1) or antagonistic (interleukin-1ß, tumour necrosis factor-α, cyclooxygenase-2, monocyte chemoattractant protein-1, inducible nitric oxide synthase) (*Particle* x *Ozone* interaction, $p<0.05$). Comparison of responses in cells recovered by bronchoalveolar lavage and lung parenchyma revealed distinct responses to the pollutants in these two lung compartments.

CONCLUSIONS: The gene expression data confirm that effects of individual contaminants are not necessarily predictive of effects of co-exposure, extending our previous observations for lung injury and cardiovascular impacts. It is likely that health effects attributed to specific pollutants are similarly altered in mixtures.

1.63 National Survey of Disinfection By-Products and Selected Emerging Contaminants in Canadian Drinking Water: Emerging Contaminants

A.-M. Tugulea[1], C. Kubwabo[1], B. Koudjonou[2], M. Giddings[2], F. Lemieux[2], and M. Servos[3]

[1] Exposure and Biomonitoring Division (EBD), Environmental Health Science and Research Bureau, Safe Environments Program, HECSB, Health Canada, Ottawa, ON
[2] Water, Air and Climate Change Bureau (WACCB), Safe Environments Program, Healthy HECSB, Health Canada, Ottawa, ON
[3] Biology Department, University of Waterloo, Waterloo, ON

SUMMARY: This CMP funded survey investigates concentrations of selected emerging contaminants (including pharmaceuticals, bisphenol A and perfluoroalkylated compounds) in Canadian drinking water. The poster presents data from 34 sites in 6 Provinces. Determinations were done in Health Canada and University of Waterloo laboratories.

OBJECTIVES/BACKGROUND/ISSUES: Emerging contaminants in drinking water are trace compounds whose potential risks have only recently been identified. They migrate into drinking water sources and not all current water treatment processes effectively remove them. Some substances in this category are known or suspected carcinogens and endocrine/reproductive disruptors. Limited data have shown that many of these compounds can be present in Canadian drinking water. This survey investigates the occurrence of selected emerging contaminants: pharmaceutical products, bisphenol A (BPA), perfluoroalkylated compounds (PFOS, PFOA) in Canadian drinking water.

DESIGN/METHOD/DESCRIPTION: This study is the result of the collaboration between research (EBD) and risk assessment (WACCB), with specific contributions from academia. Sixty water distribution systems across Canada were selected, in collaboration with the Federal-Provincial-Territorial Committee on Drinking Water. Selection was based on water source (surface water, groundwater) and factors such as the treatment process and the size of the water plant. During the study, each facility is sampled twice (winter and summer of the same year). Specific methods are used for sample collection and preservation in order to assure high quality of data.

OUTPUTS/RESULTS: This poster presents the first set of results for pharmaceutical products, BPA, perfluoroalkylated compounds from 34 water distribution systems in 6 Provinces. Concentration levels are presented in conjunction to the characteristics of the water system relevant for risk assessment. Target analytes are present at many locations in low concentrations that are not expected to affect human health.

IMPACT/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: 30 additional locations will be sampled in 2010. Data from this survey will be used for Health Canada's risk assessment/management activities under CEPA. The results will also provide the Water, Air and Climate Change Bureau with new and updated exposure data to be used in the development and revision of Guidelines for Canadian Drinking Water Quality.

1.64 National Survey of Disinfection By-Products and Selected Emerging Contaminants in Canadian Drinking Water: Disinfection By-Products

A.-M. Tugulea[1], R. Aranda-Rodriguez[1], C. Kubwabo[1], D. Bérubé[1], B. Koudjonou[2], M. Giddings[2], and F. Lemieux[2]

[1] Exposure and Biomonitoring Division (EBD), Environmental Health Science and Research Bureau, Safe Environments Program, HECSB, Health Canada, Ottawa, ON
[2] Water, Air and Climate Change Bureau (WACCB), Safe Environments Program, HECSB, Health Canada, Ottawa, ON

SUMMARY: This CMP funded survey investigates levels of contaminants including disinfection by-products (DBPs) in Canadian drinking water. The poster presents data on DBP levels from 34 sites in 6 Provinces. Levels of iodinated DBP in Canadian drinking water are presented for the first time.

OBJECTIVES/BACKGROUND/ISSUES: Reliable water quality data is essential for assessing and managing potential water-related health risks. The identification of emerging disinfection by-products challenges the basis of our current mitigating strategies, designed to reduce the amounts of well-known DBPs. This National Survey will help fill the gap of Canadian data on some of the emerging DBPs: iodinated DBPs, nitrosodymethylamine (NDMA) and other nitrosamines, Mutagen X (MX), recently detected in drinking water.

DESIGN/METHOD/DESCRIPTION: Over sixty water distribution systems across Canada were selected based on water source characteristics and factors impacting the management of DBPs, such as the treatment process used (chlorination, chloramination, etc.) and the size of the water plant. Five points (source water, finished water and three points along the distribution system) are sampled for each water treatment system twice in the same year (winter/summer).

OUTPUTS/RESULTS: More than one hundred water quality parameters are determined for each location. Concentration levels of NDMA and MX are presented in conjunction with relevant water characteristics in order to facilitate the development of risk mitigation strategies. Iodinated DBPs were found at 16 out of 34 locations tested. This underlines the need for more research on their potential health impacts. Iodinated DBP data are the first generated in Canada and the most extensive data available from a survey outside the USA.

IMPACT/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The iodinated DBP data add to a very small existing body of evidence about human exposure to this class of compounds through drinking water and contribute to the development of new research in the field. Data generated from this survey will be used for Health Canada's risk assessment/management activities under CEPAand will provide WACCB (Health Canada) with new and updated exposure data the development and revision of Guidelines for Canadian Drinking Water Quality.

1.65 Survey of Perchlorate in Dairy Milk Available in Ottawa Markets in 2006

Z. Wang[1], D. Forsyth[1], B. Lau[1], and V. Casey[1]

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

SUMMARY: In this study, 138 dairy milk samples were analyzed by stable isotope dilution ion chromatography tandem mass spectrometry (ID-IC-MS/MS) to determine the concentrations of perchlorate in dairy milk available from retail outlets in Ottawa, Canada.

OBJECTIVE: The objective of the study was to determine the baseline levels of perhlorate in major brands of dairy milk samples collected from retail outlets in Ottawa.

DESIGN/METHOD/DESCRIPTION: The determination of perchlorate in milk is of particular importance due to its potential health hazard impact on infants and children. For this study, a sampling plan was followed during sample collection. Factors considered are the brand, the percentage of fat in the milk, the type of processing of the milk, the lactose levels, the size of the manufacture, and whether the milk is organic or non-organic. Milk samples were collected from five different brands from retail outlets in Ottawa. The four types of milk processes were Reduced Lactose, Regular, Filtered, and Organic. The three levels of fat percentages were whole milk (3.25%), 2% and skim. Twenty-three diary milk samples were purchased each week from the selected stores for 6 weeks. Sample analyses were achieved by ID-IC-MS/MS after extracted with acetonitril and 1% acetic acid.

OUTPUTS/RESULTS: The perchlorate levels of milk ranged from 2.37 to 7.62 µg/L (median 6.36 µg/L) and were similar to levels reported by the United States Food and Drug Administration in their total diet study. A statistically significant difference was observed between the regular milk and the organic milk. No significant difference was observed between regular milk and filtered milk; and between regular milk and Lactose reduced milk.

IMPACTS/OUTCOMES/CONCLUSION/IMPLICATION: This project provided important information of perchlorate levels in diary milk, and the results were used, combined with perchlorate data from other food analysis studies, to estimate the dietary exposure of perchlorate through food.

1.66 Development of Modulation Transfer Function (MTF) Analysis Algorithm to Support Regulatory Assessments of Digital Imaging Equipment

G. Wardlaw[1], N. Martel[1], and K. Sears[1]

[1] Medical X-Ray and Mammography, Consumer and Clinical Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

SUMMARY: Imaging technology is rapidly changing. Consequently, Health Canada (HC) physicists must ensure that emerging products are safe and effective. This work outlines one component of current analysis methods under development to evaluate new medical digital imaging systems and support future amendments to applicable regulations and HC Safety Codes.

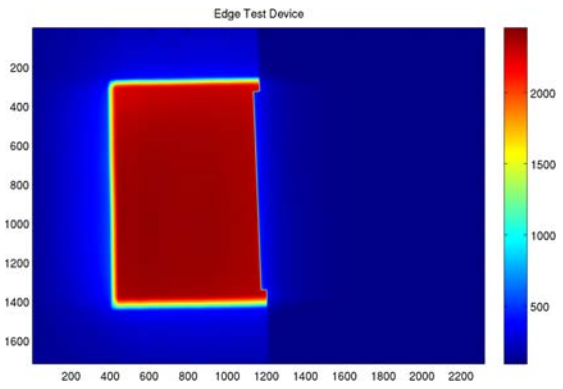
OBJECTIVE: Develop an automated algorithm to evaluate limiting spatial resolution (smallest visible structure) of digital imaging systems.

METHOD: X-ray images were obtained using a 72kVp x-ray beam directed toward a Tungsten edge device (**Figure 1**). Images were captured on an AGFA CR (Computerised Radiography) MD4.0 phosphor plate directly beneath the edge device and subsequently read-out with an AGFA 25.0 CR system. Digital images were then transferred to a workstation and analysed using customised algorithms (Matlab).

RESULTS: Analysis of pixel values along an edge device provides excellent characterisation of the system sensitivity to x-rays of varying energies and intensities (dose). **Figure 2** shows the over-sampled Edge Spread Function (ESF) obtained for this system within a 4mm wide edge-centred column. Numerical differentiation of this profile yields an over-sampled Line Spread Function (LSF, **Figure 3**), which can then be used to find the MTF (**Figure 4)** via Fast Fourier Transform.

The MTF in this case indicates that at a transfer factor of 4.64% the limiting spatial resolution is approximately 2.8 mm^{-1} (3.78% - 3.0 mm^{-1}). This range correlates well with similar CR devices reported in literature and justifies further work on large device groups. Continued development of noise spectrum and energy throughput indices is also underway.

CONCLUSIONS: Higher limiting resolution implies that systems are capable of better detecting smaller physiological anomalies and improve diagnosis. Hence, the MTF provides a potential benchmark for both HC and medical professionals to assess digital imaging system quality. Moreover, it assists HC develop effective regulation to ensure optimum care of Canadians.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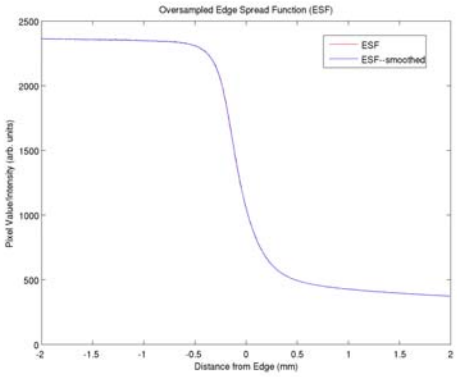
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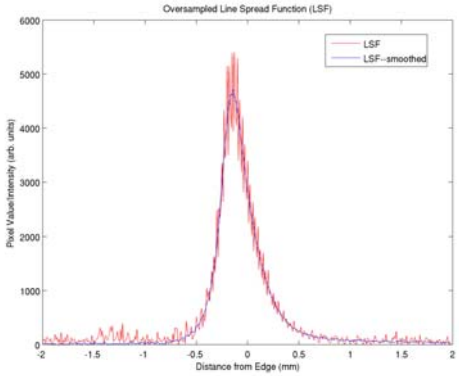
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LSF--smoothed
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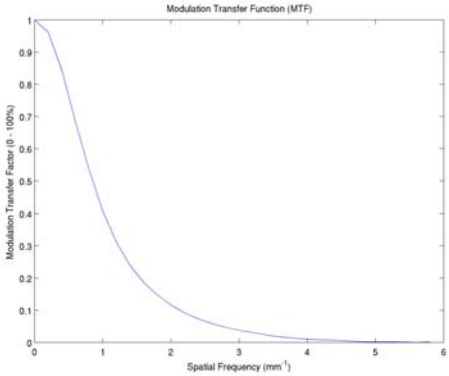
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Modulation Transfer Factor (0 - 100%)
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0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0 1 2 3 4 5 6

1.67 The Mineralogical Composition of House Dust

M. Woldemichael, MSc Candidate[1], A. Lalonde, PhD[1], and P.E. Rasmussen, PhD[1,2]

[1] Earth Sciences Dept, University of Ottawa, Ottawa, ON
[2] Exposures and Biomonitoring Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Despite the increasing demand for information on the quality of our indoor environments, little is known about the physical and chemical composition of ordinary household dust. This study represents the first systematic investigation of the mineralogical composition of indoor dust in Canada.

OBJECTIVES: To identify the composition and abundance of minerals in house dust, and to compare and contrast the mineralogy of house dust from six geographically separate localities in Ontario: two located on the Canadian Shield (Thunder Bay and Sudbury), and four located on Paleozoic sedimentary bedrock (Barrie, Burlington, Cambridge, and Hamilton).

METHODS: The composition of the mineralogical fraction of dust was determined using polarizing light microscopy, X-ray diffraction and scanning electron microscopy. Fifty-four samples of the coarse fraction (80 - 300 μm) of household vacuum dust were subjected to flotation (using water) to separate the organic components (e.g., insect fragments, dander), natural and synthetic materials (e.g., fibers, plastics) from the mineral residue.

RESULTS: The mineral fraction of dust from all six cities was dominated by quartz (17-24%), feldspar (17-20%), calcite (3-11%), and amphibole (4-5%), with various rock fragments and aggregates contributing 15-28%. There was some evidence of the influence of local geology: for example, more sulphide minerals were noted in the Canadian Shield cities compared to the other cities.

Dust samples from the six cities shared an interesting feature in common. In all localities, the quartz particles were characterized by strain features and fluid inclusions, which indicate a metamorphic-igneous bedrock source. All six cities use glacial sand derived from the Canadian Shield for ice control in the winter. Thus, tracking in sand is the most plausible mechanism by which quartz was introduced into these homes since sampling was done, in all cases, in the winter season.

IMPACTS/CONCLUSIONS: Glacial deposits dominate the mineral composition of indoor dust in Ontario cities, caused by residents and their pets tracking sand into the house. This indicates that glacial sand distributed on winter roads ends up as a major constituent of house dust.

1.68 Trypsin Inhibitor Activity in Commercial Soy Beverages and Soy-Based Infant Formulas

C.W. Xiao, PhD[1,2], and C.M. Wood, MSc[1]

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

SUMMARY: In this study, we have investigated soybean trypsin inhibitor (SBTI) activities remaining in a variety of commercial soy beverages and soy-based infant formulas. Results showed that SBTI activities are very high in most of the soy beverages and quite low in all the measured infant formulas.

OBJECTIVES: Consumption of soy products containing high levels of active soybean trypsin inhibitors (SBTI) results in decreased protein digestibility and nutritive value, and causes pancreatic hypertrophy, hyperplasia and even pancreatic carcinogenesis in certain species. This study aimed to investigate the residual activity of SBTI in commercial soy beverages and soy-based infant formulas.

METHODS: Soy beverages (8 brands), liquid (4 brands) and powder (6 brands) soy infant formulas were purchased at a local store (5 samples from the same lot/brand). A raw soybean was used as a control. Protein concentrations were determined using BioRad DC protein assay. SBTI activity was measured as the ability to inhibit degradation of casein by trypsin using a SensoLyte Red Protease Assay.

RESULTS: The average remaining SBTI activities (expressed as percentage of the raw bean) in soy beverages were 44.2% for Eden, 71.3% for Natura, 49.3% for Organics, 62.3% for Silk, 7.5% for SoGood, 12.0% for SoNice, 55.7% for SoyDream, and 27.7% for VitaSoy. The residual activities of SBTI in liquid soy infant formulas were 3.3% for Alsoy, 5.8% for Isomil Concentrate, 6.7% for Isomil Similac, and 4.7% for PC Soy; and in powder soy infant formulas were 0.7% for Alsoy, 1.8% for Enfamil, 1.6% for PC Soy, 0.5% for Isomil Advanced, 1.0% for Isomil 2 Soy, 1.1% for Organics Soy.

CONCLUSIONS/IMPLICATIONS: Compared with soy beverages, the residual SBTI activities in both liquid and powder soy infant formulas were much lower. Among the soy beverages measured, the residual SBTI activities in 6 out of 8 were much higher than 20% of the raw bean. Long-term consumption of soy beverages containing high levels of active SBTI may be harmful to human health especially young children. Set-up of a safe upper level of residual SBTI activity in soy products might be necessary in the future.

1.69 Effects of *In Utero* and/or Postnatal Exposure to Mixtures of Blood Contaminants on the Adulthood Glucocorticoid Stress Response in Male Rat

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

[1] Research and Radiation Directorate, HECSB, Health Canada, Ottawa, ON

SUMMARY: This study demonstrates a link between perinatal exposure to mixtures of Inuit blood contaminants and abnormal adulthood glucocorticoid stress response in rats. Effects were mostly attributed to the postnatal period of exposure, and less to in utero exposure. This may contribute to an understanding of stress-related chronic diseases.

OBJECTIVES: Perinatal events are suspected to reprogram glucocorticoid [corticosterone (CS) in rat] secretion for the entire lifespan, and thus we tested the hypothesis of a link between perinatal exposure to environmental contaminants and abnormal adulthood corticosterone stress response (CSR) in rats.

METHOD: The experiment included 9 treatment groups. From gestation-day 0 and until postnatal day 20, dams received corn oil (control) or a chemical mixture at 0.5 or 1.0 mg/kg/day (0.5M, and M). At birth, some control (C) and M litters were crossfostered to create 4 groups of pups with the following *in utero*/postnatal exposure: C/C, M/C, C/M, M/M. Other dams received a dose of 1.7 ng/kg/day of a mixture of aryl hydrocarbon receptor (AhR) agonists without or with 0.5M. A CSR was induced in male offspring at PND85, and the following CS drop occurring over 30 min (T30) was monitored.

RESULTS: Concentrations of CS returned to normal at T30 in group C, 0.5M, M, C/C and M/C, but it remained elevated in group AhR, AhR+0.5M, C/M, and M/M (250, 370, 310 and 250 ng/ml respectively to 189ng/ml in C). Interestingly, M had no effect on its own but it prevented the CS drop in adulthood in M/M group, in which the perinatal exposure is associated with postnatal stress created by the crossfostering procedure. This suggests that rats can tolerate exposure to M with no consequences unless they are subjected to early postnatal stress. In line with CS data, abundances of hepatic glucocorticoid receptor (GR) mRNA were significantly reduced 30% and 32% respectively by C/M and MM treatments.

CONCLUSIONS/IMPACTS: The results demonstrate that CSR and hepatic GR expression in adulthood are modified by the postnatal period of exposure to environmental contaminants and less by *in utero* exposure, and that postnatal stress might accentuate the adverse effects. These results are important in our understanding of perinatal influence of contaminant exposure on stress-induced chronic diseases.

1.70 New Methodologies to Improve the Understanding of the Dissolution and Distribution of Particulate Matter Components in Biological Media

D. Bérubé, PhD[1], T. Yapici, PhD[1], and X. Liao, PhD[1]

[1] Environmental Health Centre, HECSB, Health Canada, Ottawa, ON

SUMMARY: Airborne particulate matter and nanomaterials are examples of solid materials of concern to health risk assessment. New methodologies are developed and used to study their interactions with biological media. In addition to improve the understanding of exposure and health effects, these works contribute to develop the monitoring of these materials.

OBJECTIVES/BACKGROUND/ISSUE(S): Epidemiological and toxicological studies have demonstrated the association between health effects and metals in airborne particulate matter (PM). When also considering the emergence of nanomaterials in the environment, it becomes critical to learn about the behaviour and fate of PM components in order to better define the exposure to these materials. This presentation describes the study of factors influencing the dissolution and distribution of PM metals in biological media by newly developed methods in our laboratory.

DESIGN/METHOD/DESCRIPTION: A newly developed “on-line method” directly injects in an Inductively Coupled Plasma Mass Spectrometer (ICPMS) a small amount of a mixture of PM and simulated biological fluid as a filtrate. A second method uses a Diffusive Gradients in Thin-films (DGT) technique, with Chelex resin as complexing agent to determine diffused metal species.

OUTPUTS/RESULTS: The dissolution data generated by the “on-line method” show many advantages over the previously established sequential batch method to study metals (e.g., Ni, Pb) in smelter emissions and in ambient air PM. (1) The continuous data acquisition produces countless data points useful to understand the kinetic aspects of the dissolutions, with a multi-element perspective. (2) Dissociation rate constants ‘k_d’ can be experimentally determined, providing toxicokinetic information and allowing differentiation of dissociating species. (3) Real time monitoring of experimental changes is possible (e.g., addition of complexing agents). (4) The setup is easy to operate; the minimization of manipulations decreases data uncertainty. (5) This is a time saving methodology. Data from DGT and Chelex trapping experiments provide supplementary information on the distribution potential of dissolving metal species and on ligand competition in biological media.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The application and comparison of these methods enhance our knowledge on the behaviour of complex mixtures such as air PM when these come in contact with biological media. These works contribute to the development of exposure assessment methods.

1.71 Determination of Chlorophenols and Tetrabromobisphenol A in Water Samples Using Capillary Electrophoresis-Tandem Mass Spectrom

H. Zhang[1], J. Zhu[1], and Y.-L. Feng[1]

[1] Exposure and Biomonitoring Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: A sensitive method using capillary electrophoresis-electrospray tandem mass spectrometry (CE-ESI-MS-MS) combined to pressure-assisted electrokinetic injection (PAEKI) has been developed for the determination of three chlorophenols [2,4-dichlorophenol (2,4-DCP), 2,4,6-trichlorophenol (2,4,6-TCP), 2,3,4,6-tetrachlorophenol (2,3,4,6-TeCP)] and tetrabromobisphenol A (TBBPA) in water samples.

OBJECTIVES/BACKGROUND/ISSUE: Endocrine-disrupting phenolic environmental contaminants have attracted increasing public concerns. TBBPA, for example, is a flame retardant used in many polymer products that have been found in air, soil and sediment. Although gas chromatography (GC) analysis is commonly used to measure such phenolic compounds, the necessary derivatization procedure in the method is tedious and time-consuming. Capillary zone electrophoresis (CZE) is also a fast and low cost separation technique applicable to similar analyses. However, the small sample injection volume (nL) limits its utility for the analysis of trace analytes. By contrast, pressure-assisted electrokinetic injection (PAEKI) is a newly developed enrichment technique with powerful enhancement capability [1]. In this study, we sought to couple this technique to a capillary electrophoresis -tandem mass spectrometry (CE/MS/MS) system in order to facilitate the measurement of phenolic compounds in water and soil samples.

DESIGN/METHOD/DESCRIPTION: A capillary column was filled with 80 mM of ammonium carbonate solution (pH 9.0). PAEKI was conducted by applying a negative voltage (-7 kV) and a 50 mbar of positive hydrodynamic pressure on the sample vial at the same time. After the PAEKI process was completed, 950 mbar of hydrodynamic pressure was used to flush the injected analytes for downstream monitoring by mass spectrometry.

OUTPUTS/RESULTS: Under optimized PAEKI conditions, the four analytes, 2, 4-DCP, 2, 4, 6-TCP, 2, 3, 4, 6-TeCP and TBBPA were pre-concentrated by factors of 2554, 3046, 3557 and 6013 times, respectively, compared to conventional hydrodynamic injection. The detection limits of the four analytes were 14.2 ng/L for 2, 4-DCP, 41.4 ng/L for 2, 4, 6-TCP, 75.8 ng/L for 2, 3, 4, 6-TeCP and 6.7 ng/L for TBBPA. Relative standard deviation (RSD) was less than 10% (n=6) and thus showed good reproducibility for the method.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The method is simple and sensitive for measuring phenolic compounds in water samples and advantageous because, unlike gas chromatography methods, the derivatization procedure is not needed. Our study suggests broad applicability of PAEKI for the quantitative assessment of contaminants in water-based samples.

1.72 Monte Carlo Simulation of a Phoswatch Detector Using Geant 4 for Xenon Isotope Beta-Gamme Coincidence Spectrum Profile and Detection Efficiency Calculations

W. Zhang[1], P. Mekarski[1], R.K. Ungar[1], M. Bean[1], and E. Korpach[1]

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

SUMMARY: A Monte Carlo (MC) simulation tool has been developed using the Geant4 Toolkit [1] to simulate a low background radionuclide detection system. The tool was designed for Comprehensive Nuclear-Test-Ban-Treaty (CTBT) relevant noble gas monitoring. It can be used to for beta-gamma coincidence detection efficiency and 3D spectrum profile calculations.

OBJECTIVES/BACKGROUND/ISSUE: In preparation for entry into force of the CTBT, a sophisticated beta-gamma coincidence detector (PhosWatch) has been developed for measuring small quantities of radioactive xenon in the atmosphere that are released from underground nuclear tests. However, pure calibration standards are not yet available to do coincidence efficiency calibration for all the individual radioisotope as at least one of the other isotopes typically a significant contaminant In addition to the difficulty in isolating the daily collected 135Xe, 133mXe, 133Xe and 131mXe and determining their activity and in dealing with 222Rn interference, it is a challenge to determine the efficiency of the detector for those isotopes.

The objectives in this study were to (i) develop a simulation tool using the Geant4 Toolkit1 to produce models of each individual xenon isotope that could be used for spectral deconvolution analysis, (ii) calculate coincidence detection efficiency at the energy region of interest for each isotope individually to get a set of calibration data for their activity calculation with low uncertainty, (iii) establish interference corrections of various spectral components from radon and xenon isotopes.

DESIGN/METHOD/DESCRIPTION: The experiment consists of modeling the PhosWatch detector geometry in Geant4. The modeling is performed using the Geant4 physics processes and scintillation process to count the number of photons captured by the PMT from each scintillator individually. The validation of simulation models with experiment is included.

OUTPUTS/RESULTS: The simulated spectra could be used to calculate system coincidence detection efficiency for each xenon isotope, and the corrections for the interference of the various spectral components from radon and xenon isotopes. The calculated coincidence efficiencies have been verified with experimental results.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The MC simulation tool developed in this work can be used to model a realistic sample spectrum in two-dimensional beta-gamma coincidence histograms and three-dimensional colour surface plots with a known amount of xenon isotopic abundances, which can be used as reference spectra to test beta-gamma coincidence spectral deconvolution analysis software. The tool has been approved for use by the scientists from PNNL and XIA PhosWatch development group. The

study has enabled significant better accuracy for CTBT noble gas monitoring and led to improved knowledge of the detection system operations.

1.73 Development of a Screening Assessment Process for Micro-Organisms on the Domestic Substances List With Stakeholder Involvement

M. Breton, PhD[1], K. Yambao[1], and D. Ashby[1]

[1] New Substances Assessment and Control Bureau, Product Safety Program, HECSB, Health Canada, Ottawa, ON

SUMMARY: The New Substances Program has initiated the Screening Assessment of micro-organisms on the Domestic Substances List. To make the process as scientifically-sound and transparent as possible, a Technical Expert Group, composed of members from various stakeholder groups (government, academia, industry and NGOS) has been asked to guide in designing the process.

OBJECTIVE/BACKGROUND/ISSUE: Under 74(b) of the Canadian Environmental Protection Act, 1999, the Minister of the Environment and the Minister of Health are required to conduct Screening Assessments (SA) of the micro-organisms listed on the Domestic Substances List (DSL) in order to determine whether they are "toxic" or capable of becoming "toxic" as defined under the Act. The New Substances Program (NSP) will conduct these SA based on hazard (the micro-organism's ability to persist and survive in the environment, its invasiveness and its potential for pathogenicity/toxicity to humans and other terrestrial/aquatic organisms) and exposure (the potential for Canadians and the Canadian environment to be exposed to the micro-organism).

DESIGN/METHODS/DESCRIPTION: To ensure that the SA of DSL micro-organisms are scientifically sound and the decision making process is transparent, a Technical Expert Group (TEG) drawn from different professional areas to ensure a complete coverage of the expertise relevant to the SA was established. 10 experts were selected following an open call for nominations, from NGOs, academia, the biotechnology industry, and the federal government. The NSP also collaborates with researchers through the CRSB research strategy to support a complete SA by filling gaps in available information.

OUTPUTS/RESULTS: Under TEG guidance, DSL micro-organisms were prioritized, an SA framework was developed describing a step-wise risk assessment process, and a pilot screening assessment was prepared to test the SA framework. TEG endorsed the scientific soundness of the pilot SA of *Pseudomonas aeruginosa* based on information and data derived from scientific literature and original research conducted by CRSB-funded researchers.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Next year, the NSP will continue to fill data gaps, particularly in relation to use-patterns and exposure potential. The *P. aeruginosa* SA will undergo external scientific review, and NSP will continue to seek the valuable guidance of the TEG to ensure the scientific endorsement of the process and resulting conclusions.

1.74 Is a Separate Pre-market Review Process Justified for Toilet Bowl Disinfectant Cleaners?

J. Couture, BSc[1], L. Latifovic[2], D. Massé, BSc[2], S.C. Wright, BSc[3], and A.G. Craan, PhD[3]

[1] Faculty of Health Sciences, University of Ottawa, Ottawa, ON
[2] Faculty of Science, University of Ottawa, Ottawa, ON
[3] Bureau of Gastroenterology, Infection and Viral Diseases, HPFB, Health Canada, Ottawa, ON

SUMMARY: Scientific and regulatory literature shows that while toilet bowl disinfection claims concur with the *Food and Drugs Act* definition of disinfectant drugs, a separate pre-market review process for toilet bowl disinfectant cleaners is unwarranted. Revisions to current Health Canada guidelines for approving products with toilet bowl disinfection claims are required.

OBJECTIVES: Determine: 1) the differences between the formulation, efficacy and hygienic purpose of toilet bowl disinfectant cleaners (TBDs) and other disinfectants, particularly bathroom disinfectants (BDs); 2) the value of approving toilet bowl disinfection claims for any disinfectant; and 3) whether a separate pre-market review process is justified for TBDs.

DESIGN/METHOD: The scientific and regulatory literature was reviewed, including PubMed, Medline, federal legislation, Health Canada's (HC) Drug Product Database, guidance documents and standards pertaining to disinfectant products.

OUTPUTS/RESULTS: Of the 972 disinfectants approved for sale in Canada, only 17 TBDs and 15 BDs were identified. The active medicinal ingredients (AIs) in TBDs and BDs vary from surface-compatible quaternary ammonium chlorides, 0.2-10 %, to corrosive acidic compounds, 10% HCl and 2.5% NaClO. These AIs are common to 74.9% of all disinfectants on the market. Sharing similar formulations, both TBDs and BDs differ from toilet bowl cleaners, which are regulated under the *Hazardous Products Act,* as their antimicrobial claims, if any, do not exceed sanitization level. The microbicidal efficacy requirements are equivalent for registering all disinfectant types.

IMPACTS/CONCLUSIONS: Toilet bowls pose a low risk of transfer of pathogenic microorganisms to humans due to minimal surface-to-hand contact. A separate pre-market review process for TBDs exaggerates the hygienic benefits achieved from toilet bowl disinfection. While claims for toilet bowl disinfection are supported, TBDs should be assessed in the same manner as any other hard-surface disinfectant. As a result, the Category IV Monograph for TBDs should be removed from the *Guidance Document: Disinfectant Drugs*, and clauses regarding AIs specific to TBDs should be incorporated into the existing Category IV Monograph for hard-surface disinfectants. This proposal would help: 1) streamline pre-market approval of disinfectants; 2) simplify HC guidelines and product labelling; and 3) provide unambiguous "directions for use" to consumers.

1.75 A Statistical Profile on the Health of First Nations in Canada: Determinants of Health, 1999 to 2003

E. De Rubeis[1], C. Lei[1], J. Stokes[1], and J. Pennock[1]

[1] Health Information, Analysis and Research Division, FNIHB, Health Canada, Ottawa, ON

SUMMARY: In-line with the Aboriginal perspective of wellness, a national snapshot of social determinants of health of First Nations people on-reserve in Canada is presented, and gaps are highlighted. Findings from this report can be used to identify areas for action or future research in terms of social determinants of health.

BACKGROUND: The purpose of this presentation is two-fold: to introduce social determinants of health (SDOH) in the context of Aboriginal wellness; and to highlight observed gaps between First Nations and Canadian populations. The imbalanced distribution of health across populations is well documented, and is often associated with SDOH. This first report, in a four-report series, presents a national description of SDOH among First Nations people on-reserve in Canada.

METHODS: Analysis of several survey and administrative data sources was conducted, including Census of Population, Aboriginal Peoples Survey, and the Canadian Community Health Survey. The indicators selected to assess SDOH related to culture, personal health practices, health services, physical environment and socioeconomic status. Prevalence of SDOH indicators was also compared between First Nations and Canadian populations.

RESULTS: SDOH that were higher among First Nations on-reserve population compared to the Canadian population included prevalence of tobacco use, obesity, overcrowded housing, and inadequate water and sanitation services, with the largest gaps observed for educational attainment and employment rates. Despite these findings, more First Nations people are graduating from post-secondary education and participating in the labour force.

CONCLUSIONS: It is well known that the health status of the population as a whole is influenced by disparities, such as gaps in socioeconomic status between groups within a given population. This report used several data sources to characterize the current health determinants of First Nations populations living on-reserve in Canada, and identified gaps in SDOH between First Nations and Canadian populations. These findings will aid in the understanding of gaps in health status between populations. Furthermore, findings can be compared with available local health status and trend information to help develop community health plans and to prioritize prevention programs, interventions and services.

1.76 Monitoring the Health Status of First Nations in Canada: Where Do We Stand?

E. De Rubeis[1], and J. Pennock[1]

[1] Health Information, Analysis and Research Division, FNIHB, Health Canada, Ottawa, ON

SUMMARY: To monitor gaps in health, the World Health Organization (WHO) recommended development of health surveillance systems. Consistency of the WHO-framework with Aboriginal concepts of wellness, and ability to monitor the health of First Nations were assessed. Findings suggest that the framework will require adjustment; furthermore, data for First Nations are insufficient for monitoring gaps.

BACKGROUND: The imbalanced distribution of health across populations is well documented, and is often associated with the social determinants of health (SDOH). To monitor such inequalities, the WHO Commission on SDOH recently recommended the development of national health equity surveillance systems that include a minimum set of indicators, and a broader set of indicators on the SDOH. The health gap experienced by Indigenous populations was also identified, underscoring the need for high quality data for these populations. The objective is two-fold: to describe the current ability to monitor health outcome indicators among First Nations populations at the national-level as identified in the WHO-proposed surveillance system; and to assess its consistency with the First Nations concept of wellness.

METHODS: The minimum health outcome indicators included in the WHO-proposed surveillance framework were assessed to determine consistency with the First Nations concept of wellness. The availability and quality of First Nations data for health indicators were examined.

RESULTS: Although data exist for mortality and morbidity indicators, available data do not meet WHO-stated standards including coverage, quality, and consistency. Health outcome indicators identified in the WHO-proposed surveillance framework are generally consistent with the First Nations concept of wellness. However, an assessment of additional SDOH indicators suggests greater consistency with this concept.

CONCLUSIONS: While a national health equity surveillance system provides a basis for monitoring health inequalities across populations in Canada, current data sources for Indigenous populations are insufficient in their ability to monitor health inequalities. The framework will require some adjustment to ensure the inclusion of culturally relevant indicators. Identified gaps in data will need to be addressed together with Indigenous populations through coordinated efforts at all levels.

1.77 Release of Pharmaceuticals in the Environment by Consumers: A Canadian Perspective

E. Gagnon, MSc[1]

[1] Environmental Impact Initiative, HPFB, Health Canada, Ottawa, ON

SUMMARY: The presence of pharmaceuticals in the environment can pose environmental and indirect human health impacts. Our estimates show that human excretion is the main factor by which consumers contribute to this problem. Current disposal programs, available to consumers prevent, to some extent, improper disposal practices.

OBJECTIVES/BACKGROUND/ISSUE(S): Assess the contribution of excretion and disposal practices to the release of pharmaceuticals to the environment. Assess the extent by which disposal programs can reduce the exposure of the environment to pharmaceuticals.

DESIGN/METHOD/DESCRIPTION: Assemble statistics to estimate the amount of pharmaceuticals used/excreted and unused/disposed of by consumers. Review the literature and consult representatives from the government, industry, and academia to gather information about Canadian disposal programs.

OUTPUTS/RESULTS: On average, 54% of all pharmaceuticals purchased by consumers may enter into the environment (landfills and sewage) via excretion and disposal practices through garbage and down the drain, where contribution by excretion is 56% and contribution by disposal practices is 44%. Current disposal programs reduce the release of pharmaceuticals into the environment by less than 14%, but could achieve a reduction rate of 52% if all unused pharmaceuticals were collected and disposed of through these programs. The importance of each contribution depends on the assumption made on the percentage of pharmaceuticals that remain unused by consumers (which is uncertain).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Although human excretion has been estimated to be the main factor contributing to the environmental loading of pharmaceuticals, improper disposal practices also contribute to this problem. In order to improve proper disposal of pharmaceuticals, it is important to increase public awareness and understanding of the risks associated with pharmaceutical products in the environment and the benefits of safe disposal methods. Nevertheless, efforts should focus on programs that aim at reducing the amount of pharmaceuticals wasted by consumers. The results of this research will be used as background materials for stakeholder consultations on the needs for appropriate best management practices for substances in products regulated under the *Food and Drugs Act*. In future research, it will be important to understand how community pharmacies, health care facilities and manufacturers manage their pharmaceutical wastes.

1.78 Developing 'Knowledge to Action' Plans and Strategies for their implementation at the Bureau of Environmental Health Science and Research (EHSRB)

M. Hannan[1], R. Alwis[1], and T. Dalton[1]

[1] Business Service Unit, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: Knowledge Translation (KT) is emerging as an important field to facilitate timely and effective utilization of knowledge being created. This presentation illustrates the plans and the portals being developed by the EHSRB for 'knowledge transfer' from the knowledge developers to the knowledge users.

OBJECTIVES: To describe the structure and the plans being developed by EHSRB to generate high quality research results and to facilitate their transfer to potential knowledge users for effective knowledge utilization.

DESIGN: EHSRB conducted a thorough review of the emerging field of KT and its significance, and quickly moved to design a KT model and an organizational structure to implement its 'Knowledge Transfer' plans which include i) establishing a research planning process/body to engage knowledge creators, knowledge users and managers in the development of user-aimed research activities, ii) developing a database of emerging knowledge from the bureau, iii) preparing systematic reviews on specific topics by synthesizing available knowledge, iv) peer reviewing the synthesized information, and disseminating it to knowledge users. Primary and secondary review processes are applied to select and support the best proposals and to evaluate the quality and relevance of the results to be forwarded to knowledge users.

RESULTS/PROGRESS: EHSRB has already established a fair and transparent project review system that checks for 'relevance', scientific merit, and potential for 'knowledge transfer'. Also, an Internal Review Body (IRB) has been established to evaluate yearly project progress reports in which the investigators are asked to provide information that could be considered for 'knowledge transfer' to an identified client. The formation of a planning process and/or Research Planning and Priorities Committee is under way. Tasks such as selecting user-aimed research projects, and strengthening communication /dialogues between knowledge creators and users through holding workshops/seminars, and bilateral/multilateral discussions have been planned for the fiscal year 2009-2010.

IMPACTS/CONCLUSIONS: Once fully implemented, these structured KT methods of engaging researchers and knowledge users in research planning and communication, and rigorous review processes will help ensure scientific excellence and the transfer of appropriate knowledge from EHSRB to its clients for timely applications.

1.79 Updated Guidance for Preparing a Submission for Food Health Claims

J. Johnston, PhD[1], C. Boudrault, MSc[1], M. Eskander, MD[1], E. Chao, PhD[1], and L. Dumais, RD[1]

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

SUMMARY: The Guidance Document for Preparing a Submission for Food Health Claims provides information on the Canadian requirements to substantiate a new health claim. A step-by-step procedure outlines the submission format, how to perform the literature search, and how to review and compile the evidence.

OBJECTIVES/BACKGROUND/ISSUE(S): The Guidance Document for Preparing a Submission for Food Health Claims (GD) updates an interim GD that was in use since 2002. The revised GD was developed to provide clearer guidelines for substantiating health claims on foods in a systematic, comprehensive and transparent manner.

DESIGN/METHOD/DESCRIPTION: The GD is based on 10 guiding principles: systematic approach, transparency, comprehensiveness, human evidence, high level of certainty, demonstration of causality, biological relevance of the claimed effect, feasibility of consuming the effective dose, health claim wording, and substantiation of one food-health relationship in a submission.

OUTPUTS/RESULTS: The GD first requires general information about the petitioner and the proposed health claim. Then, the petitioner is asked to characterize both the food and the health effect. In the core section of the document called “Evaluation of Claim Validity”, an easy-to-follow 13 steps procedure is presented. During these steps, the petitioner is asked to give information about the literature search strategy, the output obtain, and the inclusion/exclusion criteria used. In addition, the petitioner has to record the number of studies excluded and the reasons for exclusion. The studies chosen are then summarized in a table format (per study design and per health outcome) and their quality is evaluated. The petitioner is also required to assess causality (consistency, strength of association, dose-response), and to discuss the generalizability of the claim to the target population, the physiological meaningfulness of the effect and the feasibility of consuming the effective amount of food. The exercise ends with the petitioner making conclusions and filling a checklist to make sure that all required items are present in the submission.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This GD will help petitioners to apply the recognized scientific principles of systematic review to the substantiation of a new health claim for food.

1.80 A Statistical Profile on the Health of First Nations in Canada: Health Services Utilization in Western Canada, 2000

C. Lei[1], E. De Rubeis[1], J. Stokes[1] and J. Pennock[1]

[1] Health Information, Analysis and Research Division, Strategic Policy, Planning and Analysis Directorate, FNIHB, Health Canada, Ottawa, ON

SUMMARY: This poster describes selected findings from a report on health services utilization among the First Nations population in Western Canada for the year 2000. Comparisons are made to the general population in Western Canada. These results can be used to track health issues and inform program and policy development.

BACKGROUND: Health services utilization data provide an indication of the diseases or disorders that place the greatest demand on health care systems. Comparisons across populations can help to identify health inequalities and to determine where prevention efforts should be concentrated to prevent illness with the goal of reducing burden on the health care system.

METHODS: Health service utilization data (reported in terms of hospital separations) in the year 2000 for the First Nations on- and off-reserve population as identified in British Columbia, Alberta, Saskatchewan and Manitoba were compared to data for general Canadian population in the four Western provinces. Crude and age-standardized hospital separation rates were calculated for the First Nations population and compared to the general population in Western Canada.

RESULTS: The leading causes (as categorized by the International Classification of Diseases, Version 9 (ICD-9) codes) of hospital separations for First Nations were ‘Complications of Pregnancy, Childbirth and the Puerperium’, ‘Respiratory Diseases’ and ‘Injury and Poisoning’. Age-standardized hospital separation rates were higher among the First Nations population in comparison to the Western population for all causes with the exception of 'Perinatal Conditions' and 'Congenital Anomalies'. The age-standardized hospital separation rate for all injuries in the First Nations population was higher than the equivalent rate in the general population in Western Canada.

CONCLUSIONS: The results presented indicate higher rates of health care utilization by First Nations than the general population living in Western Canada. Furthermore, injury is among the conditions that place the greatest demand on the health care system. Though many factors affect hospital separation data, these can help to track health issues and inform program and policy development. Hospitalization data are unavailable for all provinces/territories. As a result, more efforts are needed to be put in place to improve data collection for First Nations populations.

1.81 Impact of Socioeconomic Status on Mental Health of Canadian Seniors'

T. Messele, MSc[1]

[1] Microsimulation Modelling and Data Analysis Division, SPB, Health Canada, Ottawa, ON

SUMMARY: It examined the relationship between self-reported mental health and socioeconomic status (marital status, employment, income, educational attainment) and demographics of Canadian aging population. It looked at the magnitude of mental illness and the relationship between mental illness and socioeconomic status (SES) of seniors in Canada.

OBJECTIVES: Examine the impact of socioeconomic status (SES) on mental health of Canadian aging population and the magnitude of mental illness in seniors.

DESIGN/METHOD: Socioeconomic and demographic data from the Canadian Community Health Survey (CCHS) 2005 associated with mental health of seniors were extracted. These included age, gender, living arrangements, marital status, educational attainment, main source of income and level of income. *Self-rated mental health* questionnaire was asked respondents to rate their mental health status on a scale of "1" to "5" ("excellent" to "poor") over the previous 12 months. We employ Logistic Regression to analyze the significance of socioeconomic factors affecting the mental health and physical health of the elderly.

OUTPUTS/RESULTS: Married/common-law seniors are 74% more likely to report better mental health than single or never married seniors. Seniors with a post secondary education were 13% more likely to be satisfied with their mental health status than seniors with high school diploma. Generally, higher-income elderly individuals were more likely than lower-income elderly individuals to report satisfaction with their mental health status. Similarly, seniors who depend on superannuation, annuities, investments or dividends were about twice more likely to be in good to excellent mental health than those who depend on employment income. The prevalence of mental illness increased with age.

IMPACTS/OUTCOMES/CONCLUSIONS: Canada's aging population is growing faster, reaching the age of risk with consequent increase in the overall incidence of mental illnesses. A shift in healthcare and research priorities may be required to cope with the unique concerns of the aged population. Improvements in SES of the elderly such as affordable housing, income supports, harm reduction, and health care reform may help to improving seniors' mental health. Access to mental health services for the most vulnerable and isolated seniors is going to become essential.

1.82 Forecasting the Demand for Physiotherapy Utilization by Canadian Seniors, 2007-2016

E. Tipenko, MSc[1], B. Belhadji, PhD[2], and K. Basu, PhD[1]

[1] MSDAD, Applied Research and Analysis Directorate, SPB, Health Canada, Ottawa, ON
[2] CCCD, Health Care Policy Directorate, SPB, Health Canada, Ottawa, ON

SUMMARY: The purpose of the study is to forecast the demand for physiotherapy services by Canadian seniors in order to accommodate the needs of a growing senior population.

OBJECTIVES: Growing senior population will require physiotherapy services that manage and prevent many physical problems caused by illness, falls, disease, injury, aging, and long periods of inactivity. The primary objective of this study was to design and implement a population-based planning model to estimate the physiotherapy service requirements for seniors in Canada.

DESIGN: Four cycles of the Canadian Community Health Survey (CCHS 2001, 2003, 2005, and 2007/08) were used for forecast. Every cycle of CCHS provides the number of physiotherapy visits by each individual. Four cycles of CCHS were combined in order to get reliable estimates. Hence, for combined CCHS data, the total number of physiotherapy visits by Canadian seniors was calculated and per capita service rate was identified for the period from 2001 to 2008 for different age groups (65-69, 70-74, 75-79, 80+) and gender in order to take into account population growth, population aging and gender differences. The physiotherapy service requirements for 2009 to 2016 were estimated based on Statistics Canada's Population Projections assuming that per capita physiotherapy service rate will not change overtime. Also, difference between the non-senior population and seniors in terms of physiotherapy utilization was examined.

RESULTS: The analysis shows that seniors experience chronic illness and disability treated by physiotherapy more often than non-senior population. The projected requirements of physiotherapy services correlate well with the increasing size of the senior population and increased from 3,754,634 on average in 2001-2008 to 4,652,819 in 2011 and to 5,537,141 in 2016.

IMPACTS: Forecast of physiotherapy requirements will help governments develop and adjust programs for publically funded services and will also be useful for private insurance firms in their planning of coverage for physiotherapy services.

1.83 Development of a Synthesis Tool for Follow-Up of the Chemicals Management Plan

A. Adam-Poupart, MSc, and C. Lapointe, Eng. MSc[1]

[1] Safe Environments Programme, HECSB, Health Canada, Longueuil, QC

SUMMARY: The Quebec risk management team has been working with an industry association in the food sector to develop a tool that will promote understanding and participation among industry members with respect to the risk assessment and management processes of the Chemicals Management Plan.

One regional risk management objective is to promote industry compliance and participation in the risk assessment and management processes of the Chemicals Management Plan. Our team has begun discussions with industry associations to find out industry requirements with regard to the Chemicals Management Plan. The Conseil de la transformation agroalimentaire et des produits de consommation (CTAC), an association in the food sector, has agreed to work with Health Canada to improve follow-up of activities related to the Chemicals Management Plan. Industries are being greatly challenged by government requirements, and few actually know their legal obligations. In order to bridge the gap, CTAC and Health Canada have developed a synthesis tool to follow up on various activities related to this sector.

METHOD: Health Canada reviewed the risk management and analysis documents pertaining to substances under the Chemicals Management Plan, and categorized the data that are most relevant to the industry. The aim is to develop a tool that will promote industry compliance with the government's current and future legal requirements, and encourage industries to provide comment on the impacts of applying risk management measures.

RESULTS: The synthesis tool thus developed will greatly facilitate follow-up of various activities related to the Chemicals Management Plan throughout the risk management and analysis processes. Industries will also be able to use it to provide inside information to ensure better management of toxic substances and the reduction of health risks to the general population.

CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The synthesis document was greatly appreciated by the association. As a result, similar tools will be developed specifically for other industrial sectors. Updated data will be sent regularly to industry associations to help Quebec businesses improve their understanding and application of risk management measures.

1.84 Validation of an HPLC Method for Measuring Relative Hemagglutinin Antigen Concentration in Pandemic Influenza Vaccines

F. Bouthillier[1], C.M. Allen[1], A. Bliu[2], H. MacDonald-Piquard[1], H. Rode[3], and A. Rinfret[1]

[1] Pandemic Influenza Unit, Viral Vaccines Division, Centre for Biologics Evaluation, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON
[2] Centre for Biologics Research, Biologics and Genetic Therapies Directorate, Health Canada, Ottawa, ON
[3] Pandemic Influenza Division, Centre for Biologics Evaluation, Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: The Viral Vaccines Division (VVD) will be responsible for lot release of H1N1 and other pandemic influenza vaccines. An alternate method of determining the antigen content of the vaccine has been validated in the context of pandemic preparedness efforts and could potentially be used for regulatory lot release.

BACKGROUND: A physicochemical method using size exclusion High Performance Liquid Chromatography (SE-HPLC) has been developed for the determination of relative hemagglutinin antigen (HA) concentration in monovalent influenza vaccines. This method could represent an alternative to the internationally accepted Single Radial Immunodiffusion (SRID) assay used to measure vaccine potency.

METHODS: A SE-HPLC method was devised using a TSK-GEL G4000SWxl column alone or in series with a G3000SWxl column on a Varian HPLC system. Monovalent influenza vaccine proteins were separated using a disodium phosphate mobile phase containing SDS detergent. Of several distinct peaks, the peak containing HA was confirmed. A representative lot of vaccine with known HA content was used as a reference creating a standard curve by injecting increasing amounts of vaccine. The HA content of the sample vaccine was determined by integrating the area under the curve (AUC) and relating it to the reference curve. Validation of this method determines accuracy, precision, linearity, repeatability/ reproducibility, sensitivity, selectivity, limits of detection and range.

RESULTS: Linearity within anticipated range of use (15 µg/mL of HA) for all influenza strains (A and B) assayed has been demonstrated. Reproducibility and repeatability have been shown, by analyzing multiple lots of three influenza subtypes in triplicate. Statistical analysis suggests that the dose response is strain independent, that there is no column effect with constant parameters and no difference in sensitivity using two different detectors. The HA concentration determined by peak profile and AUC may be comparable to the potency as measured by the compendial SRID assay.

IMPLICATIONS: This SE-HPLC method has considerable potential for widespread use for HA quantification and in quality control testing for seasonal and pandemic influenza vaccines. Moreover, in the event of a global shortage of calibrated antigen/antisera reagents, this alternate method could replace the reagent-dependent SRID assay for lot release testing.

1.85 Health Canada's Participation in the Environmental Assessments of Uranium Mines in Canada

R. Grabowecky, MSc[1]

[1] Environmental Assessment Division, Chemicals, Air and Water Directorate, HECSB-RAPB, Health Canada, Winnipeg, MB

SUMMARY: The Environmental Assessment Division works with government departments towards the successful assessment of health impacts of uranium mine projects in Canada. A matrix of typical potential health impacts is provided and identifies areas of expertise offered by HC to assist with the reduction or elimination of potential risks.

OBJECTIVES: The Environmental Assessment Division (EAD) provides HC's expert advice, when requested, to federal and provincial departments that are required to undertake an environmental assessment (EA) under the provisions of the *Canadian Environmental Assessment Act* or the *Canada-(province) Agreement on Environmental Assessment Cooperation*, respectively. This poster provides insight into the uranium mining activities that may require risk assessment and mitigation to manage risks to human health.

METHODOLOGY: A matrix provides the major potential health effects for various stressors or environmental exposures, the populations at risk, types of monitoring indicators along with relevant standards or guidelines. A summary of what, when and why HC's expert advice is provided to Responsible Authorities (i.e., federal) and provinces.

RESULTS: This overview of health impacts associated with uranium mine projects forms a basis for discussion of effects not always fully assessed and understood. Federal and provincial authorities for the project may not have the in-house technical expertise to critically review EA documents for potential human health impacts. EAD can effectively co-ordinate and assist in the incorporation of HC's expert advice into the resulting EA documents and subsequent mitigation and follow-up programs. This information is valued by Responsible Authorities in their determination of significance in the assessment of potential significant adverse environmental effects.

CONCLUSIONS: The incorporation of protective and proactive assessment procedures is critical as the use of nuclear energy is expected to increase due to the forecasted increased demand for uranium in order to reduce the reliance on fossil fuel based energy sources. The public has a heightened level of concern regarding uranium mine projects due to scientific studies associating lung cancer with exposure to radon daughters. When requested, HC participates in the environmental assessments of uranium mines to promote more comprehensive and accurate evaluation of potential effects as identified to be within our core areas of expertise. Proponents, Responsible Authorities, and provincial regulators required to undertake or evaluate an environmental assessment are advised to fully consider the potential health impacts presented, and provide mitigation measures as appropriate to safeguard public well being.

1.86 Examination of the Relationship Between Endpoint and Best-Fit Model Linearity, using Benchmark Models

J. Grundy, PhD[1], L. Gorham[1], H. Izadi, BSc[1], and R. Bose, MD[1]

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

SUMMARY: Previous work compared the Benchmark method to mathematically fit toxicity data to traditional endpoints from repeated dose studies. To derive the best fit, a linear or nonlinear mathematical model is used. We found that some endpoints fit nonlinear endpoints better. This may affect how we fit these endpoints in future.

OBJECTIVES/BACKGROUND/ISSUE(S): In 2006, we began evaluating Benchmark as a tool for a non-traditional choice of point of departure in hazard assessments of chemicals and polymers. Prior work focused on comparison of the mathematically derived Benchmark dose (BMDL), to the traditional No (or Lowest) Observed Adverse Effect Level (NOAEL or LOAEL, respectively). The comparison analyzed >50 repeated oral dose rat studies. Results showed wide variation in the models, which best fit the dose-adverse effect relationship. It was hypothesized that the best-fit model could be predicted on the basis of endpoint. The significance of endpoints that best fit a non-linear model is that they may consistently yield a lower benchmark dose than those which fit linear models.

DESIGN/METHOD/DESCRIPTION: This project investigated these so-called "sensitive endpoints" to see if they should be considered differently when doing risk assessment. From previous work, several endpoints were identified which were hypothesized to best fit a nonlinear model. For comparison, other endpoints, which were hypothesized to fit a linear dose-response relationship, were also examined. In all cases the studies were run through the current version (2.0) of the US EPA's Benchmark Dose Software (BMDS) program, which fit the data to different models, then tested them according to different criteria to judge which one was the best fit.

OUTPUT/RESULTS/IMPLICATIONS: The preliminary results showed that while the majority were best fit by a linear model, some endpoints fit nonlinear models, suggesting that nonlinear fitting should always be tested during analysis of these endpoints. An additional caveat, however, was that no one endpoint fit only nonlinear or linear models. This may be because many different toxicological mechanisms may lead to one frank effect, and the dependence of the endpoint on the dose may be more of a reflection of the underlying mechanism of toxicity.

1.87 Pharmacovigilance of Subsequent Entry Biologics

S. Hashim, PhD[1], S. Semalulu, PhD[1], S. Nandram, MD[1], N. Kawsi, PhD[1], D. Vu, PhD[1]

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

SUMMARY: Health Canada's proposed new guidelines distinguishes between Subsequent entry biologic (SEBs) and generic drugs. It is a case-by-case approach, through the same regulatory pathway as New drug submissions (NDS). SEBs require extensive testing before approval, and due to potential for immunogenicity problems, they will require close post-marketing monitoring.

OBJECTIVE: This paper will examine the proposed pharmacovigilance of Subsequent Entry Biologics in light of the new proposed guidelines for regulation of these products.

BACKGROUND: A subsequent entry biologic (SEB), is a biologic product that is approved for marketing subsequent to and similar to an approved innovator biologic. SEBs are not generics. Unlike generic pharmaceuticals, SEBs being of biological origin, cannot be identical to the innovator product. SEBs are a focus of attention now because the eminent expiry of many innovative biotech products will result in substantial increase in SEB's, increasing demand for affordable alternatives, and a growing market share of biologics, which encourages development of SEB. Some SEB's have already been approved in Canada and other jurisdictions, e.g., Omnitrope* (somatropin), Binocrit** (epoetin alpha). Regulation of SEB's is challenging due to several reasons including choice of appropriate reference product, immunogenicity associated with biologics, extent of clinical studies required for authorisation, ability to address complex manufacturing process, sophisticated analytic tools for comparability assessment and substitutability with innovator product.

DESCRIPTION: This paper will examine the proposed pharmacovigilance of Subsequent Entry Biologics in light of the new proposed guidelines for regulation of these products.

OUTPUT: Health Canada introduced its first Draft Guidance Document for SEBs in March 2008. Stakeholder consultations are nearly completed and a final guidance document is expected to be released by the fall of 2009.

NEXT STEPS: Once approved SEBs will be treated in a manner similar to innovator products. Frequency of Periodic safety update report (PSUR) will be aligned with ICH requirements. Risk management plan submitted with NDS will include monitoring of immunogenicity. Canadian product monograph (CPM) for SEB will have to be developed. The CPM of reference product cannot be utilized. A unique name and label will be required for an SEB. Adverse drug reactions will have to be reported under of Food and Drug Regulation.

1.88 Risk Management Plans in Pharmacovigilance: Can They Be a Replacement for Periodic Safety Update Reports (PSURs)

S. Hashim, PhD[1], M. Mikhail, MD[1], S. Semalulu, PhD[1], A.V. Klein, MD[1], K.N. Barton, PhD[2], and D. Vu, PhD[3]

[1] Marketed Biologics, Biotechnology and Natural Health Products Bureau†, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Biologics and Genetic Therapies Directorate, HPFB, Health Canada Ottawa, ON
[3] Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: We compared the usefulness of Periodic Safety Update Reports (PSURs) and Risk Management Plan in pharmacovigilance. Controversy regarding PSURs becoming data dumps has led to regulators questioning the usefulness of PSURs. Redefinng the amount and analysis of data included in PSURs is required but they cannot be substituted with RMPs.

OBJECTIVE: To compare and contrast the usefulness of Periodic Safety Update Report (PSURs) vs Risk Management Plan (RMP) as tools of pharmacovigilance

BACKGROUND: A PSUR is intended to provide an update of the worldwide safety experiance of a medicinal product at defined time periods of post-authorisation. A PSUR contains all reports of serious and non-serious adverse events that have occured throughout the world. They also address the adverse events that are described in the literature. (Clinical trials, pharmacoepidemiological trials) The safety has to be systematically reviewed analysed and summarised in a PSUR. The methodology for identifying and evaluating the risks and process of generating intervention plans to reduce the risks to an acceptable level is generally referred to as a Risk Management Plan. In the European Union, since 2005, market authorisation holders are required to submit RMPs to the European Medicines Agency (EMEA) for new drugs and whenever a new adverse event is identified.

DESCRIPTION: This abstract will compare and contrast the usefulness of Periodic Safety Update Report (PSURs) vs Risk Management Plan (RMP) as tools of pharmacovigilance.

OUTPUTS: Recently, regulators have begun to question the value of PSURs. They are of the opinion that PSURs have become data dumps and companies are holding back critical information. Regulators may have to re-define the amount and analysis of safety data that is required in the PSUR and what use this information can be put to.

CONCLUSIONS: The PSURs remains an important tool in identifying potential safety concerns associated with a product. Identification of risk is the obvious first step to management of risk. On the other hand Risk Management Plans not only identify the risks but they also generate concrete intervention plans to minimise the identified risks. However, on their own, RMPs are not a tool to detect signals of new or unknown risks. The PSURs and RMPs are important complementary tools of pharmacovigilance, and are not mutually exclusive.

1.89 Validation of a New and Faster Method to Test Influenza Vaccine Potency for Regulatory Lot Release

S. Heidinga[1], A. Bliu[2], J. Clausen[1], A. Gauthier[1], N. Fortin[1], D. Denicourt[1], and A. Rinfret[1]

[1] Viral Vaccines Division, Centre for Biologics Evaluation, BGTD, HPFB, Health Canada, Ottawa, ON
[2] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

SUMMARY: The Viral Vaccines Division (VVD) is responsible for lot release of seasonal and H1N1 influenza vaccines. The standard method used in our labs for determining the potency of influenza vaccines has been validated to include an automated system, which has resulted in a dramatic increase in assay throughput.

BACKGROUND: The Single Radial Immunodiffusion assay (SRID) is performed to determine the potency of influenza vaccines. The size of precipitin rings formed between the vaccine sample and a reference antiserum in an agarose gel is related to the amount of haemagglutinin antigen. Currently, the diameters of the resulting rings are measured individually by a technician using Corel Draw. The purpose of this study is to validate the use of the Axiovision Zeiss automated system for reading SRID gels before implementing the method for regulatory testing. The automated system reads a scanned gel image and calculates the number of pixels in the surface area of each ring. The automated Axiovision reading system is expected to be faster, more standardized and reduce the variability of the readings.

METHOD: A validation plan was designed with the assistance of a statistician to compare the accepted method to new method for the following parameters: Accuracy, Intermediate Precision (three different analysts), Repeatability (same analyst over three different days), Robustness (varying conditions), Range and Linearity.

RESULTS:

Validation Parameter	Average Coefficient of Variation (CV) for Corel Draw Method	Average Coefficient of Variation (CV) for Axiovision Method
Accuracy	5.6	5.4
Intermediate Precision	5.5	5.2
Repeatability	2.2	0.0

In addition, there were no statistically significant differences between the two methods for robustness, range and linearity.

CONCLUSIONS: The study determined that both measurement methods are comparable and valid. The Axiovision software leads to a significant reduction in intra-assay variability allowing a 3-fold decrease in the number of replicates required for each sample and is also considerably faster leading to an estimated 10 fold increase in throughput. This is extremely valuable in the context of BGTD's regulatory preparedness efforts for the release of H1N1 pandemic vaccine lots, where Health Canada is expected to receive a large number of samples to release expeditiously.

1.90 Capacity Building in Indigenous Health Impact Assessment

R. Kwiatkowsk, D. McClymont-Peace, and C. Bourassa[1]

[1] Environmental Health Research Division, FNIHB, Health Canada, Ottawa, ON
[2] First Nations University of Canada

SUMMARY: Canada is considered a world leader in Health Impact Assessment (HIA) and the poster will highlight Health Canada's activities to enhance its influence internationally by providing assistance to Indigenous people internationally understand and participate in HIA.

BACKGROUND: Canada's wealth of natural resources (minerals, forest products and energy sources) positions Canada as a supplier for domestic and global industrial demands. As well, climate change is greatly increasing access to Canada's far north, an area rich in oil and minerals. The challenge facing the federal, provincial and territorial governments is to find ways to support economic development that enhances the health and well being of Canadians without adversely impacting the environment. Canada's Indigenous communities can be characterized as: small, young, rapidly growing, and remote. Despite expectations of significant community benefits arising from resource development, Indigenous communities continue to express concerns about the impacts that development projects are having on the environment and their health and well being.

DESCRIPTION: The First Nations University (FNUniv) has expertise in teaching, research, and service in relation to Indigenous health, the environment, and to the pure and applied sciences with an emphasis on incorporating the traditional knowledge of and contemporary issues faced by Indigenous people.

RESULTS: The Environmental Health Research Division (FNIHB, HC) is partnering with the FNUniv, the Centre Hospitalier Universitaire de Québec World Health Organization Collaborating Centre and the North American Commission for Environmental Cooperation to develop a HIA courses (starting fall 2009) for Canadian Indigenous students, community members, front-line workers or non-Indigenous individuals who work with or for Indigenous communities and would gain benefit from basic knowledge regarding HIA. A second HIA summer course will be developed for international indigenous students, starting summer 2010.

IMPACTS: The training will provide Indigenous communities with the ability to:

- fully participate in HIA decision making; thereby enhancing health and well-being; and
- identify and remediate environmental impacts associated with development projects; thereby reducing negative health outcomes.

1.91 Drug Safety and Effectiveness Network (DSEN)

S. Bayly, and R. Liteplo[1]

[1] Therapeutic Effectiveness and Policy Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: DSEN is a new initiative being led by Health Canada (HC) and Canadian Institutes of Health Research (CIHR) designed to bring decision-makers and researchers together to fill knowledge gaps on the real world safety and effectiveness of human drugs.

OBJECTIVES/BACKGROUND/ISSUE(S): DSEN is a new initiative being developed by Health Canada and the Canadian Institutes of Health Research. The DSEN's key objectives are to 1) increase available evidence on real world drug safety and effectiveness available to regulators, policy-makers, health care providers and patients, and 2) increase capacity within Canada to undertake high-quality post-market research in this area.

DESIGN/METHOD/DESCRIPTION: The key components of DSEN include a virtual network of linked research centers, a national oversight body, and a coordinating office located at CIHR. DSEN's objectives will be accomplished by building on existing Canadian research capacity and improving coordination among and between researchers and research users, to increase the quantity, timeliness and utility of available evidence.

OUTPUTS/RESULTS: Activities are being undertaken within HC and CIHR to support linkages between research and decision-making. HC and other stakeholders have been providing input to CIHR on network development. HC is working to establish a process by which it may provide input to the DSEN's research agenda, and to work towards the effective use of DSEN-generated data in its regulatory and drug plan management activities. DSEN's funding will generate studies, which will focus on post-market drug safety and effectiveness in real world environments.

IMPACTS/OUTCOMES/CONCLUSIONS: DSEN-generated evidence will be made available to support decision-making throughout the Canadian drug regulatory and health care systems. The impact will be increased collaboration and coordination among researchers, increased capacity for post-market research, and increased support for the evaluation of human drugs across the product lifecycle.

1.92 Are Anti Tumour Necrosis Factor (TNF) Alpha Drugs Associated with an Increased Risk of Malignancies in Children and Young Adults?

G. Mah-Cawthorn[1], J. Rose[1], A. Makinde[1], A.V. Klein[2], J. Karsh[3], S. Semalulu[1], and D. Vu[1]

[1] Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON
[2] Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON
[3] University of Ottawa, Ottawa General Hospital, Ottawa, ON

SUMMARY: TNF-alpha (TNF-α) inhibitors are used to treat a variety of immune/inflammatory conditions including rheumatoid arthritis (RA), Crohn disease etc. Safety data were assessed to determine whether there was increased risk of malignancies associated with these products. Except for hepatosplenic T-cell lymphomas, these drugs did not appear to have increased risk of malignancies.

BACKGROUND: Tumor necrosis factor alpha (TNF-α) is a cytokine able to lyse tumor cells, hence the name. Development of inhibitors of TNF-α as therapeutic drugs led to concerns that increased malignancies would occur among treated patients. Three TNF-α inhibitors including Humira (Adalimumab), Enbrel (Etanercept) and Remicade (Infliximab) are currently authorized for marketing in Canada. With increase in patients using these drugs, several safety concerns have emerged. This paper will focus on malignancies, particularly in children and young adults.

OBJECTIVES: To evaluate the safety data for evidence on malignancies associated with the use of TNF-α inhibitors in children and young adults.

DESCRIPTION: Authorized marketers of these products provided comprehensive safety information including up-to-date listing of Canadian and worldwide cases of lymphomas and other cancers, from time-to-market to the present. In addition, the latest Periodic Safety Update Reports (PSUR) and a meta-analysis of cancer incidence in studies of this product class were provided. With the help of an expert clinical rheumatologist, summary statistics and Bayesian Survival Analysis were used to compare the rate of malignancies in TNF-α inhibitors treated patients versus conventional therapy.

RESULTS: Lymphoma was the most common malignancy reported, which is consistent with the known increased risk of lymphoma in rheumatoid arthritis. Assessment of overall risk of malignancy in adults did not find a statistically significant increased risk. Except for hepatosplenic T-cell lymphoma, which is already labelled for these products, the assessment of malignancies in pediatric patients did not show an increased risk.

CONCLUSIONS: The TNF-α inhibitors do not appear to be associated with an increased risk of development of malignancies in the adult population. Additional data are needed on exposure to TNF-α inhibitors in the pediatric patients. The establishment of a registry of pediatric patients may be necessary to obtain comprehensive data.

1.93 Potential Framework for Therapeutic Vaccine Pharmacovigilance

B. Saïd Salim, PhD[1], E. Taylor, MD[1], A.V. Klein, MD[2], S. Semalulu, PhD[1], and D. Vu, PhD[1]

[1] Marketed biologics and biotechnology and Natural Health Products Bureau, Marketed Health Product Directorate (MHPD), HPFB, Health Canada, Ottawa, ON
[2] Centre for Evaluations of Radiopharmaceuticals and Biotherapeutics, Biologics and Genetic Therapies Directorate (BGTD), HPFB, Health Canada, Ottawa, ON

SUMMARY: The aim of this project is to develop a framework for post-market surveillance of therapeutic vaccines. These vaccines are used to treat (rather than prevent) chronic diseases such as cancer and autoimmunity. BGTD (pre-market) and MHPD (post-market) within Health Canada regulate therapeutic vaccines.

BACKGROUND: Therapeutic vaccines are used to induce/augment/modify the immune response in order to treat disease. Prophylactic vaccines are administered to a population for the prevention of disease. Postmarket surveillance or pharmacovigilance is the science of detecting, assessing, understanding and preventing adverse effects related to health products. Postmarket surveillance of therapeutic vaccines falls under the mandate of the Health Products and Food Branch (HPFB) while that of prophylactic vaccines is under jurisdiction of Public Health Agency of Canada (PHAC). BCG, a vaccine administered intradermally for the prevention of TB (a prophylactic use) is also authorized in Canada for the treatment of bladder cancer (a therapeutic use). Many new therapeutic vaccines that target conditions such as cancers, autoimmune diseases and HIV are in development. The biological complexity of these products are highlighted by the different types of vaccines under development. These include whole cell vaccines, tumour associated antigens, and DNA vaccines that utilize bacterial plasmids. Antigen-based therapies, aimed at inducing tolerance have also been used in clinical trials for treatment of autoimmune diseases.

DESCRIPTION/PROPOSAL: The framework for therapeutic vaccine pharmacovigilance will be discussed in anticipation of novel therapeutic vaccines reaching the market. The HPFB continues to develop mechanisms for a life-cycle/programme approach to pharmacovigilance for all biologic products including the monitoring of therapeutic vaccines.

IMPLICATIONS/NEXT STEPS: Pharmacovigilance of therapeutic vaccines will likely continue to follow the same legislative framework as other biological and biotechnology products, under the Food and Drugs Act and Regulations. The Canada Vigilance database is used for reporting Adverse Drug Reactions (ADR), while Periodic Safety Update Reports (PSUR) and Risk Management Plans (RMP) submitted by the Market Authorization Holder are reviewed to monitor therapeutic product safety. These tools readily apply to the post-market surveillance of therapeutic vaccines.

1.94 Case Study of an Adverse Drug Reaction: Adam, A Natural Health Product Advertised for Erectile Dysfunction

I.-N. Sully, MD, CCFP[1], M. Murty, CCFP, MD[1], and D. Vu, MSc, PhD[1]

[1] Marketed Heallth Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: The poster proposed is the history of an adverse reaction (AR) caused by a natural health product. It will show the sequence of events after a consumer reports an AR to Health Canada. This is a good example how a complaint can instigate regulatory action and it will also showcase the collaborative work that took place in the different directorates.

OBJECTIVES/BACKGROUND/ISSUE(S): The Reporting rate for adverse reaction is very low, particularly with Natural Health Products. One of the reasons is that the public and heath professionals may not be aware of the invaluable contribution and positive impact of reporting. The main objective of this poster is to emphasize the crucial role of reporting in pharmacolvigilance, and to highlight the collaborative efforts of the different Directorates, resulting in a Health Canada Public Warning notification.

DESIGN/METHOD/DESCRIPTION: A citizen was concerned that his father had an adverse drug reaction to a Natural Health Product called ADAM, and he reported the event to Health Canada. The poster chronologically details the events that took place and the contribution and involvement of the different Directorates to evaluate and respond to this signal. This included monitoring inputs from the Canadian Vigilance Program and the World Health Organization (WHO), followed by risk identification, assessment and mitigation by the Marketed Health Product Directorate (MHPD), Biologics and Genetic Therapies Directorate (BGTD), and The Health Products and Food Branch Inspectorate (HPFBI), and risk communication by the Public Affairs, Consultation and Communications Branch (PACCB).

OUTPUTS/RESULTS: After causality assessment and laboratory analysis, the product was found to be adulterated with a pharmaceutical. Health Canada issued a risk communication document warning consumers not to use ADAM, a natural health product advertised for erectile dysfunction or any Health Canada-unauthorized erectile dysfunction product.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This case study is a good example of the value of public engagement. This work demonstrates the application of the current policies and regulations towards public awareness and ultimate safety.

2.01 Oxidation and Thermal Aggregation of Interferon Alpha-2a: Impacts on Cytotoxicity and Potency

M. Alteen[1], M. Girard[1], A. Diress[1], B. Lorbetskie[1], A. Martyres[1], and R.A. Isbrucker[1]

[1] Center for Biologics Research, HPFB, Health Canada, Ottawa, ON

SUMMARY: Oxidized and thermally aggregated interferon (IFN) alpha-2a was assessed for changes in cytotoxicity and potency relative to unmodified interferon. These alterations of interferon may occur during formulation or storage and may potentially impact efficacy and safety of the drug.

OBJECTIVES/BACKGROUND/ISSUES: IFN alpha-2a is prescribed for the treatment of hepatitis, multiple sclerosis and certain cancers due to its anti-proliferative and immunomodulatory effects. However, adverse side effects are common and sometimes severe among patients prescribed the treatment. There is speculation that unintended modifications to IFN may occur in formulation and that this could be the cause of some observed side effects in addition to reducing the potency of the treatment.

DESIGN/METHOD/DESCRIPTION: IFN aggregates were prepared on-site using concentrated IFN alpha-2a from the European Directorate for the Quality of Medicines as a standard and were assessed quantitatively via size exclusion and reverse-phase HPLC. Samples were then applied to human HepG2 hepatoma cell lines and were tested for cytotoxicity with the sulforhodamine B assay. Potency was measured in a cell-based reporter gene assay after 24 hours exposure to the samples.

OUTPUT/RESULTS: Complete aggregation of IFN took place after 1.5 hours incubation time at 80º C. While the aggregated sample displayed an almost total loss of potency in this state, it did not show cytotoxicity. After 18 hours of incubation in 0.0025% H_2O_2, approximately 66% of the IFN standard were converted to its oxidized variant. This resulted in a small but significant decrease in IFN potency, from an EC50 of approximately 100 IU/ml to approximately 200 IU/ml after oxidation. Also, the oxidized protein had increased cytotoxicity relative to the standard.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Results have shown that thermal aggregation and oxidation of IFN alpha-2a had a negative impact on the biological activity of the protein, a situation that may have implications for therapeutic formulations.

2.02 Development of Analytical Method and Survey of Foods for Furan, 2-Methylfuran and 3-Methylfuran with Estimated Exposure

A. Becalski[1], S. Hayward[2], T. Krakalovich[3], L. Pelletier[4], V. Roscoe[3], and E. Vavasour[5]

[1] Food Research Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON
[2] Bureau of Biostatistics and Computer Applications, HPFB, Health Canada, Ottawa, ON
[3] Food Program, HPFB, Health Canada, Winnipeg, MB
[4] Chemical Health Hazard Assessment Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON
[5] Chemical Health Hazard Assessment Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON

SUMMARY: Furan, a possible human carcinogen, has been found to form in foods during thermal processing. A survey of canned and jarred food products for furan and its methyl analogs, 2-methylfuran and 3-methylfuran, was conducted to ascertain prevalence of these three chemicals in products on the Canadian market.

OBJECTIVES/BACKGROUND/ISSUES: The limited amount of data on concentration of furan in products on the Canadian market prompted us to conduct a survey of canned and jarred food products. Methyl analogs of furan, 2-methylfuran and 3-methylfuran, were analysed concurrently with furan via a newly developed isotope dilution method, as these analogs were detected in foods in our earlier work and are likely to undergo a similar metabolic fate as furan itself.

DESIGN/METHOD/DESCRIPTION: Analysis of furan and methylfurans was by a Headspace Gas Chromatography/Mass Spectrometry. In total 176 food items were analyzed. They consisted of 154 canned or jarred products (including 3 coffee products), 5 packaged meat pates and 17 baby foods. These data were used to derive a deterministic estimate of furan intake from the diet for various sectors of the population.

OUTPUT/RESULTS: Using this dataset, dietary exposures to furan and total furans were calculated. Average furan and total furan intakes by adults (= 20 years) were estimated at approximately 0.37 and 0.71 µg/kg of body weight/day respectively.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The levels of methyl furans in jarred food approach 50% of the concentration of furan and, in case of coffee, exceed it. Intake estimates also show that methylated furan analogues can make a considerable contribution to total furan exposure. This study is the first one to provide comprehensive data on the occurrence of furan, 2-methylfuran and 3-methylfuran in foods.

2.03 Biological Effects of Particulate Matter: Human *In Vitro* Co-Culture Model

D. Breznan, PhD[1], M. Phaneuf, MSc[1], Y. Siddiqui, MSc[1], and R. Vincent, PhD [1]

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

SUMMARY: We examined the role of lung cell interactions in modulating the biological effects of particles collected from ambient air. Cellular interactions were revealed in the differential release of cytokines and other factors in response to particle exposure. The model correlated with lung inflammation in mice after intratracheal instillation of particles.

OBJECTIVES: We assessed an *in vitro* co-culture approach for analysis of biological effects of particles with varied physicochemical properties, and the potential of the co-culture model for simulating the complexity of the *in vivo* lung alveolar milieu.

METHOD: Human lung epithelial cells (A549), macrophages (THP-1) and pulmonary artery endothelial cells (HPAE) were grown in RPMI-1640 medium in 24-well plates. For the co-cultures, A549 cells were added to THP-1 cells on the following day at cell densities comparable to the monocultures. Confluent A549 and THP-1 mono- and co-cultures were incubated with particles (EHC-93, EHC-6802, DWR1, SRM-1650, TiO_2 and SiO_2) at 0, 10, 30 and 100 µg in 1 ml of medium for 24h. HPAE cells were incubated for 24h with conditioned media obtained from particle-treated A549 and THP-1 mono- and co-cultures. EHC-6802, DWR1 and SRM-1650 particles were instilled intratracheally (0, 50, 250 µg in 50 µl of 0.9% saline, 0.005% Tween-80) into BALB/c mice using a Penn-Century aerosolizer. After 2 and 24h the mice were euthanized and lungs were lavaged with saline.

RESULTS: Epithelial A549 and macrophage THP-1 cells synergistically modulate their production of cytokines (IL-1ß, IL-6, IL-8, MCP-1 and TNF-α), ICAM-1 and VEGF in response to particle exposure. Cellular mediators from particle-exposed co-cultures can activate lung endothelial HPAE cells to produce cytokines (IL-6, IL-8, GM-CSF, MCP-1) and adhesion factors (ICAM-1, VCAM-1 and E-selectin). Intratracheal instillation of the particles in mice led to neutrophilia and elevated cytokines (IL-6, KC, MIP-1 α and TNF-α). Statistical comparison of the cell interaction model responses and PM-induced neutrophilia in mice showed good correlations.

CONCLUSION: A human cellular co-culture model was used to simulate the complexity of the *in vivo* lung micro-environment by enabling interactions between various cell types. It represents a useful approach for toxicological screening of air pollution particles and for studying the mechanisms underlying the adverse biological effects of the particles.

2.04 Application of Nanotechnology to Medical Devices: Challenges and Promises

F. Chellat, PhD[1]

[1] Medical Devices Bureau, TPD, HPFB, Health Canada, Ottawa, ON

SUMMARY: The unique properties of nanotechnology-based products are considered for many therapeutic applications, mainly because interactions with biological components/functions. The understanding derived from published studies in terms of factors that are determinants for toxicity of nanomaterials and some available data on potential applications of nanotechnology for medical devices will be presented.

OBJECTIVES: To provide an overview of cellular responses to nanomaterials based on available published data and to highlight the potential applications of nanotechnology for medical devices.

DESIGN: Analysis and discussion based on recent published findings. Examples of cytotoxicity/immunotoxicity/inflammatory reactions to some nanomaterials will be outlined. A structure-function relationship will be discussed with respect to potential applications of nanotechnology to medical devices.

OUTPUT/RESULTS: The particular properties displayed by nanomaterials make them attractive for use in biomedical applications, which represent a highly expanding domain, particularly for diagnosis and therapeutics. The unique properties of nanoscale materials/structures are associated with biological effects, which are differently expressed and are dependant of the nature of a given nanoparticulate system. Factors such as surface properties, particle size and charge have been suggested to affect cytotoxicity of nanoparticles. It has also been shown that adsorption of different proteins occur with different nanoparticle surfaces, which can in turn affect the immune system cell reactions. To compare the abilities of different nanoparticles to induce toxic effects, it has been proposed to measure the level of induced oxidative stress within cells. With respect to potential applications of nanotechnology to medical devices, benefits and advantages of using nanostructured materials to achieve optimal biocompatibility and functionality will be discussed. Surface structure modification and bioactive coatings to promote cell adherence and guided-growth on implant surface are some examples of potential applications of nanotechnology to medical devices.

CONCLUSIONS: While nanotechnology provides great promises, it also represents a great challenge in terms of understanding, predicting, and managing potential health risks. It is worthwhile to point-out that not all nanomaterial is toxic and that assessing and understanding biological responses to nanomaterials is necessary to design safe and effective products.

2.05 Lead-210 Concentration in Household Dust: A Potential Indicator of Indoor Radon Exposure

J. Chen, W. Zhang[1], D.G. Sandles[1], R. Timmins[1], and K. Verdecchia[1]

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

SUMMARY: Radon decays to a long-lived isotope lead-210. Lead-210 in the household dust could be an indicator of indoor radon levels. Measurements in over hundred Canadian homes demonstrated that measuring concentrations of lead-210 in the household dust is a viable alternative method to estimate associated indoor radon levels.

OBJECTIVES/BACKGROUND/ISSUE: Long-term exposure to radon increases the risk of developing lung cancer. The level of risk depends on the concentration of radon and length of exposure. Radon decays to a long-lived isotope lead-210. This study evaluates a novel method to estimate long-term radon exposure by measuring lead-210 concentrations in the household dust.

DESIGN/METHOD/DESCRIPTION: To determine the concentrations of radon, passive integrated radon-thoron discriminative detector (commercially RADUET) was used. RADUET detectors were placed in the lowest floor of 117 private homes. All tests began in February and ended in June 2008. The survey was designed to collect household dust during the test period. Participants were asked to change their vacuum bags at the beginning of the test, to ensure that the bags can be used for the entire test period. Dust samples were sieved to 100μm to remove the large objects from the dust, and then analyzed for activity concentrations for lead-210 by counting the 46.5keV peak on a Gamma Analyst Integrated Gamma Spectrometer.

OUTPUTS/RESULTS: Radon concentrations and dust samples were available from 111 homes. The weights of those fine dust samples varied from 3.7g to 68.8g with only 38 samples weighing more than 20g. For dust samples more than 20g, lead-210 concentration in household dust correlated well with the measured radon exposure (R^2=0.57).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This study demonstrated that lead-210 in household dust relate reasonably well to radon concentration in homes, and measuring concentrations of lead-210 in the household dust is a viable alternative method to estimate associated indoor radon levels. However, certain amount of dust must be collected to achieve the desired reliability of this estimation.

2.06 Infiltration of Particulate Matter Into Homes in Toronto, Canada: Can Commonly Available Housing Characteristics be Used to Improve Exposure Estimates?

N.A. Clark, MSc[1], A.J. Wheeler, PhD[1], A. Ryan, PhD[2], P. Hystad, MSc[3], D. Stieb, PhD[1], G. Evans, PhD[4], H. You[1], and S. Dell, PhD[4,5]

[1] Air Health Science Division, HECSB, Health Canada, Ottawa, ON
[2] Simon Fraser University, Burnaby, BC
[3] University of British Columbia, Vancouver, BC
[4] University of Toronto, Toronto, ON
[5] The Hospital for Sick Children, Toronto, ON

SUMMARY: Fine particulate matter in the air presents a health concern; however, estimating exposure is difficult because levels are measured outdoors, while in Canada most of our time is spent indoors. We investigated infiltration of particulates from outdoors into Toronto homes and found that it differs by housing characteristics and season.

BACKGROUND AND OBJECTIVE: Studies of the health effects of outdoor air pollution continue to be impacted by errors in estimating personal exposure. Differences in the infiltration of outdoor pollution between homes and over time contribute to exposure errors, but very few studies consider infiltration because it is not feasible to measure in large numbers of homes and the published literature on modeling is still scarce. This study sought to estimate infiltration efficiencies of fine particulate matter ($PM_{2.5}$) in detached residential homes in Toronto and identify housing characteristics that could be used to predict infiltration efficiencies.

METHODS: Fine particulate matter was measured continuously indoors and outdoors for 5-days at 60 detached homes in Toronto, Canada, July through November 2006 and July 2007 using a Dust-Trak. After removing peaks that resulted from indoor sources, such as cooking, an average infiltration rate for each home was estimated using a recursive mass balance model. Participating households completed questionnaires on home characteristics and house assessment values were obtained from the Municipal Property Assessment Corporation of Ontario. These variables were offered into linear regression models as predictors of infiltration efficiency.

RESULTS: After removal of incomplete and invalid data, 30 homes (50%) remained for inclusion in the analyses. Average infiltration rates were 64% (standard dev=22%); it was higher in the non-heating season (67% +/- 23%, n=21) than in the heating season (56% +/- 15%, n=9), though the difference was not significant. Predictors of higher infiltration were having an older home (R2=16%) and in the non-heating season, central air conditioning use predicted lower infiltration (R^2=10%, $p<0.05$). Other housing characteristics, including house assessment value, were not significantly associated with infiltration rates.

CONCLUSION: Although it remains challenging to predict infiltration rates for individual homes, some easily attainable housing characteristics may allow for the prediction of infiltration in future studies of air pollution.

2.07 Influenza Vaccine Proteomics as a Rapid, Comprehensive Analytical Technique for Viral and Contaminant Protein Identification and Quantification

T.D. Cyr[1], M. Cameron[1], M. Girard[1], and X. Li[1]

[1] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

SUMMARY: A method was developed to determine the amount and identity of hemagglutinin, the active ingredient in influenza vaccines. This methodology may allow more rapid vaccine manufacturing and product release because it does not require the development of specific antibodies for each influenza strain.

BACKGROUND: Influenza vaccines have been extremely successful in mitigating the morbidity and mortality of influenza. The annual flu vaccine is composed of three strains: influenza A strains (H1N1 and H3N2) as well as Influenza B strain. The individual virus strains are grown in chicken eggs, the virions collected, split and the major antigenic protein, hemagglutinin (HA) purified. Each monovalent HA stock is then quantified using a specific antibody method, currently single radial immunodiffusion (SRID). The methods presented here are intended to provide more sensitive technologies with more accurate results to augment the existing methodology.

METHOD: The protein samples were treated as follows: protein unfolding, disulphide cleavage and capping, then enzymatic deglycosylation and digestion. The resultant peptides were separated using a nanospray high performance liquid chromatography (HPLC) system coupled to a tandem mass spectrometer. The addition of standard proteins allowed individual quantitation of major proteins that were identified.

RESULTS: The method, optimized using trivalent vaccines and pre-pandemic influenza products, was highly successful in strain identification. The samples were also spiked with an internal standard to allow specific protein quantification using specialized proteomics software. Our method thus provides an alternative, spectroscopic method, to the SRID immunological method currently used for HA quantitation. Since influenza viruses are generally grown in chicken eggs, the inclusion of the chicken proteins in the search readily allows a sensitive determination of the impurity levels and is a measure of the effectiveness of the purification processes.

IMPACT: During a pandemic influenza outbreak the ability to prepare and release safe vaccines more quickly will save many lives. These methods are able to quantify and confirm identification of the influenza strains in a much faster, more accurate manner than current methodology. The methods are now being transferred to other national regulatory agencies and industry for validation and use.

2.08 A Multi-Disciplinary Approach to Determine the Impacts of Environmental Contaminants on Human Health From a Traditional Diet in the Canadian Arctic

C. Tikhonov[1], M. Feeley[1], D. Charette[1], A. Manning[1], T. Leech[1], T. Nancarrow[1], B. Adlard[1], and J. Van Oostdam[1]

[1] Primary Health Care and Public Health, FNIHB, Health Canada, Otawa, ON

SUMMARY: This paper integrates the findings from exposure, epidemiology, dietary choice and risk communication studies to determine the human health implications of exposure to contaminants from a traditional diet. Northern health professionals must have access to the best available data to provide effective dietary advice.

BACKGROUND: The objectives of this paper are to: 1) Provide the results of a number of recent biomonitoring studies that have been conducted in the Canadian Arctic; 2) to assess the impact of exposure to current levels of environment contaminants on human health; and 3) Present a framework that summarizes how risk management decisions are made. The primary exposure pathway for contaminants for various Persistent Organic Pollutants (POPs) and metals is through a diet of traditional foods. The results of the biomonitoring studies presented in the paper, indicates that exposures tend to be higher in the eastern Canadian Arctic Compared to the Western Canadian Arctic. The developing foetus is likely to be the more sensitive to the effects of POPs and metals than adults. Risk management and communication efforts integrate information on the risks and the benefits of a traditional diet. There are significant nutritional, social, cultural, spiritual and economic benefits of traditional foods that are considered in the context with the risks of exposure.

DESCRIPTION: This paper integrates the results of new follow-up Arctic biomonitoring studies (2002-2008), evaluates possible human health impacts of contaminants and a number of risk communication studies from the Canadian Arctic.

RESULTS: Exposures to Persistent Organic Pollutants and metals tend to be higher amongst Inuit of the eastern Arctic who consume marine mammals. There are significant declines in almost all contaminants in maternal blood over the last 10 years (comparisons of samples collected between 1992-1996 to samples collected between 2004-2006) for all Canadian Arctic regions studied (NWT, Nunavut and Nunavik). A number of contaminant levels are now less than one-half the levels 10 years ago. However, current epidemiological studies suggest that there may be possible subtle health effects at present concentrations of contaminants. Balancing the risks and benefits of a diet of country foods is difficult. The nutritional benefits of country food and its social, cultural and spiritual values are substantial. Country food contributes significantly more protein, iron and zinc to the diets of consumers than southern/market foods. These foods are an integral component of good health among Aboriginal northerners.

OUTCOMES/NEXT STEPS: Northern health professionals must have access to the best available data in order to provide relevant and effective dietary advice about the safety of a traditional diet. The general risk communication message states that the benefits of a traditional diet outweigh the potential risks of contaminant exposure.

2.09 A Systems Toxicology Knowledge Base for the Semantic Web

A. De Leon[1], B. Kuo[3], C.L. Yauk[4], P.A. White[4], and M. Dumontier[1,2]

[1] School of Computer Science, Carleton University, Ottawa ON
[2] Department of Biology, Carleton University, Ottawa, ON
[4] Analytical Tools Section, Biostatistics and Epidemiology Division, Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON
[4] Mutagenesis Section, Environment and Occupational Toxicology Division, Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON

SUMMARY: A significant impediment to systems toxicology research is the ongoing challenge of integrating increasingly diverse experimental data to support knowledge discovery techniques such as data mining or question answering. Here, we use semantic web technologies to simplify data integration, expose raw data for repurposing and enable questions answering using background knowledge encoded in ontologies.

OBJECTIVES: Capture diverse systems toxicology knowledge using expressive ontologies represented with the Resource Description Framework/Web Ontology Language (RDFS/OWL) semantic web languages and demonstrate sophisticated question answering involving expert knowledge over integrated datasets.

METHOD: Existing public systems toxicology knowledge bases were surveyed and analyzed for their breadth and depth. These were appropriately transformed to RDFS/OWL ontologies, and logical mappings between and across ontologies were created where none previously existed. Ontologies were enriched with expert knowledge and captured through axioms for disjointness, existential and universal quantifications as well as qualified cardinality restrictions.

Raw data from several systems toxicology databases such as CTD (chemical toxicogenomics database) were transformed into knowledge base facts using protocols established by the Bio2RDF open-source project. These were loaded into OpenLink Virtuoso 6, which is designed for browsing and querying through the SPARQL query language. OWL reasoners were used for checking data consistency, making logical links over datasets, and answering questions.

RESULTS: A survey of currently available schemas/ontologies and dataset contents and availability, have been completed. A global ontology has been designed while maintaining explicit mappings to individual schemas, which can be used to automatically transform raw data and instantiate the ontology. Transformed data are linked to Bio2RDF transformed databases such as UniProt, Gene Ontology, etc, and it is now possible to query these resources simultaneously on the Semantic Web. In addition, using services of the Virtuoso platform, the computer is now able to answer questions and make logical reasonings across varying expert knowledge.

CONCLUSIONS: This work demonstrates the advantages of using semantic web technologies as a general platform for knowledge representation, data integration and semantic query answering. By leveraging existing vocabularies and adopting web standards, this knowledge framework proves to be more useful and is able to support data repurposing beyond the original intent. The resulting knowledge base can now act as a nucleation point for systems toxicogenomics knowledge on the emerging Semantic Web. Scientists will be able to utilize and generate new

hypotheses for further researches and validations in the environmental and toxicogenomics fields.

2.10 Expression of Endoglin On Cultured Mouse Bone Marrow Cells Correlates With Mesenchymal Stem Cell Function

J. Fair[1], J. Mehic[1], and M. Rosu-Myles, PhD[1]

[1] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

SUMMARY: The assessment of mesenchymal stem cell (MSC) based biologics would benefit greatly from a rapid and efficient method for determining product purity and efficacy. Described here are experiments demonstrating the potential of using Endoglin expression as a marker of cultured MSC.

BACKGROUND/OBJECTIVE: Bone marrow (BM) derived mesenchymal stem cells (MSC), have tremendous potential as a biologic for use in regenerative medicine. Unfortunately, standard methods for detection of MSC are time consuming and non-quantitative, preventing the ability to rapidly determine product purity and predict efficacy. The development of methods for enumerating MSC has been hampered by the absence of known MSC markers. A candidate marker of MSC is the Endoglin protein, which was recently found to be expressed on a population of cells within MSC containing cultures. The objective of the present study was to determine whether the detection of Endoglin expressing cells in BM derived cultures correlates with the presence of MSC.

METHODS: Mouse BM cells were cultured in MSC expansion media for a period of ninety-six days. At fourteen-day intervals, the frequency of Endoglin expressing cells within the cultures was measured by flow cytometry and the presence or absence of MSC was determined using standard methods.

RESULTS: Cultured BM cells showed plastic-adherent properties typical of MSC and contained a distinct population of Endoglin expressing cells that was detectable up to seventy-four days. The frequency of cells expressing Endoglin was maintained at 11.7% for a period of forty days. After fifty-four days the frequency dropped to 5.7% and then decreased linearly every 14 days. By standard assay methods, MSC were detected in the BM derived cultures for a period of seventy-four days.

CONCLUSION/NEXT STEPS: These data suggest that Endoglin expression correlates with the presence of MSC in mouse BM cultures. In the future, assays comparing MSC function in purified Endoglin expressing and non-expressing cells will be completed to confirm this protein as a marker of cultured MSC.

2.11 Comparison of Cross-Interactivity of Environmental Pollutants to Double-Stranded DNA and Single-Stranded DNA

Y.-L. Feng, PhD[1], X. Liao, PhD[1], J. Zhu, PhD[1], B. Xiao[1], and M. Rubab[1]

[1] Exposure and Biomonitoring Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: The DNA relative interaction potencies of environmental contaminants have been investigated by comparing their interaction potencies to that of benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE) using a double-stranded oligonucleotide as the monitoring probe. The behaviours of the double-stranded oligonucleotide as the probe have also been compared with that of single-stranded oligonucleotide by both method sensitivity and the probabilities being attached by the agents.

OBJECTIVES/BACKGROUND/ISSUE(S): Interactions of chemicals with DNA may lead to its potential damage and instability, disruption of cellular metabolic processes, irreversible genetic damage, and genotoxicity or carcinogenicity. Information on interaction between DNA and chemicals or their metabolites is important in evaluating the potential carcinogenicity and genotoxicity of chemicals, and hence their potential risks to human health. Although DNA interactions have been well used to evaluate the activity and affinity in natural products, the uses of the interactions in estimating DNA interaction potency and the cross-interactivity of environmental pollutants especially in gas phase have not been attempted so far. DNA interaction potency of a chemical can be defined as the degree of a chemical's ability to interact with DNA. The aim of this study is to develop a chromatography-based tool by which a relative interaction potency scale can be established to estimate the DNA cross-interactivities of five test chemicals (PEQ(50) – the DNA interaction potency equivalency of testing chemical at 50% of the probe peak reduction) by the peak reduction of the DNA probe resulting from the interaction against benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE).

DESIGN/METHOD/DESCRIPTION: A high-performance liquid chromatogram method was developed to monitor the DNA probe by Diode-array Detector (DAD) detector and test chemicals were incubated with either double-stranded or single-stranded DNA, respetivley. The peak reduction on the chromatogram was used to predict the DNA interaction potency of the chemicals. A DNA interaction potency equivalency (PEQ) or called cross-interactivity at 50% of the probe peak reduction (PEQ(50)) was proposed to evaluate the relative interaction potency of test chemicals against benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE).

OUTPUTS/RESULTS: Five known direct DNA interaction chemicals BPDE, phenyl glycidyl ether (PGE), tetrachlorohydroquinone (Cl_4HQ), methyl methanesulfonate (MMS) and styrene-7,8-oxide (SO)) were employed to demonstrate the method. Two known inactive chemicals were used as negative control. Both the potency and PEQ(50) values of these five chemicals shown an order of BPDE > PGE > Cl_4HQ > MMS > SO for their DNA interaction potency. As a DNA probe, double-stranded oligonucleotides have provided similar cross-interactivities of the chemicals with single-stranded one, which may indicate that the hindrance of double-stranded chain in DNA would not affect the attacking of genotoxic chemicals.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This study provided important information that the either double-stranded DNA or single-stranded DNA can be used as the probe to estimate the cross-interactivities of environmental pollutants to DNA. The hindrance of naked double-stranded DNA will not be the issue for the attacking of genotoxic chemicals. The developed assay could be very useful to screen the DNA cross-interactivity of active contaminants in environment such as diesel exhaust gas.

2.12 Computational Tool for the Enumeration of Neutrophils in 3-D Images Generated by Confocal Laser Scanning Microscopy

R. Gagné[1], K. Nguyen[1], and A.F. Tayabali[1]

[1] Mechanistic Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Neutrophil enumeration is used by scientists to measure lung inflammation provoked by exposure to Pseudomonas bacteria. We developed an ImageJ plug-in to automate the cell counting process in 3D images. Parameters of the plug-in can be modified by the user and customized so that batch processing can be performed.

BACKGROUND: One application of Pseudomonas in biotechnology is soil bioremediation, which is efficient and costs less. However, the hazardous mammalian health effects of Pseudomonas used in for these applications on mammals have not been well characterized. One of the potential acute consequences of lung exposure to Pseudomonas is tissue inflammation, measured by neutrophils accumulating at the site of infection. To measure the neutrophil infiltration, the lungs of mice previously exposed to Pseudomonas were excised and sectioned. Two stains were applied to the tissue. One targets the cell nucleus and is non selective, whereas another targets specifically neutrophils, Confocal Laser Scanning Microscopy is then used to capture 3D images of the stained tissue.

METHOD: An ImageJ plug-in was developed to analyze the 3D images. ImageJ is a customizable Java application originally created by the NIH. When launched, the plug-in creates two copies of the image stack, where the 1st is used to segment the neutrophil nucleus and the 2nd to segment neutrophils without their nuclei. The stacks are then merged by median filter in a ternary color scheme. Particles in the stack are then enumerated and characterized by voxel propagation.

OUTPUTS/RESULTS: The plug-in was tested using 3 datasets of 60, 65 and 70 images having a resolution of 512 x 512 pixels. The confusion matrix presented below shows the output of 3 test cases. Values in the matrix represent the number of cells found in the stacks.

		actual value		
		p	*n*	total
prediction outcome	*p'*	57/24/61	0/0/1	P'
	n'	6/4/8	0/0/0	N'
	total	P	N	

Fig1. Confusion matrix of plug-in test cases

One must emphasize that “actual values” were collected by human interpretation and do not necessarily represent the accurate values, but an alternate enumeration method used for validating the performance of the plug-in.

CONCLUSIONS: This ImageJ plug-in provides a quick and easy solution for bicolour cell enumeration. The plug-in permits greater sample throughput and accuracy (reduction of human subjectiveness), as well as eliminating a tedious procedure. Adaptations to this plug-in could easily be made to perform other types of enumerations. Future work could include particles shape descriptors and classifiers to limit type I and II errors.

2.13 Blood Transfusion Chain Errors Captured in PHAC's National Transfusion Error Surveillance System (1st Two Quarters of 2008)

P.E. Alexander[1], C. Hyson[1], and P. Robillard[1]

[1] Transfusion-Transplantation Adverse Events (TTAE) unit, BSSHCAID, PHAC, Ottawa, ON

SUMMARY: Blood transfusion services must have procedures to collect error and injury information to ensure corrective actions. The Transfusion Error Surveillance System (TESS) is a hemovigilance surveillance system for transfusion errors nationally, and developed by the Public Health Agency of Canada (PHAC). The first 2 quarters of 2008 will be studied.

OBJECTIVES/BACKGROUND: The morbidity, mortality, and monetary costs associated with transfusion errors and patient recollection is significant. TESS surveillance aims to collect information on Canadian blood transfusion errors and injuries to ensure corrective actions are implemented by the users, within participating provinces. This analysis/poster presents the high severity errors (HS) with a focus on nurse and doctor involvement.

METHODS: TESS uses standardized coding. Ongoing training is provided to hospitals/provinces/territories participating in TESS surveillance. All data are captured anonymously on a web-based secured server. Among types of transfusion errors, those that could result in harm to the patient and classified as 'high severity' events, deserves particular focus for this abstract. Doctors and nurses are the focus.

RESULTS: From January to June 2008, 6,932 errors were reported of which 809 were HS (11.7%). Of these, 10.4% involved a doctor and 45.5% a nurse. For HS events involving doctors (10.4%), 13.1% occurred in emergency wards, 21.4% Intensive Care Unit (ICU), 48.8% (medical/surgical ward), 7.1% (operating rooms), 2.4% (outpatient procedures), and 7.1% (outpatients). HS were detected after issue in 13.1% and 67% occurred from 8 am to 4 pm. A no recovery-no harm error emerged in 9.5%, a near miss-unplanned recovery in 2.4%, and a near miss-planned recovery in 88.1%. A product request error emerged in 83.3% of HS, involving an inappropriate order of a blood product. In 2.4%, the product was not labelled and the label was incomplete/ illegible for key patient identifiers in 3.6%. Paperwork and sample ID did not match in 2.4%.

Of the 45.5% of HS errors involving nurses, 28.5% occurred in emergency wards, 26.0% (ICU), 26.5% (medical/surgical wards), 7.0% (obstetrics), 2.4% (operating rooms), 5.4% (out-patient procedures), 3.2% (out-patients), and 0.3% in recovery room and supplier/provider. HS were detected after issue in 9.5% of cases and 46% occurred from 8 am to 4 pm. A no recovery-no harm error emerged in 3.5% of cases, a near miss-unplanned recovery in 3.2%, and a near miss-planned error recovery in 92.9%. An order for the wrong patient emerged in 8.4%. Sample collection errors comprised 64.0%. Specifically, 5.4% were samples labelled with the wrong patient identification, 10.0% not labelled, and 46.6% involved label incomplete without key patient identifiers. In one case, the armband was incorrect. A request for pick-up of the wrong patient occurred in 7.9%. In 8.1%, the paperwork and sample ID did not match and in one transfusion HS, the product was administered to the wrong patient.

OUTCOMES/CONCLUSIONS: Most doctor and nurse HS errors occurred in emergency wards, ICUs, and medical/surgical wards, along with outpatient procedures. Serious HS, i.e., ordered for the wrong patient, requesting pickup of the wrong patient or armband incorrect, continue to occur. While a small proportion, the clinical outcome could be grave and thus the continual need for error risk mitigation. Electronic identification (barcode) technology may increase transfusion safety along with continual training of transfusion personnel, which includes support from leadership within health care institutions.

2.14 The Zoonotic Potential of Rotaviruses

S. Lamhoujeb, PhD[1], A. Cook, PhD[2], F. Pollari, PhD[2], S. Bidawid, PhD[1], J.M. Farber, PhD[1], and K. Mattison, PhD[1]

[1] Microbiology Research Division, Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON
[2] Laboratory for Foodborne Zoonoses, PHAC, Guelph, ON

SUMMARY: Rotaviuses are the common agents of diarrhoeal illness of infants. A phylogenetic characterization of VP4, VP6, VP7, and NSP4 segments using a new published classification system allowed the identification of re-assortment event between animal and human rotavirus genotypes and highlighted the zoonotic potential of theses agents.

OBJECTIVES/BACKGROUND/ISSUES: Rotavirus is the major cause of severe infantile diarrhoea worldwide and is an important pathogen in various animals. The segmented nature of the rotavirus genome provides an opportunity for genetic re-assortment and emergence of new rotavirus strains with variable antigenic properties. Characterization of domestic animal rotavirus strains is important to understand rotavirus diversity and to identify potentially zoonotic infections.

DESIGN/METHOD/DESCRIPTION: Rotaviruses were detected in a number of animal fecal samples from swine and cattle farms in southern Ontario, Canada. To evaluate the zoonotic potential and to detect re-assortment among these strains, the segments encoding for viral protein 4 (VP4), VP6, VP7 and for non-structural protein 4 (NSP4) have been sequenced from 15 fecal samples.

OUTPUT/RESULTS: The classification system proposed recently by Matthijnssens et al., (2008) allowed the identification of porcine rotavirus strains with VP4, VP6, VP7 or NSP4 genes belonging to typical human genotypes (G4 and G2). Moreover, the identification six porcine strains possessing G4P6 as genotype indicate that re-assortment between animal and human genotypes is a common event within rotavirus strains that plays an important role in their genetic diversity. Our data allowed us to identify two rotavirus strains, bovine and porcine, belonging to G10P11 and G9P6 respectively. These typical animal genotypes have been found in human cases.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The sequences will be compared to strains isolated from retail meat samples in order to determine if the genetic diversity represented in animal rotaviruses is representative of strains to which humans may be exposed.

2.15 Simultaneous Measurement of Benzo[a]pyrene-Induced pigA and lacZ Mutations, and Micronuclei in Muta™Mouse

C.L. Lemieux[1], J. Gingerich[1], L.M. Soper[1], S. Phonethepswath[2], D. Torous[2], S. Dertinger[2], P.A. White[1], and G.R. Douglas[1]

[1] Mechanistic Studies Division, Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] Litron Laboratories, Rochester, NY, USA

SUMMARY: We used transgenic mice to validate the utility of a novel mutation assay that employs the pigA gene. Here, we show that there is a strong concordance between the frequency of mutant pigA phenotypes and two well-studied genotoxicity endpoints, suggesting that this may be a promising novel mutation assay.

OBJECTIVES/BACKGROUND ISSUE(S): The aim of this study was to simultaneously measure micronuclei and mutations in the *pigA* and *lacZ* genes of Muta™Mouse following exposure to a known mutagen.

DESIGN/METHOD/DESCRIPTION: 25-week old male transgenic mice, (i.e, Muta™Mouse, strain 40.6) were dosed daily for 28 days with benzo[a]pyrene (0, 25, 50 and 75 mg/kg/day by gavage). Following a subsequent 72h expression period, mice were sacrificed, and tissues and blood were collected. The *lacZ* transgene mutant frequency (MF) was determined by PGal positive selection in DNA isolated from bone marrow. *pigA* mutants were measured by antiCD24 flow cytometry of reticulocytes (RET). Micronucleus frequencies were also measured in RETs and normochromatic erythrocytes (NCE) by flow cytometry.

OUTPUT/RESULTS: A significant dose-dependent increase in pigA phenotypes was observed in RET. Matched samples from the same animals showed a significant dose-related increase in *lacZ* MF in the bone marrow, which was approximately 25x higher than that observed for *pigA*. This difference could be due to factors such as the greater target size of *lacZ* and/or differences in the optimal sampling time for these endpoints. Significant dose-related increases in the % micronuclei were also observed for NCE and RET in these same animals.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The dose responses of all three endpoints followed virtually the same linear kinetics, suggesting that similar mechanisms were at play in their induction. Furthermore, the similarity in the response of *pigA* and *lacZ* provides evidence that pigA mutant phenotypes likely result from mutant genotypes, since there is ample evidence for the gene mutation origin of lacZ mutant phenotypes. Overall, the results of this study provide evidence toward validating the use of *pigA* as a target gene for mutagenicity testing. Further research should include testing of other compounds, and a comparison of *pigA* mutagenicity data to other genotoxicity endpoints (e.g., DNA adduct frequencies).

2.16 Gene Expression Changes in Murine Epithelial Lung Cells Exposed to Marijuana and Tocacco Smoke Condensates

R.M. Maertens, MSc[1], P.A. White, PhD[1], C.L. Yauk, PhD[1], M. Malowany, MSc[1], A. Williams, MSc[1], M.L. Charlebois, MSc[1], and S. Desjardins, PhD[2]

[1] Research and Radiation Directorate, HECSB, Health Canada, Ottawa, ON
[2] Tobacco and Drugs Directorate, HECSB, Health Canada, Ottawa, ON

SUMMARY: This study examined the relative ability of marijuana and tobacco smoke condensates to cause changes in gene expression in a mouse lung cell line. The results provide insight into the toxicological pathways that are induced when cells are exposed to marijuana vs. tobacco smoke.

OBJECTIVES: The risks of adverse effects from exposure to marijuana smoke, as compared to tobacco smoke, are not well understood. In order to gain insight into putative modes of action, the objective of this study is to investigate the toxicological pathways induced by marijuana vs. tobacco smoke condensate using genome wide expression profiling.

DESIGN: Condensates of mainstream smoke from hand-rolled marijuana and tobacco cigarettes were prepared using standard (i.e., ISO) smoking conditions. Murine lung epithelial cells (designated FE1 cells) were exposed to smoke condensates for a six-hour period, and either harvested immediately or allowed to recover for four hours. Total RNA was extracted from the cells and hybridized to whole mouse genome microarray slides. A LOWESS normalization was applied and statistically significant genes were identified using ANOVA analysis with the MAANOVA library in R.

OUTPUT/RESULTS: The results revealed 4,700 significantly differentially expressed genes (false discovery rate corrected p-value < 0.05) in cells exposed to marijuana smoke condensate. In contrast, 2,400 genes were differentially expressed following exposure to tobacco smoke condensate, and 1,422 genes were common to both condensates. Preliminary inspection of the data reveals that the genes within each condensate with the highest fold changes in expression (e.g., *Cyp1a1, Gsta1, Tiparp, Ptgs2, Maff, Casp4*) are associated with xenobiotic metabolism, inflammation, stress response, and cell cycling.

IMPACTS/OUTCOMES: Marijuana smoke contains many of the same chemical components found in tobacco smoke, and like tobacco smoking, habitual marijuana smoking causes adverse pulmonary reactions. However, the mechanisms of action and the carcinogenic potential of marijuana smoke are still unclear. The use of gene expression profiling will help elucidate the toxicological pathways induced by exposure to marijuana smoke as compared to tobacco smoke.

2.17 Evaluation of the NoroChip3.0 for Confirmation and Typing of Noroviruses

A. Martyres[1,2], N. Corneau, MSc[1], F. Pagotto, PhD[1,2], S. Bidawid, PhD[1], and K. Mattison, PhD[1,2]

[1] Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON
[2] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

SUMMARY: Noroviruses are the leading cause of gastroenteritis in the world. They are highly variable and many strains cause human illness. We have developed a DNA microarray for the confirmation and genotyping of norovirus strains in a single step. We present the evaluation of this chip in international partner laboratories.

OBJECTIVES/BACKGROUND/ISSUES: The noroviruses are detected using sensitive molecular assays. Unfortunately, because of the strain variation among human noroviruses, the specificity must be reduced to detect all strain variants. Putative isolates must be confirmed and genotyped, in a lengthy process of conventional RT-PCR, purification and sequencing. A NoroChip3.0 microarray was developed to simplify and speed up this step. We present the validation of the performance of NoroChip3.0 in norovirus typing.

DESIGN/METHOD/DESCRIPTION: Norovirus genomes were amplified by RT-PCR, labelled with Cy3 and hybridized to the NoroChip3.0. This was accomplished, in triplicate, for 22 reference strains in our lab and 10 strains each in partner labs in Norway, Spain and Chile. Data were analyzed using ArrayPro and UPGMA matrices. Clusters derived from NoroChip3.0 analysis were compared to those achieved by traditional sequencing.

OUTPUT/RESULTS: The NoroChip3.0 successfully distinguishes between genogroups in our reference set as well as in partner labs. Some cluster types are well separated by the NoroChip and some need additional work. The protocols have been successfully transferred to international collaborators.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The NoroChip3.0 represents an exciting step towards rapid methods for norovirus typing. We await data from 7 other partner labs to complete the analysis. The information from this validation study will be used to refine the design and analysis of the NoroChip3.0 data and simplify the experiment to develop a rapid and easily interpretable protocol for norovirus genetic typing.

2.18 Development of a Novel Carbohydrate Based Detection Method for Norovirus

V. Morton[1,2], J. Jean[3], J.M. Farber[1,2], and K. Mattison[1,2]

[1] Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON
[2] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON
[3] Institut des Nutraceutiques et des Aliments Fonctionnels, Université Laval, Québec, QC

SUMMARY: Norovirus is a leading cause of foodborne gastroenteritis. A method to detect norovirus contamination in food samples was developed based on the known interaction between norovirus capsids and human blood group antigens. This method is rapid, simple and able to detect low levels of contamination.

OBJECTIVES/BACKGROUND/ISSUES: Norovirus is a highly contagious human virus, which causes acute gastroenteritis. They have a very low infectious dose (10-100 viral particles) and spread easily via the fecal oral route. It is estimated that 40% of norovirus infections are caused by contaminated foods. Norovirus have been shown to bind to histo-blood group antigens (HBGA) present on the surface of red blood cells and epithelial cells of the digestive tract. This specific interaction can be used to concentrate virus particles before detection. This is extremely important because of the low infectious dose and the lack of a cell culture system.

DESIGN/METHOD/DESCRIPTION: This study developed a method for detecting noroviruses in food samples using the specific binding interaction between norovirus capsids and HBGAs. Streptavidin magnetic beads were coated with biotinylated HBGAs were added to the sample. The beads were then collected using two different magnetic collection systems, the Pathatrix™ and iCropTheBug. The amount of norovirus captured by the beads was quantified using reverse transcriptase real-time PCR.

OUTPUT/RESULTS: We successfully detected norovirus from a variety of spiked food matrices including strawberries, green onions, lettuce and deli meat. Our system was also able to recover a variety of different norovirus strains. The end goal of this project is to develop a standardized method for detection of norovirus contamination in food products.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Current work is focused on adding Feline Calicivirus as an internal process control to the method. We are also evaluating the detection limits of this method against a standard absorption/elution detection method for foodborne viruses.

2.19 Genomics Research and Development Initiative in Health Canada: Accomplishments in the Last Decade and Prospects for the Future

S. Pandian[1], B. Colton[1], S. Sloss[1], A. Newchild[1], and L. Roe[1]

[1] Science Policy Directorate, SPB, Health Canada, Ottawa, ON

SUMMARY: Genomics R&D Initiative (GRDI) established in 1999, was funded to strengthen the genomics research capacity in the federal science departments involved in biotechnology. This paper summarizes Health Canada's tremendous achievements in the past decade and outlines the strategic changes planned for the future.

OBJECTIVES: We describe here, the major accomplishments since the beginning of GRDI, in terms of scientific publications, new technology platforms developed, major conferences hosted, significant contributions to international policy harmonization, as well as scientific and technical personnel trained.

METHOD: The Science Policy Directorate has designed and developed a Genomics database, where the Principal Investigators across the department are contributing on a regular basis, not only scientific progress information but also information on financial and human resources management. This database, combined with personal consultations with scientists, has allowed us to collate this information that the department can proudly showcase.

RESULTS: As just a few examples, we cite:

- the development and application of "omics" tools for analysis and reduction of exposure to food borne pathogens;
- extensive plasmid genomic profiles have allowed us to develop surveillance and rapid response program in Salmonella outbreaks- a made in Canada innovation;
- rapid advances made in studying environmental toxicogenomics- such as multiplex liquid protein arrays to diagnose allergens and mutagenic biomarkers;
- improved pharmacogenomics methodologies developed in Health Canada have generated better analysis of potential health risks of novel therapies and therapeutics;
- genomics study of intestinal bacteria and their metabolic responses have allowed us a much better understand the dynamics of nutrigenomics,
- the Public Health Agency of Canada (PHAC) which is part of the Health Portfolio, has advanced in understanding the gene-prion interactions in pathogenesis, which also was extremely valuable in guiding pre-clinical trials of new drugs in this field;

IMPACTS: Targeted funding towards capacity building in a new technology domain has proved to be an extremely fruitful investment for Health Canada in developing into a world-class regulator of consumer products, health products and food. This funding has allowed the department to build expertise and to draw valid scientific advice to support our regulatory decisions.

2.20 Characterization of Thyroid Hormone Mediated Gene Expression in Juvenile Mice Liver

M. Paquette[1], H. Dong[2], M. Malowany[3], M. Wade[2], and C.L. Yauk[1]

[1] Mechanistic Studies Division, HECSB, Health Canada, Ottawa, ON
[2] Hazard Identification Division, HECSB, Health Canada, Ottawa, ON
[3] Population Studies Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: DNA microarrays were used to identify genes that are directly responsive to alterations in thyroid hormone (TH) levels in developing liver. Preliminary data confirmed the response of known TH-responsive genes and also identified a large number of genes that had not previously been shown to be affected by THs.

BACKGROUND/OBJECTIVES: THs play a critical role in growth, development and metabolism. The primary effect of THs is the transcriptional regulation of targeted genes. In order to develop an understanding of THs control of development, the effects of hyper- and hypothyroidism on gene expression in juvenile mice liver are currently being evaluated. The main objective of this research project is to develop a stronger understanding of the mechanisms by which TH modulates development in the liver.

METHOD: Hypothyroidism was induced from post-natal day 13 to 15 by adding goitrogens methimazole and sodium perchlorate to dams' drinking water. Gene expression was examined by hybridization of hepatic RNA to Agilent mouse microarrays (~41 000 genes) for hypothyroid and control animals. A LOWESS normalization was applied. Genes were indentified by absolute fold-change greater than 1.5.

RESULTS: Analysis of hypothyroid livers revealed 566 and 215 significantly altered genes in males and females respectively, with an overlap of 116 genes. Regulation of well-characterized TH-responsive genes was confirmed, validating the gene list. This includes spot14 and deiodinase1, which were significantly down-regulated in both males and females. The primary pathways affected by hypothyroidism were related to metabolism, more specifically a group of down-regulated genes were found to be involved in protein degradation, indicating that TH, as expected, affects the regular metabolic activity of the liver. Hundreds of novel candidate genes that are potentially directly regulated by THs are being validated using gene expression and other assays.

CONCLUSION/NEXT STEPS: Preliminary data indicate a strong hepatic response following short-term perturbations of TH levels in juvenile mice. Upcoming work will identify TR binding sites and target genes using ChIP-on-chip analysis. The long-term goal of this research is to establish a tissue specific marker of thyroid hormone action for use in studies to detect thyroid-disrupting chemicals (TDCs).

2.21 Development and Safety Evaluation of Nanomaterials for Encapsulation and Delivery of Stem Cells to Dysfunctional Heart Tissue

M. Rafat, PhD[1], J. Karov, PhD[1], M. Griffith, PhD[4], D. Courtman, PhD[3], Z. Arzhangi, MSc[4], and J.N. Daka, PhD[2]

[1] Device Surveillance Division, Medical Devices Bureau, HPFB, Health Canada, Ottawa, ON
[2] Research and Radiation Directorate, Healthy Environment and Consumer Safety, Health Canada, Ottawa, ON
[3] The Ottawa Hospital Research Institute, Ottawa, ON
[4] Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON

SUMMARY: Tissue-specific delivery of stem cells holds the potential to regenerate damaged heart tissue and to restore its functions after Myocardial Infarction. In this study we describe a novel cell encapsulation technique for target delivery of stem cells to damaged heart tissue. This research is conducted in collaboration with OHRI and UOttawa.

BACKGROUND/ISSUE(S)/OBJECTIVES: Heart failure is the number one cause of death in developed countries. Stem cell transplantation has drawn a lot of attention as a promising therapy for heart disease. However, extensive cell attrition, and loss at the site of transplantation present a limit to therapeutic efficacy. We have hypothesized that by encapsulating the cells in naturally-derived materials, e.g., collagen and alginate, cells viability, and target delivery can be enhanced. Our main objective is to develop encapsulation techniques for effective delivery of stem cells. The other objective is to develop characterization techniques for safety evaluation of such systems at nano and micro scales.

DESIGN/METHOD/DESCRIPTION: Novel collagen-alginate microspheres loaded with GFP-BOEC cells (green florescence expressing -blood outgrowth endothelial cells) were developed. The method involves the gelation of a hybrid collagen-alginate-cell solution using a drop-wise technique in a calcium chloride bath. Microspheres were washed and transferred to a Petri dish containing culture medium and incubated at 37°C. Microspheres formation, and morphology (shape and size) and viability of the cells were monitored using a Nikon inverted light microscope.

OUTPUTS/RESULTS: Light microscopy images suggest successful formation of hybrid collagen-alginate microspheres in a size range of about 1000-2000 µm. The images also show that cells fluoresce an apple green when excited with near UV light implying that most of the cells are viable.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Preliminary results from these experiments reveal that GFP-BOEC cells can be encapsulated in collagen-alginate microspheres. The results suggest that cells are viable over a period of three days. Also, light microscopy techniques were successfully utilized for physical (i.e., shape and size) and biological (i.e., viability) characterizations of microspheres. The next steps will include the use of Mesenchymal Stem Cells instead of GFP-BOEC, fine-tuning of material formulations, and further characterizations, i.e., scanning electron microscopy (SEM). We anticipate that this work will help us to better understand new emerging technologies such as nanotechnology, stem cells therapeutics, and tissue

engineering that will ultimately benefit the regulatory process of medical products that are based on such technologies.

2.22 Cross-Platform Comparison of MicroRNA Techniques

A. Rowan-Carroll, MSc[1], A. Williams, MSc[2], K. Jackson, PhD[3], C.L. Yauk, PhD[1]

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

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

SUMMARY: Largely unstudied for the last 15 years, microRNAs regulation of the genome is a major focus of research into gene regulation. MicroRNAs have been found in a wide variety of plant and animal tissues, and have been implicated in numerous disorders and diseases. In this study we compare the technical and biological reproducibility of two microRNA platforms (Agilent and Exiqon) to ensure that the platforms produce reproducible results.

DESIGN: MicroRNA are short single stranded RNA molecules that range in length from 19-23nt. Although microRNAs are not translated to functional proteins, they are partially homologous to many messenger RNA (mRNA) sequences, which they bind to and down regulate. The ability of a single microRNA transcript to regulate hundreds of mRNA transcripts indicates their importance in the transcriptome. MicroRNAs have been implicated in numerous disorders and disease. In particular, deregulation of microRNAs has been implicated in the development of certain cancers. In this study we performed a referenced based dye swap comparison between Agilent and Exiqon microRNA microarray platforms, in order to assess 1) reproducibility of microarray data within a platform, 2) to examine cross platform variability between two highly used commercially available microRNA platforms and 3) to carry out technical validation exercises to ensure that the platforms used produce reproducible, accurate and sensitive results.

Two standard references microRNA samples where made and technical replicates, as well as dye swap experiments where preformed using both Agilent and Exiqon chips. Data was normalized using quantile normalization and technical replicates were averaged. Using the collapsed technical replicates, a fold change ranking comparison was generated for each platform and compared using the concordance at top plot (CAT plot) (3,4) to examine the percent of overlap between the top changing genes from each of the platforms.

OUTPUT: Technical reps within platforms were found to be highly reproducible. The average correlation within a platform was 0.9415 for Exiqon and 0.9943 for Agilent. Matched probe cross-platform concordance analysis of the top ranked 100 genes revealed a 65% concordance between platforms, which is consistent with previous published findings.

IMPACTS: The result of this study provides valuable information about advantages/ disadvantages of using two widely used microRNA microarray platforms. In conclusion, results from this basic analysis of platform design will effectively allow us to interpret data derived from these two types of arrays.

2.23 A Simple GC-(ion trap) MS/MS Based Analytical Method for the Measurement of 8-Epiprostaglandin F2α (8-isoprostane) in Human Plasma

G. Saravanabhavan[1], R. Vincent[2], and P. Kumarathasan[1]

[1] Proteomics Laboratory, Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON

[2] Inhalation Toxicology Laboratory, Environmental Health Sciences and Research Bureau, HECSB, Health Canada, Ottawa, ON

SUMMARY: The lipid metabolite 8-isoprostane is an established biomarker of oxidative stress. Current methods for analysis of 8-isoprostane are cumbersome and require extensive sample purification. We report the use of immunoaffinity purification to recover 8-isoprostane from a complex matrix followed by GC-(ion trap) MS/MS analysis. While simpler and faster, the procedure retains the analytical performance of existing standard methods.

BACKGROUND AND OBJECTIVES: The attack of arachidonic acid by reactive oxygen species forms a family of compounds that resemble prostaglandins in structure. Among these compounds, 8-epiprostaglandin F2α, or 8-isoprostane, has been shown to result from free-radical damage to lipids and has been adopted as a biomarker of oxidative stress. Several analytical procedures based on chromatographic techniques such as gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) have been developed for 8-isoprostane analysis from biological fluids. However, due to the presence of other prostaglandin-like compounds structurally very similar to 8-isoprostane, most of the existing analytical methods require extensive sample purification steps. Moreover, multi-step derivatization procedures are applied to increase detection of 8-isoprostane in GC-MS analysis. In those assays, sample preparation becomes cumbersome and incompatible with high throughput analyses. Commercial immunoassays are available for 8-isoprostane, but sensitivity and assay-to-assay performance are less reliable. We report a simpler and faster method for the analysis of free 8-isoprostane present in human plasma samples. The method is based on immunoaffinity purification followed by one-step derivatization prior to GC-(ion trap) MS/MS analysis.

METHOD: Two hundred microliters of plasma sample was diluted to 1 mL with eicosanoid affinity column buffer and spiked with deuterated 8-isoprostane standard. The sample was applied to a preconditioned eicosanoid affinity column and the entire sample was allowed to pass through the column by gravity. After washing the column buffer followed by ultrapure water, 8-Isoprostane was eluted with 95% ethanol. The sample was evaporated to dryness under nitrogen stream and then derivatized with N,O-bis(trimethylsilyl) trifluoroacetamide. After derivatization the sample was evaporated to dryness and reconstituted in isooctane prior to final GC-(ion trap) MS/MS analysis.

RESULTS: Our imunnoaffinity purification procedure coupled to GC-MS/MS detection can quantify as low as 2 ng (injected mass) isoprostane with a linear dynamic range of 1-1000 ng. The recovery of a deuterated internal standard was always better than 90%. The intra- and inter-assay imprecision was less than 7%.

IMPACT/OUTCOME: The improved procedure for analysis of 8-isoprostane in human plasma is simpler and faster, while retaining the excellent analytical performance of the standard methods. The new procedure will be valuable in a number of active studies in which we are monitoring oxidative stress in human subjects in response to exposure.

2.24 Analysis of Tyrosine Metabolites as Oxidative Stress Biomarkers in Human Urine Using HPLC-EC Array Technique

G. Saravanabhavan[1], E. Blais[1], R. Vincent[1], and P. Kumarathasan[1]

[1] Environmental Health Centre, Health Canada, HECSB, Health Canada, Ottawa, ON

SUMMARY: Oxidative stress can be assessed by measuring specific biomarker levels in body fluids, such as urine. Oxidative metabolism of tyrosine produces several stable metabolites that are widely used as markers of oxidative stress. In this work an analytical method was developed to measure simultaneously several tyrosine metabolites in human urine using liquid chromatography-coularray detection technique.

BACKGROUND: Oxidative stress has been implicated in various pathologies as well as in environmental pollutant-induced negative health outcomes. Proteins are one of the primary targets for the attack by reactive oxygen and nitrogen species. Phenylalanine and tyrosine residues when oxidized form stable metabolites that are widely used as biomarkers for oxidative stress. Several analytical methods exist for the analysis of tyrosine metabolites in human plasma. These metabolites are eventually excreted in urine. Moreover, collection of human urine is easy and non-invasive compare to that of plasma. Hence, in this work we have developed a HPLC-coularray based analytical method for the simultaneous analysis of p-,o-,m-tyrosine, 3-nirotyrosine, 3-chloro tyrosine, and the DNA damage marker 8-hydroxy deoxyguanosine (8-OH dG).

ANALYTICAL APPROACH: Sample preparation involves the base hydrolysis of urine followed by solid phase extraction of target analytes using reverse phase polymeric sorbent. The purified sample was then analyzed using HPLC-coularray technique. The coularray detector consists of 12 electrochemical cells that were maintained at increasing positive potentials (0 – 800mV). The analytes were identified at different detector channels based on their oxidation potential. Each analyte was quantified using an eight-point external calibration curve.

RESULTS: The developed analytical method can detect the target analytes at concentrations as low as 5 pM with a linear dynamic range between 150 nM and 2 pM. Recovery of target analytes, measured by spiking different concentration of individual analytes to the urine matrix, showed reproducible recoveries and were generally over 50%. Inter- and intraday variation of the assay was lower than 7%. The applicability of the method was demonstrated by measuring these compounds in healthy human urine (n =10) samples.

OUTCOME/IMPACT: Our group has been involved in the analysis of biomarkers in various biological fluids such as plasma, saliva and lavage. This current method would enable us to expand our field of investigations into urine analysis and this method will be used to investigate samples received through the HC-mandated MIREC (Maternal-Infant Research on Environmental Chemicals) objectives.

2.25 Characterisation of the Interactions Between the Conserved Hydrophobic Region of the Prion Protein and a Model Membrane by NMR

S. Sauvé, PhD[1], D. Buijs, MSc[1], and Y. Aubin, PhD[1]

[1] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

SUMMARY: Transmissible spongiform encephalopathy diseases, also named prion diseases, result from the conversion of the normal cellular prion protein to a misfolded, infectious form that is responsible for neurodegeneration. There are scientific evidences suggesting that the cellular membrane may be a potential player in the generation of some types of infectious form. Here we present an atomic-level characterisation of the interactions between a domain of the prion protein and a model membrane system.

OBJECTIVE: Determine the structure of the conserved hydrophobic region (CHR) of the prion protein in dodecyl phosphocholine (DPC) micelles as a membrane model.

METHOD: A labelled peptide representing the CHR from residue 110 to 136 of the prion protein was produced in *E. coli* and purified. The labelled peptide was dissolved in DPC micelles and the three dimensional structure was determined by NMR. Titration of paramagnetic ions such as gadolinium and manganese allowed the determination of the position of the peptide relative to the micelle surface.

RESULTS: A high resolution, three-dimensional structure of the CHR peptide in the micelle has been calculated from NMR data. The peptide adopts an alpha helical conformation in DPC micelles. Paramagnetic relaxation enhancement (PRE) experiments indicate that the helix spans the micelle with residues near or above the surface. Titration of a DPC solution into a solution of labelled peptide revealed that the latter first binds to the surface of the micelle before insertion. In addition, PRE experiments showed that the surface- bound specie interacts strongly with the surface, probably below the lipid headgroup-water interface.

IMPACT: The causative agent of prion diseases is a misfolded form, called the scrapie or infectious form, of the normal cellular prion protein. This conversion can occur in a sporadic fashion or by ‘contact’ with infectious material. To date, the factors responsible for the sporadic conversion are still unknown and it has been postulated from work on transgenic mice that CHR-membrane interactions could modulate this process. Our findings provide an atomic-level description of these interactions.

2.26 Development of a Rapid Imunochromatographic Test for the Detection of Norovirus

A. Shukla[1], V. Morton[1], S. Bidawid[1], and K. Mattison[1]

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

SUMMARY: The detection and identification of foodborne pathogens can be time consuming. This project aims to develop a rapid test for foodborne pathogens that functions on the same principle as a pregnancy test. It will provide a method for rapid diagnosis and screen food samples prior to consumer exposure.

OBJECTIVES/BACKGROUND/ISSUE(S): Norovirus is the leading cause of infectious gastroenteritis worldwide. It has been estimated that 40% of norovirus (NoV) infections are transmitted by food and water. The objective of this project is to design a rapid test for diagnosis of foodborne pathogens using both the carbohydrate viral receptors and antibodies designed to detect NoV. Other rapid systems to date rely only on antibodies for capture and they are hampered by too much specificity and a lack of sensitivity.

DESIGN/METHOD/DESCRIPTION: Synthetic carbohydrates representing the NoV receptors have been tested and found to increase the efficiency of viral capture as compared to antibodies. Polyclonal antisera (JTa, JTb, HMa, HMb, KMa and KMb) were produced against fragments of the NoV capsid protein. Their affinities have been estimated by Western blot analysis.

OUTPUTS/RESULTS: Synthetic histo-blood group antigens have the ability to capture noroviruses from solution as well as from foods. The polyclonal antibodies display varying affinities for NoV collected from clinical samples. These two binding events are not mutually exclusive. The antibodies with the highest affinity will be used in the mobile phase combined with a carbohydrate capture phase to develop a rapid chromatographic test for the detection of NoV.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The affinities for each of the antibodies have been characterized using Western blotting analysis of a dilution series (using Tris-buffered saline) of a subset of clinical samples. The next steps are to determine the appropriate conjugates that are required to make a rapid test on absorbent paper and to ensure that it is cost effective. Waiting for results is often the hardest part of suffering not only for the infected individuals, but for those involved in prevention and containment of outbreaks. Development of this rapid test will help to not only diagnose patients quickly, but will also help to control the spread of NoV outbreaks.

2.27 Transcriptional Responses of Macrophage-Like Cells to Domestic Substance List Pseudomonas Strains in Biofilm and Planktonic States

P.S. Shwed, PhD[1], J. Crosthwait, BSc[1], and V.L. Seligy, PhD[1]

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

SUMMARY: In natural environments, microbes may exist in biofilms that are structured microbial communities. This study aims to adapt a mouse gene expression assay to biofilm microbes, measure gene responses and compare to microbes in suspension.

OBJECTIVES: *In vitro* testing of Domestic Substance list (DSL) microorganisms, in support of the Canadian Environmental Protection Act (1999), is mostly carried out with microbes in suspension. However, in natural environments, microbes can co-exist, associate and form structured biofilm communities. There is a lack of information for the safety assessment for microbial biofilm states. The aim of this study was to determine if the transcriptional responses of mouse macrophage cells are different in response to DSL *Pseudomonas* biofilm and suspension cells.

DESIGN: Triplicate 200 minute exposures of mouse macrophage like cells (J774A.1) were carried out with *P. aeruginosa* (Pa) (ATCC 15692, 31479, 31480) biofilms or planktonic cells. Biofilms were established on polycarbonate membrane inserts or polystyrene blocks and quantitated by staining and colony counting. Real time reverse transcription PCR was used to quantify receptor, immune response and house keeping genes in RNA samples from exposed macrophage and control (mock-exposed) cells.

OUTPUTS/RESULTS: Transcriptional response in J774A.1 cells exposed to biofilm cells of Pa strains was similar at the level of transcription magnitude and type of toll like receptor gene and accessory pathway gene response, consistent with earlier immune indicator studies involving vegetative forms of these microbes and measurements of cytokines. Preliminary exposure studies involving biofilms established on polycarbonate membrane inserts appeared to attenuate or eliminate transcriptional response of some macrophage genes.

IMPACTS/OUTCOMES/CONCLUSIONS: This study shows that *in vitro* exposure testing of *Pseudomonas* biofilms can be carried out by adapting a mouse macrophage assay and that some transcriptional responses are consistent with *in vivo* studies using vegetative cells. Additional exposure studies involving suspension cells and biofilms formed on polystyrene inserts will provide additional comparative data. Development of *in vitro* models that employ planktonic and biofilm forms of bacteria can enhance risk assessment.

2.28 The Community Heat Index: Implementation of a Novel Community Heat Metric in Canada

U. Bickis, PhD[1], C. Simpson, MSc[1], and A. Yagouti, MSc[1]

[1] Climate Change and Health Office, WACCB, HECSB, Health Canada, Ottawa, ON

SUMMARY: Extreme heat events will become public health threats. We are supporting pilot Heat Alert and Response Systems (HARS). We are determining "heat" (a composite of temperature, humidity, wind and radiation) in communities, comparing this to illness/death data, to establish the level at which health effects begin, leading to HARS triggers.

BACKGROUND: Extreme heat can be a serious Public Health issue, as evidenced by some 70,000 related excess deaths in Europe in 2003. "Despite limited research on heat waves in Canada, this study demonstrates that the effects of heat are profound and far-reaching". (Smoyer-Tomic et al, 2003). Also, in the deadliest extreme heat event on record in Canada, there were 1180 deaths (back in 1936). The point is, with Climate Change, events such as these are more unpredictable, but are expected to occur with greater frequency, intensity and duration. Without preparation(s), what happened in Europe could happen here.

Physiologically, heat is a composite of temperature, humidity, solar load and air movement. Present indices used for heat in Canada disregard several of these components. Accordingly, the existing heat "thresholds" (levels below which adverse effects are not seen) and/or HARS "triggers" (the point at which a HARS is activated) are based on incomplete data. It should be noted that a World Meteorological Organization endorsed project is developing a Universal Thermal Climate Index, incorporating the same four parameters. The Science Section of the Climate Change and Health Office (CCHO), in conjunction with both its Outreach and Policy Sections, is conducting heat monitoring in nearly 20 communities across the country. This is in order to apply a scientifically-defensible and physiologically-based metric for the implementation of (HARS) by public health and emergency response officials in participating communities. HARS are important because of the expected increase in the frequency, severity and duration of extreme heat events in Canada.

DESCRIPTION: With industry collaborators, CCHO has developed environmental heat monitoring systems (EHMS), based on the well-established principle of the "wet-bulb globe temperature-outdoor" index (WBGTo). It incorporates, by algorithm, all four of the physiologically-significant environmental heat parameters. Heat will be continuously monitored over the summer of 2009 and 2010. The levels of heat will be correlated with various indices of illness and death to arrive at heat-health relationships.

OUTPUT: The output from the EHMS will be termed Community Heat Indexes (CHI). From these, CCHO will develop health thresholds, and the participating communities can derive their respective HARS triggers.

OUTCOMES: This presentation will show the results of the 2009 monitoring and analysis, outlining its human health significance.

2.29 Development of a Canadian Pharmaceuticals and Personal Care Products Research Network and Data Portal

A. Socha[1], and K. Ostapyk[1]

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

SUMMARY: Significant research on pharmaceuticals and personal care products (PPCPs) occurs in Canada. However, coordination, communication, funding mechanisms and networking could be improved. Health Canada leads a collaborative effort to establish a research network, a web-accessible information portal, an analytical chemistry research and development program, and a monitoring program for PPCPs in the Canadian environment.

BACKGROUND: Health Canada has co-sponsored workshops on PPCPs in the environment. Feedback as well as internal analysis demonstrate a need for: a network to improve communication and collaboration and investigate the presence and risks of PPCPs in the environment; a centrally-coordinated data portal for research and collaboration; standardized analytical methods; and a priority list for monitoring.

METHOD: The recommendations of the research community, obtained through workshops series and direct communication have guided the work. Environmental Assessment Unit (EAU) staff studied several existing data portals to determine their suitability. A business case was prepared describing the pros and cons of adopting an existing portal, creating a new portal based on an existing model, and creating a new portal from scratch.

RESULTS:

Data Portal: Health Canada will join the European *Network of Reference Laboratories for Monitoring of Emerging Environmental Pollutants* (NORMAN), using their data portal. It is web accessible and includes searchable fields for researchers' profiles, contact information, environmental fate, monitoring, effects and analytical chemistry data

PPCP Network: A Canadian PPCP Network will be established to facilitate communication, distribute current information and provide a mechanism for exchange of physical-chemical data.

Analytical Chemistry Program: The Network will coordinate collaborations to standardize the target list of compounds and develop analytical protocols. An inter-laboratory study will build capacity and establish a network of analytical laboratories. Quality assurance/quality control (QA/QC) protocols will be validated, standardized and adopted. Certified reference samples will be shared.

Canadian PPCP Monitoring Program: The Network will coordinate a monitoring program, centralize data and provide a common format.

CONCLUSIONS/NEXT STEPS: Health Canada will work to secure funding for capital investments, collaboration, human resources and standards development.

- Health Canada will take the lead in establishing a Canadian PPCP Network.
- Health Canada and the Ontario Ministry of the Environment will coordinate an inter-laboratory study to build capacity and standardize analytical methods.

2.30 Using Exotic Atoms to Keep Borders Safe

T.J. Stocki, PhD[1], E.-I. Esch, PhD[2], N.J. Hoteling, PhD[2], A. Adelmann, PhD[3], R.H. Heffner, PhD[2], A. Jason, PhD[2], L. Mitchell, PhD[4], and H. Miyadera, PhD[2]

[1] Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON
[2] Los Alamos National Laboratory, New Mexico, USA
[3] Paul Scherrer Institut, Swtizerland
[4] U.S. Naval Research Laboratory, Washington, DC, USA

SUMMARY: Muons, which are produced naturally in the upper atmosphere or artificially by a particle accelerator, can be used to scan cargo for special nuclear materials (e.g., Uranium or Plutonium). Preliminary results show that by measuring the x-rays induced by these muons one can detect the presence of these materials.

OBJECTIVES: Cosmic rays are composed of different particles (protons, neutrons, muons, pions, kaons, etc.). One of these particles, the muon, exists long enough and is penetrating enough that it can be used to actively scan cargo to ensure the non-proliferation of special nuclear materials (SNM). A set of “proof of concept experiments” have been performed to show that active muon analysis can be used for this purpose.

METHODS: Experiments with muons were performed at high-intensity, medium-energy particle accelerators (TRIUMF, Vancouver, and Paul Scherrer Institut, Switzerland). These muons, like any negative particle, were used to form exotic atoms with one electron replaced by the “exotic” particle. Since the muon is captured in an excited state, it will give off x-rays, which can be detected by high-purity germanium detectors. These x-rays are of relatively high energy (between 100 keV and 7 MeV), because the muon is 207 times more massive than the electron. The energies of these x-rays can identify the element and the isotope in which the muon has been atomically captured.

RESULTS: The muonic x-rays corresponding to the SNM of interest, have been detected, even with the use of various shielding configurations composed of lead, iron, polyethylene, or fibreglass. Other muonic x-rays were also used as to act as calibration lines.

CONCLUSIONS: It has been shown from these preliminary results that muons can be used to find special nuclear materials by measuring the energies of the muonic x-rays, even in various shielding configurations. Further experimentation is underway to better understand backgrounds.

IMPLICATIONS: The security of mankind can be protected by the use of this technology.

2.31 Method for Studying Potential Immune Responses from Repeated Exposures of Biotechnology-Related Bacteria

A.F. Tayabali, PhD[1], K. Nguyen, BSc[1], and V.L. Seligy, PhD[1]

[1] Biotechnology Laboratory, Mechanistic Studies Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: Several bacterial strains are currently used or considered for use in biotechnology. Human exposures to these biotechnology-related bacteria could occur repeatedly over time. These exposures could be from either environmentally stable spores or at low bacterial doses. In order to determine whether immune effects could arise from these repeated exposures, we developed a mouse exposure regime to test for potential immunological effects.

OBJECTIVE: Our studies with *Bacillus* species demonstrated that doses over 10^5 cfu/mouse of actively growing cultures (~90% vegetatively growing cells, ~10% spores) caused severe toxicity and inflammation. However, a single low dose at or below 10^4 cfu/mouse, or doses using only spores caused no toxicity or immune effects. The objective of this study was to develop an exposure regime to test whether repeated exposures to spores could cause innate or acquired immune effects.

METHOD: Balb/c mice were exposed endotracheally to 10^6 spores of *Bacillus cereus* (ATCC 14579) weekly for four weeks. Mice exposed to saline alone or single spore doses were used as controls. A proportion of animals was sacrificed every week. Bacterial clearance was measured by tissue homogenization and colony enumeration. Pulmonary and blood inflammatory cytokines (interleukin (IL) -1 beta, IL-6 and tumour necrosis factor-alpha), Th1 and Th2 cytokines (IL-2, IL-4, IL-5, IL-12(p70), granulocyte macrophage-colony stimulating factor, interferon-gamma), and serum immunoglobulin (Ig) (IgG1, IgG2a, IgG2b, IgG3, IgE, IgM) were monitored using multiplex bead arrays. Blood leukocyte counts were determined using a haematology analyzer.

RESULTS: All animals tolerated exposures without showing signs of distress seen with actively growing cultures (respiratory distress, ruffled fur, hunched appearance, watery eyes, lethargy). Pulmonary clearance occurred within a week regardless of the number of doses administered. Pulmonary and blood inflammatory markers, Th-1 and Th-2 cytokines and immunoglobulin levels were unaltered compared to treatment with saline or single dose.

CONCLUSIONS: The repeated exposure method showed that *Bacillus cereus* spores do not cause changes in markers of innate or acquired immunity. Our analysis will continue with excised lymphoid tissue, and exposures to other bacteria that failed to yield acute effects with high doses. Repeated dosing assays will be added to the repertoire of tests available to Health Canada evaluators for screening assessments of Canadian Environmental Protection Act Domestic Substance List organisms.

2.32 Dietary Iron Bioavailability: Validation of Newer *In Vitro* Methods

M. Tsirigotis[1], P. Griffin[1], and K.A. Cockell[1]

[1] Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Low iron bioavailability is a main cause of iron deficiency in Canada and worldwide. We are establishing a cell culture based protocol using a human-derived cell line to compare the bioavailability of different forms of dietary iron and the effects of factors that enhance or inhibit iron absorption from foods.

OBJECTIVES/BACKGROUND/ISSUES: Health Canada polices, regulations and evaluation activities relating to iron nutrition are often guided by assumptions or approximations of iron bioavailability. Studies of iron bioavailability are an identified research priority from the Dietary Reference Intakes process. We are comparing *in vivo* and *in vitro* methods used to measure iron bioavailability, including the Health Canada standard rat haemoglobin repletion assay and the newer simulated digestion/Caco-2 human intestinal epithelial cell culture model.

DESIGN/METHODS/DESCRIPTION: Caco-2 cells are cultured in six-well plates with an upper chamber separated by a dialysis membrane. The food sample to be analyzed is placed on top of the dialysis membrane in a solution of peptic and pancreatic enzymes to simulate gastric and intestinal digestion. The membrane protects the Caco-2 cells from damage by the digestive enzymes and allows iron solubilised in the digest to diffuse through the membrane. The cells in the lower chamber can take up the free iron and use it to synthesize the iron storage protein, ferritin. The production of ferritin in response to cellular iron uptake is used as an indicator of iron bioavailability.

OUTPUTS/RESULTS: Iron, supplied as $FeCl_3$, has been shown to be bioavailable in this assay system. Addition of ascorbic acid (a known enhancer of iron bioavailability) increased $FeCl_3$ bioavailability more than three-fold in preliminary experiments. We are proceeding to testing of other iron salts and foods containing iron.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: This cell culture-based protocol will provide Health Canada with a cost- and time-saving alternative for determining iron bioavailability that will avoid ethical concerns that arise with the use of laboratory animals. Validation of the *in vitro* method will permit its use to address knowledge gaps identified by Nutrition Evaluation personnel and to test hypotheses generated through the use of the Food Iron Bioavailability Index developed at Health Canada.

2.33 Microarray Analyses of Methoxyacetic Acid-Induced Toxicity to Spermatogenesis: Comparison of Approaches to Functional Analyses

M. Wade, PhD [2], A. Williams, MSc[1], A. Kawata, BSc[2], and C.L. Yauk[3]

[1] Hazard Identification Division, EHSRB, HECSB, Health Canada, Ottawa, ON
[2] Population Studies Division, EHSRB, HECSB, Health Canada, Ottawa, ON
[3] Mechanistic Studies Division, EHSRB, HECSB, Health Canada, Ottawa, ON

SUMMARY: Microarray data of testis gene expression changes in response to methoxyacetic acid (MAA) treatment were used to examine multiple methods of data mining for functional analysis. Several approaches were used to identify the biochemical and physiological processes most altered by MAA treatment. These results are compared to the observed morphological changes induced by MAA treatment.

BACKGROUND/OBJECTIVES: Toxicogenomics holds much promise for discovering mechanism(s) of toxicity by monitoring changes in expression of the entire transcriptome. The greatest challenge in making use of genomic data comes in distilling large amounts of data into a clear picture of changing cell/tissue function in response to chemical insult. A variety of tools were used to examine functional changes in gene expression profiles from a microarray study of testis toxicity and results were compared with respect to the observed changes in testis histology and function.

METHOD: Microarrays (Agilent 20K oligoarrays) were used to examine time-dependent changes in testis gene expression in response to *in vivo* treatment with MAA. At 12 and 24 hour post exposure (PE) – corresponding to major increase in death of germ cells - large numbers of genes were found to be significantly altered. A variety of statistical, relational and data-mining approaches were used to predict the toxicological and biochemical responses to MAA treatment from a whole testis or testis cell type-specific perspective.

RESULTS: Functional analyses of significantly altered genes was performed by investigating the KEGG pathway or Gene Ontology enrichment in lists of significantly altered genes (using online tools DAVID or Fatigo) or by performing microarray ANOVA on genes clustered by recognized biochemical pathways (e.g., KEGG, PANTHER). These approaches led to similar results (Reduced expression of genes associated with RNA splicing, intermediary metabolism, increase genes associated with oxidative stress response, apoptosis). In addition, publicly available datasets of testis cell type-specific gene expression were mined to create lists of genes associated with each cell type. These were then used to predict target cell type of MAA action and functional responses within these populations.

CONCLUSION: This approach accurately identifies reduced gene expression in germ cell populations shown to be dying in response to MAA while increases in oxidative stress response genes are supported by literature on biochemical responses to MAA. These studies will help devise effective procedures for interpretation of toxicogenomic data. The use of multiple tools in concert improves the predictive power over single tools.

2.34 QuickScan Dicentric Chromosome Analysis for Radiation Biodosimetry

R.C. Wilkins, PhD[1], F.N. Flegal[2], Y. Devantier[2], and J.P. McNamee, PhD[1]

[1] Consumer and Clinical Radiation Protection Bureau, RRD, HECSB, Health Canada, Ottawa, ON
[2] Atomic Energy of Canada Limited, Chalk River Laboratories, Chalk River, ON

SUMMARY: Biodosimetry is a method that provides dose estimates for individuals exposed to ionizing radiation by examining damage to chromosomes. In a mass casualty situation, it is imperative to supply timely dose estimates to provide critical information to the medical community. This study evaluates a method for increasing throughput for biodosimetry.

OBJECTIVES/BACKGROUND/ISSUE(S): The dicentric chromosome assay (DCA) is the 'gold'-standard assay for accurately estimating unknown radiological doses to individuals following radiological or nuclear accidents. However in a mass casualty scenario, this assay is not well suited for providing timely dose estimates due to the time- and expertise-intensive nature of this assay. In an attempt to increase triage-quality biodosimetry throughput, the National Biological Dosimetry Response team is evaluating an alternative scoring technique, termed DCA QuickScan.

DESIGN/METHOD/DESCRIPTION: The basis for the DCA QuickScan approach is that, unlike conventional DCA scoring, individual centromeres are not counted, but the metaphase spreads are rapidly examined for obvious damage. If the metaphase spread appears to be complete with no damage, then it is scored as normal. If damage is observed (i.e., fragments, visible rings and/or dicentrics), the scorer carefully enumerates the damage, but the total number of chromosomes is not recorded. Using the DCA QuickScan approach, 50 metaphase spreads were examined unless five dicentrics were observed in less than 20 metaphase spreads. Results were compared to conventional DCA scoring.

OUTPUTS/RESULTS: Dose estimates for the conventional DCA were found to be within 0.5 Gy of the actual dose for 83% of the unknown samples, while DCA QuickScan dose estimates were within 0.5 Gy for 80% of the samples. Of the dose estimates falling 0.5 Gy or more outside the actual dose, the majority were dose over-estimates. Scoring by the QuickScan method reduced the scoring time by a factor of 6.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The results indicate that for emergency situations a QuickScan approach should be implemented. This would quickly prioritize samples for full DCA analysis, thereby allowing biodosimetrists to focus their efforts on providing high accuracy dose estimates to those individuals that received clinically-significant radiological doses. Future studies will further evaluate the accuracy of the DCA QuickScan method.

2.35 A Novel Luminex System to Measure the Lot-to-Lot Variability in Flavivirus Vaccines

A. Farnsworth, PhD[1], and J. Whitteker, MSc[1]

[1] Centre for Biologics Research, HPFB, Health Canada, Ottawa, ON

SUMMARY: Flaviviruses, which include Yellow Fever virus (YFV), Dengue virus (DV), Japanese Encephalitis virus (JEV), and West Nile virus (WNV) among others, are a significant burden on public-health agencies across the world. Using West Nile virus as a model we are developing new tools for lot-testing live-attenuated flavivirus vaccines.

BACKGROUND: While effective vaccines are currently marketed and available for some flaviviruses group (YFV, JEV) vaccines against others are still under development. A significant focus is on the production of various types of Live-Attenuated Virus (LAV) vaccines due to their inherent economic and immunological advantages. Lot testing of LAV vaccines is usually preformed by confirming the numbers of active attenuated viruses in the vaccine lot through a Plaque Forming Unit (PFU) or Tissue Culture Infectious Dose 50 ($TCID_{50}$) assay. While necessary, these assays are not well suited for assessing lot-to-lot variability that may be occurring due to deviations in manufacturing protocols.

DESIGN: Two viral products are predominately released from cells infected by flaviviruses; whole virions and non-infectious virus-like particles. Changes in virus seed stock, host cells and growth conditions can result in alterations in the infective virus to virus-like particle (VLP) ratio. Using the Luminex xMAP system we will design assays that measure virus genome and structural protein content. Fluctuations in the ratio of virus to VLPs will be detected by changes in the ratio of genome to protein content as detected by our assay.

OUTPUT: Currently we have designed a West Nile virus that is limited to a single round of replication. This attenuated virus allows us to begin testing our bead-based assays on the Luminex 100 platform and to determine which antibodies and oligonucleotides provide reproducible and sensitive detection of West Nile virus genomes and proteins.

IMPACTS: If a reproducible and sensitive assay is achieved using West Nile virus as a model, identical assays can be designed for use with other flavivirus LAVs or similar assays can be designed for LAVs derived from other virus families.

2.36 Database of Radiogenic Cancer in Experimental Animals Exposed to Low Doses of Ionizing Radiation

J.M. Zielinski[1], H. Jiang[2], S. Shilnikova[2], D. Krewski[2], and P. Duport[3]

[1] Environment Health Science and Research Bureau, HECSB, Health Canada, Ottawa, ON
[2] McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, ON
[3] International Centre for Low Dose Radiation Research, University of Ottawa, Ottawa, ON

SUMMARY: The database including virtually all publicly accessible data on the induction of radiogenic cancer in laboratory mammals has been used to address the question of whether or not the dose-response curve for radiation carcinogens is linear at low doses.

OBJECTIVES/BACKGROUND/ISSUE(S): To address the question of whether or not the dose-response curve for radiation carcinogens is linear at low doses.

DESIGN/METHOD/DESCRIPTION: A comprehensive database (hereafter referred to as Database) of animal carcinogenesis experiments involving exposure to different types of ionizing radiation was created. The experiments were identified through the International Radiobiology Archives of Long-Term Animal Studies (1996) and a MEDLINE search using the keywords: rat, mouse, dog, ionizing radiation, alpha, beta, gamma, X-rays, neutrons, cancer, and neoplasms. Paper copies of identified publications appearing in peer-reviewed journals, annual reports of research institutions, and conference proceedings were obtained. Each of these articles was reviewed to ascertain its relevance to radiation carcinogenesis in animals. Papers containing all of the information necessary for inclusion in the Database (species and strain of experimental animal, type of radiation, mode of administration, body or organ doses, dose rate, and type of cancer of interest) were selected as appropriate sources of data.

OUTPUTS/RESULTS: The Database on radiogenic cancer in animals consists of 800 datasets drawn from 262 experiments. The Database includes 87,982 exposed and 37,111 unexposed (control) animals. This represents the largest Database on experiments on radiation carcinogenesis in animals assembled to date. Based on visual examination of the data six major patterns of dose-response were observed: four patterns (U-shape, J-shape, no apparent effect, no cancers in exposed and control animals) showed no evidence of effect or a decrease in cancer incidence at low doses and two patterns (dose-related increase in cancer incidence inverse U-shaped) showed some evidence of a radiation effect at low doses. Based on visual examination, there were more datasets with no evidence of an effect or a decrease in cancer incidence at low doses than datasets with a positive dose-effect relationship. Subsequently, we conducted a rigorous statistical analysis to determine the meaning of frequently observed crude negative dose-response slopes at low doses.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: A descriptive overview of the experiments included in the Database, along with a qualitative assessment of the shape of the dose-response relationship for radiation carcinogenesis at low doses in experimental animals is presented.

2.37 Clarity of the Health Risk Message Through Simplicity and Use of Relativity of Risk

M. LeBrun[1], S. Forsen[1], N. Blackburn[1], F. Hallé[1], S. Reid[1], and V. Hogan[1]

[1] Office of Risk Management and Science, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Health Canada regularly issues public communications (PCs). These tools are important to patients and consumers and so must be easy to read and understand. Many PCs use text above the literacy proficiency of the average Canadian adult. PCs must better reflect the public's ability to read, understand, and use the risk information they contain.

OBJECTIVES/BACKGROUND/ISSUE(S): Identify different techniques that will help simplify and clarify the risk messages Health Canada issues to the public.

DESIGN/METHOD/DESCRIPTION: An Issue Analysis Summary (IAS) was authored examining PCs Health Canada had issued in the past. These PCs often used language that went beyond the identified health literacy levels of the general public. The PCs were examined using various programs that assess the literacy level of a text such as: the Flesch Reading Ease Test, Flesch Reading Grade Level, Gunning Fog Index, the Simple Measure of Gobbledygook (SMOG), Automated Readability Index, and the Coleman-Liau Index. Collectively, these tests demonstrated that a post-secondary education reading skill level was required in order to understand the risk information presented in these messages intended for the general public.

The IAS was performed by consulting publications and websites to identify possible techniques to better communicate risk messages to the public. Two general categories for improvement were created from this research: simplification of the message and inclusion of relativity of risk messages.

OUTPUTS/RESULTS: Health Canada PCs were evaluated on their required reading skill levels and demonstrated that a post-secondary education level of literacy would, on average, be required for sufficient understanding. This level of skill is far above the recommended grade 8 literacy levels deemed appropriate for the average Canadian adult to understand health risk information.

The two categories for improvement identified a variety of approaches: 13 for simplicity of the message and 6 for relativity of risk statements. Each approach was brought forward to the Expert Advisory Committee on the Vigilance of Health Products where consultation supported the principle of clarifying the messages.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Further study as to the effectiveness of each of these options will need to be investigated before a decision as to which approaches would be feasible and most likely to result in clarifying the health risk message.

2.38 Food Security Knowledge Initiative: A Case Study in Knowledge Development and Exchange Innovation

D. Sheppard, MSc[1], K. Robinson, PhD[1], T. Morrison[2], I. Sirois[3], and M. Hooper[3]

[1] Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, Ottawa, ON
[2] Community Programs Directorate, FNIHB, Health Canada, Ottawa, ON
[3] Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON

SUMMARY: Food security is an important issue facing multiple levels of government and with clear links to chronic disease. This presentation will highlight the learnings from an innovative multi-partner initiative designed to advance knowledge development and exchange in the area of food security and chronic disease in Canada.

OBJECTIVES/BACKGROUND: The Food Security Knowledge Initiative represents an experiment in bridging science and practice. Since fall 2008, PHAC has brought together researchers, policy makers and practitioners to identify knowledge gaps and opportunities in order to enhance learning exchange and joint problem-solving on food insecurity and chronic disease to accelerate effective action. The initiative aims to increase awareness of evidence-based policy and practice options, improve access to effective and innovative interventions, and increase evaluation and sharing of practice-based learning.

METHOD/DESCRIPTION: This work is informed by a knowledge cycle framework that depicts how knowledge is produced, shared and used and as such, another objective of the initiative is to assess the knowledge cycle framework's utility as a knowledge-to-action tool. Finally, the initiative centres on building connections and collaboration among multiple partners. This presentation will outline the initiative's collaborative processes, knowledge development, and experiences to date in linking government with civil society organizations and the academic community to contribute to informed decision-making and evidence-based programming and policy development.

RESULTS: Activities completed to date include: mapping of key organizations and initiatives aimed at reducing food insecurity in Canada, stakeholder consultation and engagement, knowledge syntheses on the relationship between food security and chronic disease and food security intervention effectiveness, and a pan-Canadian needs assessment workshop to identify knowledge gaps and specific knowledge transfer and exchange opportunities.

CONCLUSION: This session will conclude with reflections on implementing knowledge to action initiatives with research, policy and practice perspectives in chronic disease prevention including progress in documenting learnings through a case study methodology that can inform similar knowledge development and exchange undertakings.

2.39 Rapid Detection of *Giardia* sp. and *Cryptosporidium* sp. in Formalin-Fixed Holstein Calf Fecal Samples: A Correlation Study With Fluorescence Microscopy

E. Chomyshyn[1], M. Parenteau[1], L. Parrington[2], and B.R. Dixon[2]

[1] Scientific Services Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON
[2] Microbiology Research Division, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

SUMMARY: Confirming the presence of *Giardia* sp. and *Cryptosporidium* sp. in fecal samples has always presented a significant challenge with regards to misidentification and false negatives. Here the importance of proper sample handling and preparation are discussed, as well as the advantages of flow cytometry as a rapid diagnostic tool.

OBJECTIVES: Confirming the presence of *Giardia* and *Cryptosporidium* cysts and oocysts in fecal samples has always presented a significant challenge with regards to misidentification and false negatives. Rapid and precise diagnosis allows for the treatment of patients affected by these parasites quickly and appropriately for faster resolution of illness. Flow cytometry has shown great promise as an accurate and sensitive tool for screening a large number of samples in a relatively short period of time, which is difficult and tedious to accomplish by fluorescence microscopy.

In the past, some have reported difficulties correlating flow cytometry and fluorescent microscopy data, but it is our belief that this may be due to improper sample handling and a lack of consistency in preparation.

DESIGN: Fecal samples from very young Holstein calves were prepared using the optimized preparation protocol developed in-house, as well as with slight variations representative of different techniques found in literature. Samples were then examined by fluorescent microscopy and results were correlated with those obtained by flow cytometry.

OUTPUT: It was found that when samples are correctly handled and processed in an appropriate and consistent manner, the results obtained by flow cytometry correlated very highly with those obtained by fluorescent microscopy.

IMPACT: The speed at which a large of samples can be screened and the precision with which this can be done makes flow cytometry an invaluable tool for parasitologists with regard to food safety and policy development.

2.40 Challenges of Post-Market Surveillance of Nanotechnology-Based Health Products

S. Drmanic Storbeck, MSc[1], A. Tonary, PhD[1], S. Semalulu, PhD[1], R. Leitch, MSc, MEng[1], and D. Vu, PhD[1]

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

SUMMARY: There are many nanoparticle-based health products approved by Health Canada. Appropriate signal detection, assessment, adverse reaction reporting, and risk management planning requires a greater understanding of the key mechanisms underlying adverse events, to accurately interpret the safety implications of this new technology.

ISSUE(S): To assess the state of knowledge with respect to nanotechnology-based health products and discuss the challenges encountered during post-market surveillance of these products.

DESCRIPTION: A nanomaterial is a man-made object ranging in size from 1 nanometre to 100 nanometres, while a nano-object is any material with any dimension in the nanoscale. There is no one agency or organization that regulates nanotechnology-based health products in Canada. Rather, the products are regulated according to the type of product (e.g., biological, natural health product). The scientific knowledge on which one can quantitatively assess the risks associated with nanomaterials is limited, and uncertainties associated with risk assessment and risk management of nanomaterials have been addressed using a precautionary approach that gives priority to ensuring the safety of Canadian consumers and the environment.

OUTPUTS: Due to potentially unique physicochemical properties of nanomaterials, questions have been raised about their safety. In Canada, approved nanoparticle-based health products include pegylated interferons used for hepatitis treatment, Abraxane for metastatic breast cancer, silver-containing products and sunscreens. This list expands when radio labelled pharmaceuticals, and imaging and drug delivery products are included. The potential to cause harm will be negligible for some nanomaterials. For example, a recent report suggested that pegylation does not appear to result in more side effects than standard interferon. However, in other situations where a clear health risk has been identified for a product, regulatory action may need to be taken.

NEXT STEPS: From a scientific perspective, there is still a tremendous amount that is not known about how to develop and use nanotechnology-based products safely. However, knowledge from other materials can be used to reduce potential risks, and existing regulations can be applied to nanomaterials. Strategic research will be essential to support the long-term safety of increasingly sophisticated nanotechnology-based materials and products.

2.41 A Novel Skin Soap Washing Method for Predicting Dermal Absorption of Soil Contaminants

R.P. Moody[1], A. Yip[1], and A.V. Tytchino[1]

[1] Bureau of Environmental Health Research, Exposure and Biomonitoring Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Dermal absorption of soil contaminants is a major exposure route. *In vitro* human skin tests were conducted for five contaminants, both with and without soil. Good correlations of chemical removed by skin washing with that not absorbed suggested a simpler method to predict absorption.

OBJECTIVES/BACKGROUND/ISSUE(S): Data from soil contaminant tests conducted in collaboration with the Bureau of Impact and Risk Assessment suggested a new method using skin soap wash data for predicting dermal absorption. This method has advantages to earlier more invasive punch biopsy and adhesive tape skin stripping methods, which also predict absorption by difference from the applied dose.

DESIGN/METHOD/DESCRIPTION: Human skin specimens obtained following informed consent from Ottawa Hospital were tested *in vitro* in Bronaugh Teflon® flow-through cells using a receiver solution of Hanks modified saline (pH 7.4) to simulate blood flow. Tests were conducted with soil spiked with five radiolabeled chemicals (^{14}C-benzo[a]pyrene (B[a]P), mercury-203, nickel-63, ^{14}C-ethylene glycol (EG) and ^{14}C-nonyl phenol) with concurrent controls without soil. B[a]P was tested after 24 and 42 hrs to examine skin depot bioavailabiliity. Samples were analyzed by Liquid Scintillation Counting.

OUTPUTS/RESULTS: In all cases lower % absorption and greater % removed by soap wash was observed in tests with spiked soil *versus* concurrent controls without soil. Good correlations of the % of applied dose washed-off with soap *versus* the % dermal absorption were obtained for tests with (r^2 = 0.88 (n = 6)), and without (r^2 = 0.96 (n = 6)), soil for five chemicals including two B[a]P tests. Data for EG was corrected for evaporative loss. For data with and without soil pooled together, the correlation was not as good (r^2 = 0.85; n = 12).

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Analysis of soap washes could provide a simple, fast, and relatively cost-effective *in vitro* method for predicting dermal absorption, and reduced animal testing. Additional *in vitro* tests, particularly of other chemicals, soils, skin cleansers and methods of skin washing are needed. Linear regression slopes of with and without soil data were significantly different ($p < 0.05$) suggesting a complex sorptive interaction of soil with contaminant physicochemical properties and dermal absorption.

3.01 The Importance of a Community-Based Approach to Health Research in the Arctic

D. Charette[1], S.G. Donaldson, PhD[1], A. Manning, BES (Hons.) [1], T. Leech, MSc[1], T. Nancarrow, MSc[1], B. Adlard, BSc (Hons.) [1], and J. Van Oostdam, DVM[1]

[1] Safe Environments Directorate, HECSB, Health Canada, Ottawa, ON

SUMMARY: Community-based health research (CBHR) has maintained an important role in understanding the complexity of northern health issues by actively involving researchers and community members in research.

OBJECTIVE: The objective of this paper is to outline a community-based methodological approach that was applied to a human health research project in Nunavut, Canada.

RESEARCH DESIGN: Health Canada's International Polar Year dietary choice community-based health research (CBHR) project is designed to engage northern communities in the research process to help understand the factors influencing peoples' dietary choices in Nunavut.

A variety of mediums where employed to engage participants, community members, organizations and local governments.

DATA COLLECTION: During 2007-2009, in-depth semi-structured interviews (n=128) were conducted with men and women in Cape Dorset, Iqaluit, and Kimmirut, Nunavut, Canada.

In total, 128 interviews were analyzed using NVivo 8; a qualitative data analysis software package. Grounded Theory methods (Strauss and Corbin, 1990) were employed to analyze the transcripts in NVivo 8 for: (1) emergent themes and relationships; (2) exploring gender differences; (3) building analytic categories through further interviews; (5) making gender comparisons and comparisons between each set of interviews; (6) making cross-community comparisons between each set of interviews by community.

OUTPUT: The research showed the importance of community research partnerships, the involvement of community members in all phases of research, the process that was employed to collect, analyze and interpret the findings, and the mediums used to communicate the research results.

IMPACTS: The results of this paper provide a new foundation that could be used to build future community-based health research projects in the circumpolar region.

3.02 Statistical Considerations in the Treatment of Nutrient Data from SNAP-CAN

J. Deeks[1], R. Klutka[1], and M. Munro[1]

[1] Nutrition Research Division, HPFB, Health Canada Ottawa, ON

SUMMARY: The Sampling and Nutrient Analysis Program (SNAP-CAN) generates a large amount of raw nutrient data that must be aggregated into a single profile for each food, prior to entry in the Canadian Nutrient File (CNF). This poster will outline the statistical procedures employed to ensure accuracy and consistency when reviewing and compiling data.

OBJECTIVES: To develop objective criteria for aggregating analytical composite data from SNAP-CAN for entry into Canada's food composition database, the CNF. The data should be statistically and scientifically reviewed to ensure that the variation is reasonable, outliers are properly dealt with and values are consistently imputed for trace (<LOQ) and not detected (<LOD) measurements.

DESCRIPTION: When analytical nutrient datasets are collated, the goal is to return a mean value and a standard deviation to indicate the variation. Rules are needed for attaining this goal in the unique environment of a nutrient database where consistency is key, natural variation is expected, and it is only possible to report one numeric data point for each nutrient. Several techniques were applied to identify potential outliers. Unlike many forms of analytical work, there can be true zero values when reporting nutrient levels in foods. A number of criteria were tested to determine the most appropriate cutpoints that would allow the reporting of 0 and take into account the uncertainty of data below detection and quantification limits.

OUTPUTS/RESULTS: The following procedure is followed for each set of data.

1) A value is imputed for all uncensored data utilizing the instrumental LOD and LOQ.
2) After examining the effect of using available statistical techniques, suspicious data were determined to be most effectively flagged by a calculation of data outside of 2 standard deviations from the mean. These are excluded if determined to be in error.
3) The dataset is aggregated. Datasets for each nutrient are a single value based on the proportion of values below LOD and between LOD and LOQ.

IMPLICATIONS: This work has allowed us to determine rules, which result in the long-term aim to provide a means whereby there can be uniform reporting of data particularly in regard to outliers and non-quantified data.

3.03 Regulatory Impact of Updating a Pesticide Exposure Parameter

S. Farah[1], A. Poliquin[2], and P. Brassard[3]

[1] Exposure-1 Section, Health Evaluation Directorate, PMRA, Health Canada, Ottawa, ON
[2] Stakeholder Engagement and Outreach Section, Policy Communications and Regulatory Affairs Directorate, PMRA, Health Canada, Ottawa, ON
[3] Re-Evaluation Section, Health Evaluation Directorate, PMRA, Health Canada, Ottawa, ON

SUMMARY: Area treated per day (ATPD) is a required parameter to estimate exposure to workers applying pesticides. New ATPD default values were generated by performing a statistical analysis of an existing database, considering the type of applicators, techniques of application, crops and farm sizes. The new higher percentile ATPD values were selected to better represent exposure to workers.

OBJECTIVES: Deriving ATPD default values for specific pesticide uses strongly depends on the type of applicator, method of application, crops and farm size parameters required to apply the pesticide efficiently. This project was initiated to update existing values, taking into account the need to obtain an overall high-end value (˜ 90th percentile) for estimating worker exposure (daily dose), for which the ATPD is one of the constitutive variables.

METHODS: ATPD data from a recent agricultural census database were separated into the four major equipment groups: Aircraft, Groundboom, Airblast and Hand-Held. Further separation into type of applicator (farmer or custom) or crops occurred if the resulting groups were significantly different. Parameters of best-fitted distributions were then generated for the resulting groups, along with estimates of central values and percentiles. ATPD defaults were set as the values required to reach the 90th percentile of worker exposure, based on propagating uncertainty in the daily dose equation.

RESULTS: Non-cancer ATPD defaults were set at the arithmetic mean for log-normal distributions, and at the 75th percentile for normal distributions. Cancer exposure is averaged over a lifetime and only required a 50th percentile to be representative. These values were summarized in a table which also contained previously used ATPD values from other specific sources that could be used when pesticide application scenarios do not fit the resulting group's classification.

CONCLUSIONS/IMPLICATIONS: Health Canada has a regulatory obligation to provide a transparent framework for selecting and using data critical to risk assessment. The present science-based ATPD default values are generated to obtain a representative estimation of mixer/loader/applicator exposure. The method provides a classification scheme based on specific application scenarios with propagation of uncertainty analysis to report values at the proper percentile. This approach to risk assessment is transferable to other parameters of exposure.

3.04 Data Flow for Microarray Experiments

R. Gagné[1], B. Kuo[2], L. Berndt-Weis[1], and C.L. Yauk[1]

[1] Mechanistic Division, HECSB, Health Canada, Ottawa, ON
[2] Biostatistics and Epidemiology Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Microarray experiments (ME) are conducted to measure gene expression. From experimental design to identifying genes that show significant expression, many steps involve data storage and retrieval, and statistical and bioinformatics analyses using various software. This poster summarizes the crucial steps involved in MEs and displays the data flow diagram (DFD) routinely used by biologists to manage their data. This data flow is intended to help direct the development of bioinformatics and statistical support for MEs at Health Canada.

BACKGROUND: Microarray technology is widely used by scientists to measure the expression of genes in a high throughput manner. MEs generate large amounts of information, which include experiment design, quality assurance, images, results and analyses. This information needs to be archived, retrieved, processed, and analysed quickly and easily to draw meaningful conclusions and for publication purposes.

DESCRIPTION: We propose a pipeline that describes information management of MEs performed at the Environmental Health Science Research Bureau. Represented in a data flow diagram (DFD), information flows through laboratory equipments and computers on and off the Health Canada Network. Transfer of information between equipment on and off the network is done through portable memory devices. Nodes for statistical and bioinformatics analyses on the DFD are shown only as examples since they tend to have a high variability depending on the nature of the ME.

OUTPUTS: A DFD was created for visualization of the information archiving, retrieving, processing, and analyses pipeline. The proposed pipeline serves as a high-level overview of how information generated from MEs are processed in the EHSRB. Due to the nature of this cutting-edge technology, the information management pipeline is constantly being revised and optimized to yield better results.

CONCLUSIONS: The proposed ME information management pipeline provides a training tool for laboratory personnel and decision makers in the microarray laboratory. Not only it will be used to manage information and draw meaningful results from analyses, it will also help scientists quickly identify and locate experimental deficiencies, thus, improving the overall efficiency of genomic research.

3.05 The First Nations Addictions Evidence-Base Process: Renewing First Nations Addiction Prevention and Treatment Services in Canada

D. Harris, MSW, MBA[1], C. Hopkins, MSW[2], G. Graves, MA[1,3], and D. Stoneadge, MS[1]

[1] Addiction Programs, FNIHB, Health Canada, Ottawa, ON
[2] Nimkee Healing Lodge, Muncey, ON
[3] Canadian Centre on Substance Abuse, Ottawa, ON

SUMMARY: The Impact of substance use problems has been identified as a significant concern among First Nations communities. In response, Health Canada, along with its First Nations partners, has initiated a comprehensive, evidence-informed and culturally relevant review of the National Native Alcohol and Drug Abuse Program (NNADAP).

OBJECTIVES: The First Nations Addictions Evidence-base Process is a multi-pronged research initiative focused on enhancing, renewing and validating on-reserve addiction services in Canada. In partnership with First Nations communities and representative organizations, the Evidence-based process has been developed to consolidate the best available evidence, health information and community knowledge to guide policy and program decision-making at both regional and national levels. The synthesis of this data will culminate in a Renewed Program Framework for NNADAP by Spring of 2010 that will guide service delivery and planning over the next five to 10 years.

METHODS: The Addictions Evidence-base Process draws upon several related research initiatives, including regional needs assessments, a national expert's panel and a series of commissioned research papers. Through a variety of research methods – focus groups, key informant interviews, blogs, and surveys – First Nations communities and representative organizations will participate in both developing and refining renewal priorities for NNADAP. The priorities identified in the needs assessments will inform a new framework for NNADAP, which will be undertaken by the First Nations Addictions Advisory Panel – a national group of First Nations and other addiction experts – and will be completed by 2010.

OUTPUTS: Both the regional needs assessments and the NNADAP research papers have engaged First Nations communities (south of the 60th parallel) in the renewal of the NNADAP. These two sub-components of the process will be complete by August 2009. Based upon the outputs of needs assessments, research papers and other lines of evidence the First Nations Addictions Advisory Panel – a national group of First Nations mental health and addiction experts – will develop a renewed program framework for NNADAP by Spring of 2010.

RESULTS/CONCLUSIONS: The goal of this initiative is to systematically enhance, renew and validate on-reserve addiction services through a collaborative and transparent process with First Nations. As such, this process has been designed work in partnership with First Nations communities in developing a renewed vision for NNADAP that is both grounded culturally relevant approaches and evidence-based practices. Priority areas for this process are reducing barriers to service access for remote/isolated communities; increasing federal/provincial collaboration on First Nation mental health and addictions issues; and enhancing the evidence-

based and culturally relevant continuum of services accessible to First Nations communities in Canada.

3.06 Adverse Effects of Indoor, Outdoor and Personal Exposure to Particulate Air Pollution on Cardiovascular Physiology and Systemic Mediators in Seniors

L. Liu, PhD[1], T. Ruddy, MD[2], M. Dalipaj, MSc[2], R. Poon, PhD[1], M. Szyszkowicz, PhD[1], H. You, MSc[1], R. Dales, MD[1], and A. Wheeler, PhD[1]

[1] Research and Radiation Directorate, HECSB, Health Canada, Ottawa, ON
[2] University of Ottawa Heart Institute, Ottawa, ON

SUMMARY: We monitored fine particles indoors, outdoors and at personal level for 28 seniors, and measured their cardiovascular physiology, and blood mediators of inflammation and vascular function. We found that exposure to particulate pollution, may result in adverse effects on cardiovascular function and blood mediators modulating vascular system in seniors.

OBJECTIVE: To investigate the associations between an acute exposure to particulate air pollution monitored indoors, outdoors and at personal level and changes in cardiovascular function and blood mediators of vascular function, inflammation and oxidative stress in seniors.

METHODS: We monitored indoor and outdoor concentrations of black carbon (BC) and fine particulate matter ($PM_{2.5}$) and personal $PM_{2.5}$ over 24 hours for 28 non-smoking subjects, median age 78 years old, who lived in Windsor Ontario. We then measured their blood pressure, heart rate, brachial artery function, and determined C-reactive protein, endothelin-1 (ET-1), vascular endothelial growth factor (VEGF), interleukin-6 and tumor necrosis factor-a, and oxidative stress markers thiobarbituric acid reactive substances (TBARS) and 8-isoprostane in plasma. The procedure was repeated over 7 weeks. We tested associations using mixed-effects models adjusting for confounding variables.

RESULTS: We found that increases in BC and $PM_{2.5}$ were significantly ($p<0.05$) associated with increases in blood pressure, heart rate, vascular regulators ET-1 and VEGF, and oxidative stress marker TBARS, and a decrease in brachial artery diameter. For example, in all subjects, personal $PM_{2.5}$ (7.1 $\mu g/m^3$) was associated with a 3.43 mmHg increase in systolic blood pressure, indoor BC (0.17 $\mu g /m^3$) associated with a 3.20 mmHg increase in diastolic blood pressure, outdoor BC (0.48 $\mu g/m^3$) associated with a 0.04 mm decrease in brachial artery diameter, indoor $PM_{2.5}$ (3.5 $\mu g/m^3$) associated with 0.28 pg/ml increase in ET-1; personal $PM_{2.5}$ (7.1 $\mu g/m^3$) was associated with a 0.29 ng/ml increase in VEGF in females, and a 0.41 nmoles/ml increase in TBARS in subjects not taking antihypertensive medication. BC, a marker for traffic emissions, seemed to have larger adverse impact on health measurements than did $PM_{2.5}$.

CONCLUSION: Daily exposure to particulate pollution, likely traffic-related, may result in adverse effects on cardiovascular function and blood mediators that modulate vascular system in seniors.

3.07 Determination of Microcystins and Anatoxins in Fish, Plankton, and Water by LC-MS/MS

G. Neumann[1], V. Roscoe[1], G.A. Lombaert[1], and T. Rawn[2]

[1] Food Program Laboratory, RPB, Health Canada, Winnipeg, MB
[2] Bureau of Chemical Safety, Food Research Division, RAPB, Health Canada, Ottawa, ON

SUMMARY: Six liver toxins (microcystins) and neurotoxic anatoxin-a were monitored in fish tissue, livers, plankton, and water from Lake Winnipeg, Canada using liquid chromatography-tandem mass spectrometry. Sample extraction and cleanup were matrix-dependent. Only microcystins were detected and only in plankton samples, where they were found in 10 of 12 (83%) samples.

OBJECTIVES: Cyanobacteria (blue-green algae) can produce hepatotoxic and neurotoxic compounds. In collaboration with Department of Fisheries and Oceans, Lake Winnipeg Research Consortium, and Freshwater Fish Marketing Corporation, determine anatoxin-a and microcystins levels in fish tissue, fish livers, as well as water and plankton from Lake Winnipeg to establish if these compounds are present and available for human uptake during fish consumption.

DESIGN: Samples were extracted and cleaned up using commodity-specific techniques. A single chromatographic separation and detection method was developed using reverse-phase liquid chromatography-tandem mass spectrometry. Detection limits ranged from 0.01 to 1.7 ug/g for the microcystins and from 0.03 to 0.4 ug/g for the anatoxins, dependant upon the specific toxin / matrix combination.

OUTPUTS/RESULTS: Microcystins were detected in 10 of 12 (83%) of plankton samples. No microcystins or anatoxins were detected in fish tissue, liver or water samples tested.

IMPACTS/OUTCOMES/CONCLUSIONS: Neither microcystins nor anatoxins were detected in the fish tissue, liver, or water samples analyzed. Microcystins were present in the lake plankton, with MC-LR being the most commonly found, as expected. Recent work by others indicates that protein-bound microcystins are more toxic than the free molecular forms and may result in underestimation of the microcystin content (F. Jüttner, H. Lüthi, Toxicon 51, (2008), 388-397). This may be an avenue to pursue in future work.

3.08 The Global Health Research Initiative

J. Rae[1], and C. Clemenhagen[2]

[1] International Affairs Directorate, SPB, Health Canada, Ottawa, ON
[2] Global Health Research Initiative Secretariat, IDRC, Ottawa, ON

SUMMARY: Health Canada is a founding member of Canada's Global Health Research Initiative (GHRI), a partnership of five agencies of the Government of Canada established in 2001 to promote and facilitate inter-disciplinary research to address the global health challenges of the 21st century.

OBJECTIVES: To explore the questions: "How do Canadians benefit from Canada's investments in global health research?" and, "How can we engage more fully with the GHRI?"

DESCRIPTION: GHRI sponsored projects produce specialist knowledge from new research as well as syntheses of the most relevant existing research findings in a number of high priority subject areas, such as: prevention and control of pandemics and emerging infectious diseases; prevention and control of chronic diseases; health policy and health systems; the interaction of health, environment and development.

Between 2001 and 2009, the GHRI supported over 100 projects in 60 countries involving researchers from Canada working closely with researchers from Sub-Saharan Africa, Asia, and the Americas.

This work has involved close to 200 Canadian researchers affiliated with 61 research institutions and universities across Canada collaborating on projects and working in teams with over 500 researchers based in 172 research settings in low-to middle-income countries.

Total GHRI investments from 2001 to 2011 are estimated at $50 million, including approximately $7.9 million for the 2009-2010 fiscal year. By 2015, total investments though the GHRI partnerships are expected to reach approximately $60.9 million.

RESULTS: What does the Global Health Research Initiative accomplish?

GHRI partners are able to, for example: increase the total amount of, and pool, available resources for longer term research initiatives that address common priorities; identify research-based interventions that contribute practical solutions to implement on a larger scale in response to global health problems.

One of the far-reaching examples of development impact from GHRI funded research is the Centre for Development of Best Practices in Health at the Yaoundé Central Hospital in Cameroon. The Centre, created through a Teasdale-Corti Research Partnership Global Health Leaders Award, is now producing evidence syntheses, health technology assessments and knowledge translation training programs to link research evidence with policy and practice in the central African sub-region. An area of particular focus is improving health care delivery to manage the growing burden of chronic disease in central Africa. When the G8 Leaders at the L'Aquila Summit in July 2009 spoke of creating networks and centres of research excellence in Africa, this GHRI funded initiative could very well be considered a forerunner.

CONCLUSION: The five GHRI partners continually seek to increase the effectiveness of their partnership in order to take full advantage of its collaborative potential. As findings are coming together now from the early phases of some GHRI research programs, a key activity will be capturing lessons learned and communicating findings to translate research into action.

3.09 Drug Seizures: What Can the Data Tell Us About the Demand for Treatment?

K. Richard, MA[1], and C. Landry[1]

[1] Office of Drugs and Alcohol Research and Surveillance, CSTD, HECSB, Health Canada, Ottawa, ON

SUMMARY: Where illicit drugs are concerned, evidence-based is often diverse and somewhat elusive. However, there are some sources of information that may be useful to help predict the demand for drug treatment services.

OBJECTIVE: Given the illegality of many of the substances, which are abused and lead to the need for treatment, there is limited availability of reliable and timely information on the types and nature of substances being used. However, data on the types of illicit drugs, which are seized by police and border services has been collected on a continual basis since 1989. As a result, it provides a good indication of the trends in the availability of illicit drugs across the country and over time.

DESIGN: Based on statistical analysis of data on drug seizures and treatment in Ontario, this presentation will review the comparability of drug seizures trends with prevalence of use and discuss the extent to which the drug seizures data can be useful as a leading indicator of the demand for substance use treatment.

RESULTS: This presentation will discuss the linkages and correlations between general population surveys (demand information) and drug seizure information (supply information) to drug treatment intake data, by type of substance, to help determine the usefulness of such data sources to predict the demand for certain treatment options. Data from general population surveys and drug seizure information from Health Canada will be compared across jurisdictions on several indicators of drug use in Ontario with linkages to treatment information from the provincial Ministry of Health.

CONCLUSIONS: The data from general population surveys and drugs seizures have great potential as an important and complementary source of information for treatment facilities. Through the triangulation of these data platforms, a more robust assessment of drug use patterns and the need for treatment services can be estimated.

3.10 Neuroprotective Efficacy and Correlated Markers of Preconditioning, Postconditioning or Progesterone Treatments of *In Vitro* Cultured Cortical Neurons Following Oxygen and Glucose Deprivation

M. Russell[1], M. Nowakowska[1], A. Williams[2], C.L. Yauk[2], and S.S. Prasad[1]

[1] Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON
[2] Mechanistic Studies Division, HECSB, Health Canada, Ottawa, ON

SUMMARY: Stroke is a major cause of disability/death and necessitates the exploration of new therapeutic strategies. Using an *in vitro* cortical neuronal model, we measured the effectiveness and molecular mechanisms of treatments for injurious ischemia: pre-conditioning - preceding short duration of oxygen-glucose deprivation (OGD); post-conditioning - following OGD; or progesterone.

BACKGROUND: Animal studies have demonstrated that ischemia (restricted blood supply) for short periods before or after long ischemia or progesterone administration following brain injuries are neuroprotective. Our objective is to assess an *in vitro* neuronal OGD ischemia model to measure the effectiveness of such potential CNS therapies and identify corresponding biomarkers. These biomarkers may delineate the efficacy and safety of neuroprotective treatments and offer novel therapeutic targets.

METHODS: E18 rat cortical neuron cultures were subjected to OGD in an anaerobic chamber. For pre-conditioning, cultures were exposed to 45 minutes OGD followed by overnight reperfusion in regular media at normal conditions prior to OGD insult. For post-conditioning, OGD insult was followed by 3 cycles of 15 min OGD and 15 min reperfusions. For progesterone treatments, progesterone was added in the media following OGD insult. After each treatment, cell survival was evaluated by quantifying lactate dehydrogenase release after 3h and overnight reperfusion. Gene expression analyses were also performed using real-time-PCR based arrays and microarrays.

RESULTS: Optimal protection was achieved with 2h OGD insults. Average cytotoxicity after 3h reperfusion in each group was as follows: 2h OGD = 37$\pm$3%; preconditioning = 0$\pm$3%; postconditioning = 15$\pm$3%; and progesterone = 24$\pm$7%. After 16h reperfusion the average cytotoxicity was as follows: 2h OGD = 41$\pm$3%; preconditioning = 1$\pm$5%; postconditioning = 10$\pm$4%; and progesterone = 15$\pm$8%. Apoptosis genes were most significantly altered, several of which attenuated during preconditioning and postconditioning.

CONCLUSIONS: The *in vitro* neuronal culture is an effective model for examining neuroprotective efficacy and mechanisms of neuroprotection since the OGD induced cytotoxicity mimics stroke and both pre- and postconditioning treatments provide significant protection. Gene expression analysis identified biomarkers of neurodegeneration and neuroprotection during ischemic and neuroprotective periods which offer novel therapeutic targets and provide tools to assess the efficacy and safety of emerging neuroprotective treatments.

3.11 Mutagenic Activation of Domoic Acid Through Reaction With Nitrous Acid

T. Schrader, PhD[1], and I. Langlois, BSc[1]

[1] Toxicology Research Division, HPFB, Health Canada, Ottawa, ON

SUMMARY: Domoic Acid is a toxin causing amnesic shellfish poisoning when ingested. Incubation of domoic acid with nitrous acid, formed in the stomach/saliva, generated a direct-acting mutagen in the Ames Assay, suggesting that exposure to non-symptomatic levels of domoic acid could be a cancer concern deserving consideration in regulatory reassessment.

OBJECTIVES/BACKGROUND/ISSUE(S): Domoic Acid is a cyclic toxin found as a shellfish contaminant and was responsible for an outbreak of amnesic shellfish poisoning in Canada in 1987. Published *in vitro* mutagenicity studies have shown that native domoic acid is not mutagenic. However, the existence of an amino group within the structure of domoic acid provides a possible site for mutagenic nitrosamine formation upon exposure to nitrous acid, found in the gut and saliva. The possibility of mutagenic activation through this mechanism was therefore tested including the related compounds kainic acid and glutamic acid for comparison.

DESIGN/METHOD/DESCRIPTION: Domoic, kainic and glutamic acids were incubated with nitrous acid and the reaction stopped by addition of ammonium sulfamate. Mutagenicity was examined with the Ames *Salmonella* microsome assay using the frameshift sensitive strains TA97, TA98 and basepair sensitive strains TA100, TA102, TA104.

OUTPUTS/RESULTS: When tested up to 1 mg/plate, all three compounds were non mutagenic in the absence of nitrous acid. Incubation of domoic acid with nitrous acid was found to generate a direct-acting frameshift and basepair mutagenic activity in all strains except TA104. No activation of glutamic or kainic acids was observed.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The mutagenic activation of domoic acid points towards a mechanism needing further characterization but which should be factored into future risk assessments.
The unsaturated carboxylic acid side chain present in domoic acid but missing in kainic acid suggests that it, rather than the amino group, is responsible for the observed mutagenicity. Similarities between this side chain and unsaturated fatty acids have initiated an examination of nitrous acid effects upon the activation of both essential, unsaturated fatty acids and trans fatty acids. This work may also influence regulation of allowable levels in food. Finally, these results suggest a very fundamental role for nitrogen oxides in carcinogenesis.

3.12 Machine Learning for the Comprehensive Nuclear-Test-Ban Treaty: Contest Results for the 2008 IEEE International Conference on Data Mining

T.J. Stocki[1], R.K. Ungar[1], J.G. Li[2], N. Japkowicz[2], I. Hoffman[1], J. Yi[1], M. Bean[1], L.-E. De Geer[3], and A. Ringbom[3]

[1] Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, Health Canada, Ottawa, ON
[2] HECSB, Health Canada, Ottawa, ON
[3] School for Information Technology and Engineering, University of Ottawa, Ottawa, ON
[4] FOI, Swedish Defence Research Agency, Stockholm Sweden

SUMMARY: Health Canada conducts explosion detection for the Comprehensive nuclear-Test-Ban-Treaty inter alia by monitoring radioactive noble gases in the atmosphere. Synthetic nuclear explosion data based on realistic atmospheric transport modelling with environmental background data were used as training datasets to establish an optimal classification model employing state-of-the-art technologies in machine learning.

OBJECTIVES: Since January 1959, Health Canada has measured radioactive fallout on air filters. Since 1996, compliance verification of the Comprehensive Nuclear-Test-Ban Treaty (CTBT) has employed noble gas monitoring of four radioisotopes of radioxenon, namely, ^{131m,133m,133,135}Xe. The activity concentrations of these isotopes can help distinguish normal reactor emissions from a nuclear explosion. In locations where radioxenon background emissions are high, classification of these two sources becomes difficult. Machine Learning (ML) is employed to overcome this difficulty. Health Canada successfully organised and sponsored an international ML contest held in conjunction with the IEEE International Conference on Machine Learning in Pisa, in December 2008. The participants designed and ran ML algorithms.

DESIGN: Real radioxenon measurements from 5 international monitoring stations were combined with synthetic explosion data. This synthetic data was created by using realistic fission yields from an explosion to estimate the amount of each radioxenon isotope. Then the activity concentrations of those isotopes were calculated as if they were measured at the station taking into account atmospheric transport. This then created a realistic dataset. State-of-the-art technologies in ML were employed by the contestants who submitted their results to Health Canada for evaluation.

OUTPUTS/RESULTS: Classification results for modern machine learning technologies used by the contestants were compared. These algorithms were judged for best overall performance and for best balance (in terms of different station types and learning curve effectiveness). A blind test was performed to verify the results of the contestants. Further study into improving these algorithms and the synthetic dataset is ongoing.

IMPACTS/CONCLUSIONS: Improved accuracy in discriminating a nuclear explosion from regular anthropogenic sources of radioxenon is achieved. These algorithms can be used by Canada's National Data Centre and by the Comprehensive nuclear-Test-Ban Treaty Organization to better identify radioxenon sources and hence make policy decisions.

3.13 Creation of an exchange network on environmental health issues: an example of horizontality that promotes science integration throughout Quebec

F. Valcin[1], M. Verge[1], C. Viau[2], S. Bisaillon[2], M. Mikhail[2], C. Laliberté[3], D. Bolduc[3], M.-J. Nadeau[4], M.F. Blain[1], C. Handfield[1], and E. Boivin[1]

[1] Safe Environments Programme - RAPB - Health Canada – Longueuil, QC
[2] Département de santé environnementale et santé au travail - Faculté de Médecine - Université de Montréal – Montreal, QC
[3] Unité scientifique Santé et environnement - INSPQ – Quebec City, QC
[4] Direction de santé publique - Agence de la santé et des services sociaux de la Montérégie – Longueuil, QC

SUMMARY: A Francophone exchange network on environmental health issues was created to enable environmental health professionals to exchange information on current and emerging issues. The network is made up of over 150 participants from various federal and provincial organizations and universities.

DESIGN/METHOD/DESCRIPTION: The network was created in partnership by Health Canada, the Université de Montréal and the Institut national de santé publique du Québec. The network is a virtual group of professionals who exchange their knowledge and experiences on various scientific issues in environmental health. Participants come from government departments and agencies, universities and other organizations working in Quebec. The network primarily shares information via Web conferences (interactive online seminars) held every month.

OUTPUTS/RESULTS: An assessment survey of potential members' needs guided the development of the network. The subjects of interest mentioned by members cover disciplinary approaches such as epidemiology, risk management and biological monitoring, knowledge summaries on current subjects as well as the presentation of field interventions. Four Web conferences were conducted to test the Web platform before the network was launched (September 2009).

IMPACTS/EFFECTS/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Nine Web conferences are planned for the first year (until May 2010). The Safe Environments Programme (Quebec Region) can use the network to work more closely with industries. The information disseminated during the Web conferences will help members conduct research or transfer knowledge to stakeholders in environmental health and the communities they serve. Links can also be forged with other groups, such as the Great Lakes group.

3.14 Development of the Health Canada Scientific Integrity Framework

L. Boettger, MA[1], and Z. Master, PhD[1]

[1] Research Policy and Outreach Division, Science Policy Directorate, SPB, Health Canada, Ottawa, ON

SUMMARY: This presentation will outline the components of Health Canada's Scientific Integrity (SI) Framework and specifically discuss the development of the Health Canada draft SI policy and procedure for addressing allegations of scientific misconduct.

Instances of scientific misconduct have been reported in Canada and within the Department. Cases of scientific misconduct at Health Canada have potential risks that include affecting the health and safety of Canadians, damaging the reputation and credibility of the department, and misusing public funds.

OBJECTIVES: The SI Framework seeks to promote SI at Health Canada and address the current policy gap in this area. To determine the behaviours that undermine SI, an examination of national and international policies and procedures and academic literature on scientific and research integrity was performed. Ongoing discussions with Health Canada's Legal Services Unit, Human Resources/Labour Relations, Strategic Communications Division and the Centre on Values and Ethics are performed.

DESIGN: Group consultations with Health Canada's regulators and researchers on the policy and procedure have been conducted and the feedback received has helped further refine the policy. External consultations with science-based departments and agencies that have SI policies were also performed.

OUTPUT/RESULTS: Although not yet approved, the SI Framework currently contains four components: 1) a policy; 2) a procedure for handling allegations of scientific misconduct; 3) a training program; and 4) a mentorship guide. The draft SI Policy covers: (i) falsification, fabrication and plagiarism; (ii) authorship and publications practices; (iii) respect for research subjects (both human and animal); (iv) scientific reporting; (v) the use of scientific evidence during decision-making; (vi) interpretation of scientific data during regulatory examination; and, (vii) good faith reporting of allegations and protection against reprisal. The draft procedure for handling allegations of misconduct reflects existing HC procedures with the notable addition of a Designated Person and a Scientific Review Committee to address the science-laden nature of the misconduct allegations.

NEXT STEPS: The SI policy and procedure for handling allegations of scientific misconduct will be further developed and, once both are approved, a communications strategy will be devised. Moreover, a training program designed for researchers will be developed that will teach on the ethics of science and the responsible conduct of research. Lastly, a Guide to Research Mentoring will also be developed.

3.15 10 Years of Integrating Science and Indigenous Knowledge: BC First Nations Environmental Contaminants Program

Z. Fabian[1], R. Lawrence[1], C. Tikhonov[2], and R. Kwiatkowski[2]

[1] Environmental Public Health Services, FNIHB, BC Region, Health Canada, Vancouver, BC
[2] Environmental Research Division, Primary Health Care and Public Health Directorate, FNIHB, Ottawa, ON

SUMMARY: Since 1999, the BC First Nations Environmental Contaminants Program (BCFNECP) has provided First Nations people in British Columbia with a means to address their human health concerns regarding the potential for exposure to chemical environmental contaminants. The Program is focused on policy development, capacity enablement, developing partnerships, and youth engagement.

OBJECTIVES:

- Support BC First Nations in developing projects that explore the link between human health and chemical environmental contaminants
- Build and enable scientific research and proposal-development capacity at the individual and community levels
- Apply the principles of ecosystem research and encourage the integration of Indigenous ways of knowing with conventional scientific methodologies
- Serve as a starting point for First Nation communities to investigate local environmental health issues

DESCRIPTION: The BCFNECP was established in 1999 as part of a cross-Canada initiative to help First Nations people address their environmental contaminants concerns. It is a community-based program, funded by Health Canada, that focuses on the human health links to chemical environmental contaminants.

The Program's design and administration has been significantly influenced by the Health and Environment of Aboriginal Life (HEAL) project, which ran from 1993-2000.

OUTPUTS/RESULTS: Since 1999, the BCFNECP has supported more than 85 projects. An annual conference has been held since 2005 for project teams to share their research with one another. Conference presentations and projects are increasingly involving First Nation students pursuing higher education. In addition to the conference, a more recent capacity-enabling strategy has been to effort provide detailed qualitative feedback to proposal applicants along with connections to potential resources.

There are several instances of how the outcomes of BCFNECP projects have been applied to remedial activities, more advanced research, consumption recommendations for specific traditional foods, and other such value-added benefits.

NEXT STEPS: While feedback from Program participants has been largely positive, the BCFNECP is presently focused on:

- developing an operational management guide and program policy document
- encouraging the participation and interest of youth in environmental health science
- increasing linkages to researchers, institutions, and organizations that can provide financial and/or human resources assistance to project teams and applicants
- improving target distribution of annual call for proposals

3.16 Heat Alert and Response System (HARS) Best Practices for Canadian Communities

A. Rogaeva[1], A. Wilk[1], and P. Berry, PhD[1]

[1] Climate Change and Health Office, Health Canada, Ottawa, ON

SUMMARY: Heat-related illnesses and deaths are preventable. The Climate Change and Health Office (CCHO) initiative is to develop heat resilient individuals and communities in Canada. The HARS Best Practices Guidebook will be used by health and emergency management officials to develop, implement, evaluate and modify their activities aimed at reducing health risks from extreme heat events.

OBJECTIVES/BACKGROUND/ISSUES: Climate change is expected to exacerbate many current climate hazards, including an increased frequency, severity and/or duration of extreme heat events (EHEs). Heat-related illnesses and deaths are preventable with appropriate planning by public health officials. To reduce increasing risks to Canadians from EHEs, HARS Best Practices Guidebook is being developed to assist communities with implementing and modifying their heat warning systems.

METHOD: HARS best practices were identified with input from four Canadian pilot communities. CCHO consulted with key experts and stakeholders from these communities to identify their needs for the content of the Guidebook. In addition, CCHO evaluated HARS practices in Hamilton, Montreal and Toronto. The analysis included literature review of best practices, an examination of the accuracy, validity and consistency of health promotion factsheets and public opinion research. Focus groups comprising of medical personnel, caregivers and municipalities, identified the needs and behaviours of vulnerable groups.

OUTPUTS: The HARS Best Practices Guidebook emphasises the importance of long-term planning, mid-term prevention and short-term emergency measures to reduce the impacts of heat-related illnesses. Community level interventions such as the identification of and outreach to vulnerable populations (e.g., seniors) and the availability of services to avoid heat stress (e.g., cooling centres) are essential adaptations. These must be complemented by targeted dissemination of information to increase Canadians' knowledge of effective measures for reducing heat health risks.

Preventative measures such as modifications to the environment (e.g., reducing urban heat island effect) and behaviour (e.g., increase fluid intake) are essential to develop heat resilient individuals in Canada.

IMPACTS/NEXT STEPS: The HARS Best Practices Guidebook will serve to protect Canadians from the impacts of EHEs. It will allow for a better understanding of the needs of vulnerable populations and municipalities.

Future efforts will focus on developing evaluation strategies for HARS and gathering feedback on behaviour changes of vulnerable populations during an EHE.

3.17 Guidance for Health Canada: Biobanking of Human Biological Material

Bioethics, Innovation and Policy Integration Division[1]

[1] Science Policy Directorate, SPB, Health Canada, Ottawa ON

SUMMARY: Development of the Guidance for Health Canada: Biobanking of Human Biological Material has been informed by input from the health portfolio and external stakeholders. It provides comprehensive guidance that aligns the department's biobanking activities with international norms and ethical principles in order to help ensure consistency.

OBJECTIVES/BACKGROUND/ISSUE: A 2003 Statistics Canada survey found that Health Canada (HC), which at that time was responsible for the work currently undertaken by the Public Health Agency of Canada (PHAC), maintained approximately 92% of all federal holdings of human biological material. In the absence of comprehensive and harmonized biobanking guidance in Canada, HC embarked on an initiative to develop a departmental guidance document with the objectives of clarifying the principles applicable to departmental biobanking activities and aligning HC's biobanking activities with international norms and ethical principles.

DESIGN/METHOD/DESCRIPTION: Development of the Guidance began in 2004 and has been informed by ongoing feedback from within the health portfolio, including HC Branches, PHAC, Legal Services, and Access to Information and Privacy. Other important considerations have included input and analysis from external experts, existing departmental policies and practices, and recent guidance developed by other organizations, including the Organisation for Economic Co-operation and Development. Feedback has been obtained through the use of workshops, interviews, electronic consultations, meetings and presentations to the HC Research Ethics Board and HC Senior Management.

OUTPUT/RESULTS: The guidance is intended to apply to biobanking activities that are carried out on HC premises, performed in collaboration with external researchers, under contract with HC, and/or funded by HC. It applies to biobanking activities carried out for the purpose of research, surveillance, risk assessment or biomonitoring, and addresses diverse areas such as governance, biobank development, recruitment, consent, collection, storage, processing, handling, quality, disclosure, sharing and disposal.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: The guidance document aligns the department's biobanking activities with international norms and ethical principles, and clarifies principles applicable to departmental biobanking activities. This will ultimately help ensure consistency in departmental biobanking activities, and may also help inform the development of biobanking guidance for other audiences. Implementation of the guidance will include outreach/education activities with affected groups, and an evaluation will be carried out after 3 years.

3.18 The Northern Contaminants Program: Integrated Science and Policy for Canada

J. Van Oostdam[1], S. Donaldson[1], M. Feeley[2], and C. Tikhonov[3]

[1] Chemicals Surveillance Bureau, HECSB, Health Canada, Ottawa, ON
[2] Bureau of Chemical Hazards, HPFB, Health Canada, Ottawa, ON
[3] Primary Health Care and Public Health, FNIHB, Health Canada, Ottawa, ON

SUMMARY: The Northern Contaminants Program (NCP) is a multi-agency program undertaking research on environmental contaminants in arctic Canada. Integrated research has identified source regions in the globe and possible arctic human health impacts. Canada and the seven other arctic countries have used this information to push for international controls on contaminants.

BACKGROUND: The Canadian Northern Contaminants Program (NCP) is a federal multi-agency program that involves federal and territorial departments, aboriginal organizations, community groups and university researchers in Arctic contaminant research to protect humans and the environment. Since 1991 the NCP has undertaken three major assessments with each one presenting new knowledge and making stronger connections between long-range transport of contaminants and their impacts on human health in the Arctic.

DESCRIPTION: The NCP has involved environmental and wildlife scientists, plus human dietary and health impact scientists. This integrated contaminants research monitoring and modelling has attempted to identify source regions in the globe plus extensive human biomonitoring and health effects research has attempted to identify possible human health impacts.

RESULTS: Through back trajectory modelling, contaminant source countries in Asia, Europe and North America have been identified. In addition, human and environmental monitoring and research has identified the bioaccumulation of these contaminants in the marine mammal food chain. Human biomonitoring has found that Inuit populations of the eastern Arctic have up to ten times higher concentrations of contaminants such as PCB, DDT and mercury than concentrations seen in southern populations. Through the Arctic Monitoring and Assessment Program (AMAP), Canada and the seven other Arctic counties have been able to use this information, on a policy level, to press for global controls on persistent organic pollutants through treaties such as the United Nations Environment Program 2004 Stockholm convention.

OUTCOMES/NEXT STEPS: The data generated through the Canadian NCP and AMAP have played an important role at an international policy level. Initial trend monitoring have found that there have been significant declines in a number of contaminants but new contaminants are also being identified in the Arctic environment and its peoples so further monitoring / research is needed for input to various international fora.

3.19 Collaborative Public Health Program Evaluation: The Toronto Hot Weather Response Program (HWRP)

A. Yusa[1], S. Gower[1], S. Dolan[1], M. Campbell[2], E. Pacheco[2], and U. Bickis[1]

[1] Climate Change and Health Office, Water, Air and Climate Change Bureau, Chemicals, Air and Water Directorate, HECSB, Health Canada, Ottawa, ON
[2] Toronto Public Health, Toronto, ON

SUMMARY: Health Canada's Climate Change and Health Office (CCHO) and Toronto Public Health (TPH) have initiated an evaluation of the Toronto "Hot Weather Response Program" (HWRP). The evaluation will: 1) identify effective adaptations, and 2) develop a framework to best assess heat alert and response system (HARS) "effectiveness".

OBJECTIVES/BACKGROUND/ISSUE(S): Toronto has one of the longest operating HARS and has evolved continuously since its inception. CCHO and TPH will jointly identify best practices and assess system effectiveness to support system improvement and decision-making in Toronto and other Canadian communities. There are currently few examples of HARS evaluations

DESIGN/METHOD/DESCRIPTION: TPH and CCHO adopted a collaborative approach to developing and initial implementation of an evaluation of Toronto's HWRP. The resulting Evaluation Framework identified project methods such as environmental data collection and surveys.

OUTPUTS/RESULTS: The Evaluation Framework outlined a multi-faceted study including both science and program-related evaluation themes. Formal evaluation activities are expected to begin in the summer of 09/10. The results of a media analysis and preliminary results of an analysis of heat health massaging are expected for the fall of 2009.

IMPACTS/OUTCOMES/CONCLUSIONS/IMPLICATIONS/NEXT STEPS: Many existing extreme heat health studies have focussed on one aspect of a HARS. Few examples of HARS evaluations exist. This study will address this gap and contribute to climate change and health knowledge by providing a more comprehensive understanding of the impact of a HARS on reducing heat-related health risks by evaluating a full system.

The identification of effective aspects of the Toronto HARS will allow public health and emergency management decision-makers in Toronto as well as other Canadian communities to implement the most effective heat health interventions (e.g., health messaging, heat alerts, cooling centres etc.) in the face of limited resources.

3.20 Implementation of a Systematic and Coordinated Signal Detection Model in the Marketed Pharmaceuticals and Medical Devices Bureau (MPMDB): One Year Experience

A.E. Arias, MD, PhD[1], N. Irfan, PhD[1], K.N. Barton, MSc[1], and L. Laforest, MSc[1]

[1] Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, HPFB, Health Canada, Ottawa, ON

SUMMARY: Identifying signals on new drug safety issues require careful analysis of information from various sources. We present results from recent experience in the Bureau after implementing a model for the systematic and coordinated analysis of distinct types of information aiming at their identification.

BACKGROUND: New information on drug safety or adverse events constitute safety signals in pharmacovigilance. Identification and subsequent assessment of new signals, i.e., of hypothesis on the possible causal relationship between an adverse event and a drug, are core responsibilities of the Marketed Health Products Directorate (MHPD). They are part of MHPD's broad mandate ensuring a consistent approach to post-approval safety surveillance for regulated marketed health products.

DESCRIPTION: Effective detection of new drug safety signals requires analysis of multiple sources of information. Because the previous approach was reactive and not as well structured, three working groups have started to assess distinct types of information in a systematic and coordinated way for signal detection purposes. Taking advantage of individual professional expertise within MPMDB, groups conduct systematic screening and preliminary assessment of: 1) information discussed in articles recently published in relevant scientific journals; 2) communications from major foreign regulatory agencies; or 3) information voluntarily submitted by marketing authorization holders as post-marketing safety reports. Coordination is ensured by weekly meetings of group Chairs and shared project management support. Signal identification is based on quality and strength of the evidence, and seriousness of the adverse event. Further assessment steps are discussed at MPMDB management level.

RESULTS: Out of 345 potential drug safety topics assessed, 94 signals on different pharmaceuticals and possible drug reactions have warranted further analysis since 2008. Signals identified after implementation support the strengthening and streamlining of detection activities in MPMDB. Relevant preliminary information on potential new signals is now systematically collected and included with the rationale for further assessments in the Bureau. Importantly, it is also being used to document and/or explain the reasons why further assessment was not considered necessary.

CONCLUSIONS: Results after implementation of the systematic and coordinated signal detection model in MPMDB, support its role as a valuable complementary approach to the one based on data mining analysis from the Canada Vigilance ADR database.

3.21 Linking Primary Care and Public Health: Opportunities for the Canadian Task Force on Preventive Health Care

K. Robinson[1], C. Makris[1], and K. Elmslie[1]

[1] Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada (PHAC)

SUMMARY: PHAC has re-established the Canadian Task Force on Preventive Health Care. The field of primary care has evolved; scope of practice and supports for guideline implementation are key challenges. This presentation will review the renewed Task Force and present opportunities and challenges to strengthening primary care and public health connections.

OBJECTIVE: Widespread support exists for the Canadian Task Force on Preventive Health Care and its previous 25-years of work pioneering the development of preventive care guidelines. This provides an opportunity to build on this foundation and ensure that the renewed Task Force model is appropriate to the current context of a health care system burdened by chronic disease and where primary care and public health issues increasingly intersect. This presentation will enhance understanding of priorities, opportunities and challenges to strengthening connections between public health and primary care in the context of development, dissemination and use of practice guidelines.

METHODS: This presentation is based on: descriptive analysis and review of key international and Canadian policy reports and literature syntheses relating to the intersection and interaction between primary care and public health sectors; and thematic analysis of purposefully sampled key informant interviews with regional and national primary care and public health researchers and practitioners.

RESULTS: Preliminary analysis indicates several key themes: the importance of combining practice guidelines with continued focus on patient/community need; identifying opportunities for service coordination and referral; the need to situate practice guidelines in a comprehensive range of services to improve population health from personal care to health promotion; improving care by applying a population perspective to medical practice; and the importance of regional, provincial and national efforts to support joint sector policy, training and research.

CONCLUSIONS: Based on the findings of this analysis, opportunities to further complementary efforts between primary care and public health sectors will be presented. In addition, implications for the Canadian Task Force on Preventive Health Care and other relevant primary care and guideline/advisory groups will be proposed in order to contribute to interdisciplinary and collaborative preventive care and public health practice.

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