

Book of Abstracts

Message from the Chief Scientist

It is my great pleasure to extend greetings and heartfelt appreciation to each of you for your contributions of enthusiasm, energy and expertise that continue to make the Health Canada Science Forum an important annual event. It is only through the continuing support of the scientific community and Health Canada that we have this critical opportunity to celebrate our successes, share our challenges, and to develop opportunities for the collaborations that hold so much potential for our future.

The discipline of science, and related scientific activity, encompass so many fields of endeavour. The natural sciences, mathematics, life sciences, social sciences and the humanities - each generate important, specific and relevant questions and knowledge in our collective pursuit of scientific excellence. The health and science related issues and opportunities we face are complex, requiring evermore knowledge, capacity, interconnections, and robust policies.

I am well aware that few among us were initially motivated to become scientists in order to participate in the implementation of public policy. The inevitable frustrations inherent in the important but difficult process of policy implementation are all the more reason to be mindful of the values which brought us here. There is nothing trite about the independent pursuit of truth with integrity, much to respect about the dedication and effort to develop the necessary skills, acumen - and even perhaps, irreverence – to make an original or substantive contribution.

This year, our sub-themes of Innovation, Information, Integration and working Internationally echo Health Canada's objective of making the best possible ethical and evidenced-based decisions, both on behalf of the Canadian public and the wider global population. I applaud the organizers for having the foresight to stimulate our thinking by inviting a very impressive and inspiring group of guest speakers; and I look forward to hearing what each of you will contribute.

Pierre-Gerlier Forest, Ph.D.
Chief Scientist

Foreword

I am honoured to chair this year's Science Forum, which I hope you will find stimulating as well as varied. The forum truly encompasses the whole range of science, from social to biological and health sciences, done in our department. This year, we have endeavoured to provide the maximum time for participants to meet and speak to the authors of posters. For the first time, an invitation will be sent to universities and places will be reserved for students to participate.

I would like to extend my gratitude to the members of the Organizing Committee, the Scientific Review Committee, the Office of the Chief Scientist staff and many others in Health Canada who worked hard to ensure that this event continues to grow successfully and continues to enhance the understanding and professional development of our scientists and all Health Canada employees.

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Chair, Health Canada Science Forum 2006

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HPB

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Research Scientist
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Food Directorate, HPFB

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Biologist
Safe Environments Programme, HECSB

Aline Rinfret
A/Manager
Biologics and Genetic Therapies
Directorate, HPFB

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Science Policy Analyst
Office of the Chief Scientist

Vern Seligy
Research Scientist
Safe Environments Programme, HECSB

Phil Shwed
Research Scientist
Safe Environments Programme, HECSB

Heather Simmons
Senior Evaluation Office
Environmental Assessment Agency, PMRA

Judy Snider
Manager of Surveillance
Tobacco Control Programme, HECSB

Azam Tayabali
Research Scientist
Safe Environments Programme, HECSB

Francine Villeneuve
Senior Program Officer
Health Research Secretariat
Office of the Chief Scientist

Mike Wade
Research Scientist
Safe Environments Programme, HECSB

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

FNIHB: First Nations and Inuit Health Branch
HECSB: Healthy Environments and Consumer Safety Branch
HPFB: Health Products and Food Branch
HPB: Healthy Policy Branch
PMRA: Pest Management Regulatory Agency

1.01 Do Newly Patented Cancer Drug Treatments Imply Increasing Prices for Existing Brand-Name Cancer Drugs?

Z. Adatia, M.A.¹, A. Constant, M.A.¹, and C.D. Mallory, PhD¹

¹ Health Supply and Demand Analysis Division, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: New drugs tend to be more expensive, which drives up the proportion of drug costs out of total health care expenditures. We have found that the growth of costs in cancer drugs has exceeded growth in utilization. Also, in certain circumstances, new brand name products can increase the price of existing patent products, treating the same therapeutic condition.

DESIGN: We examined the price reaction of brand name cancer drugs when a new patented cancer drug enters the market. Canadian drug data from IMS Health for the five most recent years is used to estimate price equations. Both linear random and fixed effect models were used to account for product/formulation and province specific effects. Province specific effects (such as varying provincial drug coverage plans) were captured through the use of regional data.

RESULTS: Results were compared with findings that prices of existing brand-name hypertension drugs increase with the number of nearby competitors, but decrease with the number of brand-name products in the same sub therapeutic drug class. These results support theoretical findings that new and different drugs competing in a market for a given set of clinical indications can shrink the market share of the existing products, causing the makers of those products to increase prices.

CONCLUSIONS: If prices of existing brand name cancer drugs increase due to the launch of new patents, this would affect consumer access to effective and crucial cancer drug treatments in Canada. For policy makers, although new products may increase total costs, the new products also bring better health outcomes. A fuller examination of net effects on social welfare is warranted.

1.02 The Fingerprint Assay: Characterization of Protein-Based Biologics Using 2D Nuclear Magnetic Resonance Spectroscopy

Y. Aubin, PhD¹, G. Gingras¹, and S. Sauvé¹

¹ Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

OBJECTIVE: Development of a methodology based on 2D Nuclear Magnetic Resonance spectroscopy to characterize protein-based subsequent entry biologics.

DESIGN: The methodology had first been developed on human granulocyte-macrophage colony stimulating factor (rhGM-CSF). The human cytokine had been cloned, expressed in *E. coli* as inclusion bodies, and refolded to its active conformation. The protein was then studied by 2D NMR experiments to obtain contour maps where every single amino acids could be identified. Then data were collected to determine the three dimensional structure of rhGM-CSF in solution. NMR spectra recorded for this study were used as benchmark fingerprints for comparison with NMR spectra collected on commercially prepared rhGM-CSF.

Unglycosylated rhGM-CSF expressed in yeast produces a well-folded cytokine that is active in a cell-based assay. NMR spectra of this material have been recorded.

OUTPUTS/RESULTS: Comparison of the 2D-NMR contour maps of human ¹⁵N-rhGM-CSF produced in *E. coli* with rhGM-CSF produced in yeast are practically identical. These results demonstrate that the *E. coli* material that was refolded *in vitro* shares the same active conformation as the rhGM-CSF produced in the yeast expression system. The latter secretes the recombinant protein that folds readily into its active conformation.

IMPACT/OUTCOMES/CONCLUSION: Protein-based biotherapeutics such as hormones, and insulin, are very complex molecules that are very difficult to characterize at the atomic level. Therefore, current methods used to assess the quality and efficacy of biologics rely on *in vitro* and biological assays. These only provide an indirect characterization by inferring the identity of the active ingredient via the measurement of an effect. The methodology presented here provides a clear demonstration that a protein such as rhGM-CSF prepared via two very different procedures harbour an identical active three-dimensional structure. This method will be especially useful for the comparison of subsequent entry biologics with existing brand name products.



1.03 Lipid and Fatty Acid Metabolism is Modulated by the Source of Protein in the Diet

A. Aziz, PhD¹, L. Plouffe¹, C. Wood, MSc¹, C.W. Xiao, PhD¹, P. Griffin¹, K. Cockell PhD¹, R. Peace, PhD¹, G.S. Gilani, PhD¹, and W.M.N. Ratnayake, PhD¹

¹ Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

BACKGROUND: Cardiovascular diseases (CVD) are the major cause of death in Canada. Since defective lipid metabolism is a key risk factor for CVD, understanding the effect of dietary components on lipid metabolism is crucial to develop dietary strategies aiming at reducing the risk for CVD. In contrast to fat and carbohydrate, the effect of protein on lipid and fatty acid metabolism has received little attention despite evidence showing improved lipid metabolism with high protein diets. Also, the effect of protein on many physiological functions appears to depend on its source.

OBJECTIVES: The aim of this study was to determine the effect of protein source on lipid and fatty acid metabolism in the liver and plasma.

DESIGN: Male hamsters were fed four diets consisting of one of these four different proteins (casein: CA; beef: BF; wheat gluten: WG; and soy: SOY) for eight weeks. At the end of this period, hamsters were killed after an overnight fast, and liver and blood were collected for the measurement of fatty acids by gas-liquid chromatography, total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG) by a colorimetric method and gene expression of key liver enzymes involved in lipid and fatty acid metabolism by RT-PCR.

RESULTS: Our data show that in the liver, WG and SOY led to higher concentrations (% of total) of docosahexaenoic acid (22:6n-3), total and long-chain n-3 polyunsaturated fatty acids (PUFA) ($P < 0.05$), and higher gene expression of $\Delta 6$ desaturase ($P < 0.05$), but lower concentrations of total and long-chain n-6 PUFA, total monounsaturated fatty acids, arachidonic (20:4n-6), oleic (18:1), and palmitoleic acids (16:1) ($P < 0.05$). In plasma, TC, but not LDL-C, HDL-C and TG concentrations, were lower after WG than after BF ($P < 0.05$).

CONCLUSIONS: These data show that lipid and fatty acid metabolism in the liver is regulated by the source of the protein in the diet.



1.04 Brand Name and Generic Pharmaceutical Pricing in Canada

M.-C. Benda, PhD¹

¹ Applied Research Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: The purpose of this study was to assess the price reaction when new drugs are launched into the market, for a better understanding of the source of the increase in the pharmaceutical expenditures observed during the last decade.

DESIGN: We estimate price equations for cardiovascular brand name and generic drugs in Canada. The estimation approach incorporates a product specific effect and includes the level of differentiation of the products based on therapeutic class of the drug and on its formulation in order to take into account of the heterogeneity of the products. Specifically, we consider two families of pharmaceuticals competing for the treatment of hypertension, namely Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin receptor blockers (ARBs), which have been in the Canadian market since the 1980s. Using Canadian drug data provided by IMS Health from February 1997 to February 2006, we analyze prices within models for panel data.

RESULTS: We found that the prices of existing products decrease when the number of products in the same sub therapeutic class increases, but the prices increase with the number of nearby competitors. Our results indicate that generic products drive down prices of very close substitutes, but are likely to result in higher prices for other products treating the same clinical conditions.

IMPACTS/OUTCOMES/CONCLUSIONS: Closeness of drug products is an important variable in pharmaceutical pricing. This suggests that, in Canada where pharmaceutical products account for sizeable proportions of total expenditure on health care, increasing generic products on the market could contribute to pharmaceutical cost containment.

1.05 The Use of Inductively Coupled Plasma Mass Spectrometry (ICP-MS) to Study Dietary Iron Absorption Using Stable Isotope Tracers

K. Benkhedda, PhD¹, H. Chen, PHD^{1,2}, and K. Cockell, PhD¹

¹ Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

² Food Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVE: To develop an accurate and precise analytical protocol to measure iron (Fe) stable isotope tracer ratios. This work is conducted to support a human study using a double stable isotope tracer protocol to assess the effect of calcium supplementation on dietary Fe absorption in a group of young women.

DESIGN: Fe stable isotope ratios are measured in blood samples after chemical sample purification. Microwave digestion was used for sample decomposition before matrix separation and Fe purification using an anion exchange resin AG 1-X8. A multi-collector ICP-MS was used for Fe isotopic ratio measurements and an Aridus nebulizer and desolvating system was used to overcome the numerous and severe interference on the four Fe stable isotopes, that otherwise would affect the accuracy and the precision of Fe stable isotope ratios that need to be determined.

RESULTS: The factors affecting the precision and the accuracy of Fe isotopic ratios have been identified and optimized. Quantitative recoveries of Fe from different steps of sample preparation were obtained. Effective matrix separation has permitted resolution of the major interference on the Fe isotopes. External precision on the order of 0.008 (% RSD) and 0.04 (% RSD) were obtained for $^{57}\text{Fe}/^{56}\text{Fe}$ and $^{58}\text{Fe}/^{56}\text{Fe}$, respectively, for 10 replicate measurements of a Fe standard. For blood samples, external precision in the range of 0.007 - 0.02 (% RSD) and 0.04-0.1 (% RSD) were obtained.

CONCLUSIONS/IMPACTS: The analytical protocol developed in this work will be used in determining iron absorption in young women with marginal iron status, before and after long-term calcium supplementation. We have established the technical expertise to answer whether iron absorption is compromised by long-term calcium supplementation in this sensitive sub-group of the population. The results of this study will have important implications regarding food fortification and calcium supplementation policies.

1.06 Cigarette Smoke Causes Heritable Genetic Mutation

M.L. Berndt¹, A. Rowan-Carroll¹, A. Williams², G.R. Douglas¹, M.R. Stämpfli³, and C.L. Yauk¹

¹ Environmental and Occupations Toxicology Division, HECSB, Health Canada, Ottawa, ON

² Biostatistics and Epidemiology Division, HECSB, Health Canada, Ottawa, ON

³ Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON

OBJECTIVES: To test the hypothesis that exposure to cigarette smoke results in heritable DNA sequence mutation arising in spermatogonial stem cells of male mice.

DESIGN: Mature male C57Bl/CBA mice were exposed to mainstream tobacco smoke (MTS) from two cigarettes daily, 5 days/week for 6 or 12 weeks, using a smoking apparatus for mice. Sham-exposed mice were placed in restrainers only. Mice were sacrificed six weeks following the last cigarette smoke exposure. This waiting period ensured that sperm samples collected from the caudal epididymus were pre-meiotic spermatogonial stem cells throughout the exposure periods. Single molecule PCR (SM-PCR) was used to examine the expanded simple tandem repeat (ESTR) *Ms6-hm* locus from MCS- and sham-exposed sperm DNA. Mutations, resulting from gains and losses of repeat units, were scored blindly by two observers.

OUTPUTS/RESULTS: Exposure to MTS resulted in a 1.5- to 2-fold increase in ESTR mutation over sham-exposed males. ESTR mutation was consistently elevated across the germline of all exposed mice.

IMPACTS/OUTCOMES/CONCLUSIONS: The work presented here demonstrates that exposure to MTS causes heritable DNA sequence mutation in pre-meiotic spermatogonial stem cells. These mutations result from the induction of genetic instability in the paternal germline and are heritable in subsequent generations. The findings suggest that cessation of smoking should be undertaken in all males prior to conception.

1.07 Determination of the Three Dimensional Structure of the Conserved Hydrophobic Region of the Recombinant Human Prion Protein in a Membrane Environment by NMR

D. Buijs, BSc¹, G. Gingras, BSc¹, and Y. Aubin, PhD¹

¹ Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa ON

OBJECTIVE: To characterize the structure of the conserved hydrophobic region (CHR) of the prion protein in a model membrane environment, with multidimensional nuclear magnetic resonance (NMR) spectroscopy techniques.

DESIGN: The CHR of the human prion protein (PrP) has been cloned and expressed in *E. coli*. The purified protein was dissolved in dodecyl phosphocholine (DPC) micelles to mimic a membrane environment. Three dimensional NMR experiments were performed, and tertiary structures calculated.

RESULTS: The three dimensional structure of the human PrP in DPC micelles was found to be in dynamic exchange between random coil and α -helix in micelles at pH 6.3. Upon raising the pH to 7.6, the peptide assumed a predominantly helical conformation.

IMPACT/CONCLUSIONS: Prion diseases result from a conformational change of the prion normal cellular form to an abnormal form that causes neurodegeneration. Observations have implicated the CHR in this conformational change. Interactions between the CHR and the cellular membrane have been associated with certain forms of prion diseases. In particular, the A117V mutation in the CHR region has been found in patients with the Gerstmann-Sträussler-Scheinker syndrome. This study provides the first atomic model of this region in a membrane environment. The characterization of this pH-dependent conformational behaviour may help identify the interactions that modulate the unfolding of the normal cellular form of the prion protein.

1.08 Laboratory Interoperability for PU Urinanalysis

C. Li, PhD¹, D. Lariviere, PhD¹, M. Zamora, PhD¹, S. Kiser¹, G. Moodie¹,
R. Falcomer¹, and J. Cornett, PhD¹

¹ Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau,
HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Following a radiological/nuclear (R/N) incident where plutonium is involved, bioassay of the first responders and the public is important to assess potential internal contamination. If the incident is of a large scale, hundreds or even thousands people need to be assessed in a timely manner. Many laboratories will be called upon to work on the analysis. This project was to test the interoperability among laboratories via a proficiency test program.

DESIGNS: Plutonium isotopes (^{239}Pu and ^{240}Pu) were spiked in pre-stabilized urine from healthy human at five different concentration levels (from $\mu\text{Bq/L}$ to mBq/L) and shipped to six laboratories across Canada and two laboratories in the U.S.A. The samples were analyzed by inductively coupled plasma mass spectrometry (ICP-MS), alpha spectroscopy (α), or thermal ionization mass spectrometry (TIMS).

OUTPUTS/RESULTS: The results from all of the participating laboratories were received by the end of May 2006. Data analysis will be conducted in June and July. Data will be pooled and analyzed according to acceptance criteria. Interoperability will be assessed as: 1) same method in different laboratories, e.g., α in AECL and NIST; 2) different methods in the same laboratory, e.g., α and TIMS in NIST; and, 3) low-level assay, e.g., at $\mu\text{Bq/L}$ level.

IMPACT/CONCLUSIONS: Good interoperability helps improve laboratory reach-back capability and capacity, which is important for consequence management following an R/N incident.

1.09

[Withdrawn]

1.10 A Study of Processing Parameters for Manufacturing Porous PLGA 85/15 Scaffolds for Tissue Engineering

J.K. Perron, MASc¹, J.N. Daka, PhD², H. Naguib, PhD³, and A.S. Chawla, PhD²

¹ Department of Mechanical Engineering, University of Ottawa, Ottawa, ON

² Medical Devices Bureau, Therapeutic Products Directorate, HPFB, Health Canada, Ottawa, ON

³ Department of Mechanical and Industrial Engineering, University of Toronto, Toronto, ON

OBJECTIVE: To manufacture and to study processing parameters to optimize the production of PLGA 85/15 porous scaffolds with a high level of porosity and interconnectivity, using a gas foaming/salt particle leaching technique.

DESIGN: The design of the scaffolds was based on using materials that are biocompatible with human cells and can degrade into non-toxic by-products. The technique does not use high temperatures or organic solvents which may be harmful to cells. It therefore fits the HC mandate that requires all medical devices used in Canada to be safe and effective. In this study, 85/15 poly (DL-lactide-co-glycolide) acid, commonly known as PLGA 85/15 was used. Also used were sodium chloride, distilled water and carbon dioxide.

OUTPUTS/RESULTS: Samples of porous PLGA 85/15 scaffolds were produced by applying high pressures, using carbon dioxide, at selected lengths of time, to a matrix of PLGA 85/15 and NaCl particles. The final porosity and interconnectivity in the scaffolds were obtained by leaching out the salt particles using distilled water. The fabrication parameters studied included gas saturation pressure, gas saturation time, and NaCl/polymer mass ratio. The physical properties examined were the density, the porosity, and the average pore size of the scaffold. The Young's modulus in compression, as well as the pore density inside the scaffold were also studied. In general, all scaffolds showed a porosity of more than 90%, a relative density of 0.0534 to 0.149 g/cm³, a pore density of 1.51x10⁶ to 6.72x10⁶ pores/cm³, and a compression modulus of 0.07 to 0.84 MPa. The NaCl/polymer mass ratio was the parameter that had the most significant effect on the physical properties of the scaffold. The average pore size was affected by the saturation pressure only slightly, and the pore size was equivalent to the size of the NaCl particles used to make the scaffold.

CONCLUSION: The present technique is attractive for preparing laboratory scaffolds designed for evaluating the physical properties, biocompatibility and biosafety of implantable medical materials. The results also provide HC with an improved understanding of polymer/cell interactions in scaffolds.

1.11 Interactive Access for the Canadian Nutrient File, 2005

J. Deeks¹, M.F. Verreault¹, and M. Munro¹

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

OBJECTIVE: The Canadian Nutrient File is Canada's national standard reference food composition database. In 2003, consultations with stakeholders revealed that a vital requirement was to have a more user-friendly program with which to access the nutrient data, since only a small number of clients were able to utilize the electronic relational files available for download.

METHODS AND MATERIALS: A program had previously been developed in order to edit and maintain data updates. A component of this software served as the JAVA template in which users are able to search either in English or French, by partial foodnames or foodcodes. Once one has located the food of interest, the next screen presents choices among reasonable serving sizes including one, which corresponds to the Canada's Food Guide for Health Eating (CFGHE). Upon choosing a serving size a report is generated profiling the available nutrient data in the chosen portion of the food.

RESULTS: Consumer response for the new service is very positive as indicated by enthusiastic feedback from clients and a significant reduction in the number of queries to CNF staff as clients can now locate the data independently. We are planning to conduct a consumer satisfaction survey in 2007.

SIGNIFICANCE: The CNF continues to fill the need for reference nutrient data for use on population nutrition studies that investigate diet and disease/risk assessment. The new interactive web program makes accessing the database more user-friendly allowing greater dissemination to a greater number of users who can now utilize this nutrient data to positively influence healthy eating and better food choices.

1.12

[Withdrawn]

1.13 Rapid and Selective Characterization of Influenza Virus Constituents in Monovalent and Multivalent Preparations Using Non-Porous RP-HPLC Columns

V. Garcia-Cañas¹, B. Lorbetskie¹, and M. Girard¹

¹ Centre for Biologics Research, BGTD, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To develop a method based on reversed-phase high performance liquid chromatography for the characterization of constituents in influenza vaccines.

DESIGN: Influenza vaccines are preparations containing influenza virus components. Among these compounds the membrane glycoproteins, haemagglutinin (HA) and neuraminidase (NA) are the major surface antigens and the reference base for the classification of the influenza strains by subtypes. Every year, the composition of influenza vaccine formulations depends on the most widespread strains in the world population and usually includes three strains. With the increasing requirements in terms of purity and quality of vaccines, the ability to detect and characterize specific constituents contained in these preparations becomes an important additional feature for any detection method. However, the highly hydrophobic nature of such proteins and hence, low solubility and the number of different antigens in influenza trivalent vaccines (containing three strains) make these mixtures difficult to characterize using conventional techniques.

In this work, characterization of influenza vaccines composition has been approached by a new methodology that is suitable for routine analysis. It includes a sample processing step and its subsequent analysis by RP-HPLC.

Several parameters affecting the solubility of hydrophobic proteins were tested. Using different detergents (Zwittergent 3-14 and *n*-octyl- β -D-glucopyranoside), dithiothreitol and hexafluoroisopropanol good solubilization of the hydrophobic protein fraction was achieved.

Adequate RP-HPLC conditions that can provide fast, reproducible and highly resolved separations of hydrophobic proteins using different stationary phases were investigated. For the initial studies conventional porous stationary phases were used, but some difficulties related to low sensitivity and peak carryover were encountered. These difficulties were circumvented by using a non-porous silica stationary phase, which minimized adsorption, increased the recovery, and decreased the analysis time. The effect of some parameters (i.e., organic modifier, temperature and gradient) on the resolution, selectivity and separation efficiency was studied using these columns. Under optimum separation conditions, the developed method demonstrated to be suitable for the characterization of processed monovalent preparations (containing influenza virus constituents from a single strain) and allowed to detect simultaneously three different influenza subtypes in trivalent vaccines in the same analysis.

OUTPUTS/RESULTS: Novel chromatographic separation method based on non-porous silica-based stationary phases that provided high selectivity for the characterization of several influenza vaccine components; simultaneous detection of different influenza haemagglutinins in trivalent vaccines; sample preparation procedure that improves solubilization of highly hydrophobic protein fraction.

IMPACTS/OUTCOMES/CONCLUSIONS: First report of the separation of three hemagglutinins by reversed-phase HPLC; routine testing of vaccine components by physico-chemical method.

1.14 Work and Life Stressors: Barriers to Physical Activity?

B. Haddy, candidate for BSc¹, and E. Tipenko, MSc¹

¹ Data Development and Dissemination Division, HPB, Health Canada, Gatineau, PQ

OBJECTIVES: The purpose of this study is to determine if work/life stressors act as a barrier to physical activity. There is an abundance of research showing that physical activity is used as a coping method to decrease stress levels, but the possibility that psychological stressors themselves impede, (or facilitate), physical activity levels should be explored.

DESIGN: Analysis was conducted using the 2005 Canadian Community Health Survey (CCHS).

Logistic regression analysis stratified by sex and employment status was performed to identify the odds of physical activity status (active or inactive) being related to stress factors while controlling for: age, sex, Canadian regions, restriction of activity, sense of belonging to community, education, provincial income, immigrant status and parental status. Also, through gender analysis, it will be determined whether there are gender-specific differences for physical activity behavior when experiencing different levels of work/home stress. The bootstrap method was used for logistic regression in order to control for the complex survey design.

OUTPUT/RESULTS: Self-perceived stress has been associated with a decrease in physical activity only for unemployed Canadians of both sexes. For employed males and females in Canada, having children in the household under the age of five is associated with decrease in the likelihood of being physically active.

For employed males and females in the province of Quebec, having an increasing number of close family and friends increases the likelihood of being physically active. Only in employed males, satisfaction with: neighborhood, friends and financial situation significantly related to physical activity. Unemployed females in Quebec are affected by the number of close family and friends they have, as well as their satisfaction with their neighborhood, friends and financial situation.

Total hours worked per week was the most significant predictor for both sexes across Canada and but not in Quebec. Self-perceived work stress and physical activity behavior show negative relationship only for Canadian women who work part-time hours and men who work overtime.

In Quebec, men are significantly affected by their job security when predicting physical activity status. Self-perceived work stress is insignificant for both sexes as well as job satisfaction.

IMPACTS/OUTCOMES/CONCLUSIONS: Answering this research question holds the potential to change and structure health policies and interventions such that barriers to physical activity due to work and life stressors are reduced.

1.15 Global Transcriptional Analysis of the Cardiovascular Effects of Mainstream Tobacco Smoke: Identification of Novel Biomarkers of Effect

S. Halappanavar, PhD¹, M.R. Stampfli, PhD², M.L. Berndt, MSc¹, A. Williams, MSc³, G.R. Douglas, PhD¹, and C.L. Yauk, PhD¹

- ¹ Environmental and Occupational Toxicology Division, HECSB, Health Canada, Ottawa, ON
² Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON
³ BioStatistics and Epidemiology Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To test the hypothesis that mainstream tobacco smoke (MTS) induces changes in gene expression in heart that will be predictive of eventual pathophysiological changes. To evaluate whether the measured changes will provide novel biomarkers of the effects of smoking.

DESIGN: Male C57B1/CBA mice were exposed to MTS from two cigarettes daily, 5 days/week for 6 or 12 weeks, using a smoking apparatus for mice¹. Sham-exposed mice were placed in restrainers only. Mice were sacrificed immediately after or six weeks following the last cigarette smoke exposure. Whole heart was removed and flash frozen. Total RNA was isolated from a small part of the heart and was hybridized against universal mouse reference RNA to Agilent Oligo DNA microarrays (Agilent Technologies) containing 22,000 transcripts^{2,3}. Microarrays were normalized using a global LOWESS approach, MAANOVA 2.0 and SAM.

OUTPUT/RESULTS: We have identified 20 genes that were significantly differentially expressed (2.0 to 14- fold higher or lower). Functional classification of the 20 genes demonstrates severe alteration in biological pathways regulating xenobiotic metabolism, proangiogenesis and inflammatory response. These genes include, Cyp1a1 (14 fold up-regulated), cysteine rich protein 61, Sprr1A, Lipid3 Lipin3, macrophage colony stimulating factor 1, Akap12 (gravin).

IMPACTS/OUTCOMES/CONCLUSIONS: Gene expression profiling of heart tissue provides a novel approach to study the cardiovascular effects of exposure to MTS. This work identifies several candidate biomarkers of exposure and potential adverse effect.

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1.16 Assessment of Cytotoxic and Genotoxic Effects of Diesel and Biodiesel Fuels and their Combustion Exhausts on Murine Cells

C. Healy¹, C. Parfett¹, D.E. Arnold², A. McMahon³, M. Wade³, R. Poon³, and I. Chu³

- ¹ Mutagenesis Section, Environment and Occupational Toxicology Division, Environmental Health Science Bureau, Safe Environment Programme, HECSB, Health Canada, Ottawa, ON
- ² Biochemistry Department, University of Ottawa, Ottawa, ON
- ³ Systemic Toxicology and Pharmacokinetics Section, Environment and Occupational Toxicology Division, Environmental Health Science Bureau, Safe Environment Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVE: Diesel powered vehicles, fuels and their combustion exhausts represent a significant source of urban air pollution, soil contamination, and potentially hazardous occupational exposure. To decrease health risks, attempts have been made to develop less polluting fuels. As a preliminary evaluation, we compared *in vitro* cytotoxicity and genotoxicity of different fuels and combustion exhausts: ultra-low sulphur diesel (ULSD), low sulphur diesel (LSD) and biodiesel from fish, canola and soybean in C3H10T1/2 cells.

DESIGN: Cytotoxicity was established through cellular growth assays, testing concentrations of 0, 0.01, 0.1, 0.5, 1% for fuels and exhausts extracts, for 24 hours and 48 hours respectively. Genotoxicity endpoints include a DsRed reporter gene reversion assay for tandem repeat sequence mutations, cytokinesis block micronucleus assay to detect unincorporated chromosome fragments and a microarray study using the Health Canada ToxArray™ to examine diesel-induced gene expression changes.

OUTPUTS/RESULTS: At concentrations of 0.01-0.1, DMSO exhaust extracts were not significantly more toxic than solvent controls, all maintaining 80% relative cellular proliferation (RCP), relative to untreated controls. At 1%, cytotoxicity ranking was: DMSO, Filter Blank, Soy (40%RCP)<ULSD, ULSD/Soy mix (30%RCP)<LSD/Soy mix, LSD (15-20%RCP). In fuels, fish biodiesel showed the highest cytotoxicity with 15%RCP at the mid-concentration of 0.1%. For all other fuels, 60-80%RCP was observed at 0.01-0.1%, 20-40%RCP at 0.5% and less than 20%RCP at 1%. Initial data reveals some exhaust extracts and fuels induced 2 fold increases in the DsRed assay at 0.5% concentrations. Further comparisons with fuels and exhausts are ongoing.

IMPACT/OUTCOMES/CONCLUSIONS: The outcome of these experiments will help rank potential health hazards. The observed variation within fuel types may be due to differences in fuel formulations, feed stocks, and additives. Initial toxicity data shows low toxicity from all types of exhausts extracts relative to DMSO controls, but genotoxicity may provide further insights on the long-term health effects of these substances.

1.17 Safety Assessment of Consumption of Conjugated Linoleic Acid Isomers During Early Development in Rats: Effects of Dietary CLA on Long-Chain Pufa Status

C. Cruz Hernandez, PhD¹, W.M.N. Ratnayake, PhD¹, and L.J. Plouffe¹

¹ Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Conjugated linoleic acid (CLA) is naturally found in beef and dairy products. CLA has exhibited anticarcinogenic properties and other beneficial physiological properties. However, evidence from cell culture and animal studies suggests that CLA inhibits several enzymes involved in the metabolism of linoleic (18:2n-6) and α -linolenic acid (18:3n-3) to long-chain polyunsaturated fatty acids (LCPUFA). The objective of this study was to assess, using rat as the experimental model, whether maternal intake of CLA during pregnancy and lactation has an effect on LCPUFA status on the brain and other tissues of pups.

DESIGN: Female rats (n=20 per group) were fed diets containing 0%, 0.5%, or 1% CLA. After 14 days on the diet, they were mated by overnight pairing. Litters (10 males and 10 females per group) were weaned at postnatal day 21. On postnatal day 23, 2 male and 3 female pups (50% per litter group) were killed and tissues were collected for fatty acid analysis by gas liquid chromatography.

OUTPUTS/RESULTS: The results showed that 18:2n6 decreased in blood and increased in adipose, heart and brain ($P<0.05$); 18:3n6 decreases in adipose and liver ($P<0.05$) and remain the same for the other tissues; 20:4n6 decreased in adipose, liver and increased in heart ($P<0.05$); 18:3n3 did not change; 20:5n3 decreased in liver and increased in heart and blood ($P<0.05$) with no significant differences in brain; 22:6n3 decreased in liver and increased in heart ($P<0.05$) with no significant differences in brain. Total CLA increased in tissues ($P<0.05$) dose dependently except in the brain.

IMPACTS/OUTCOMES/CONCLUSIONS: These findings do not support that CLA adversely affects LCPUFAs in various tissues of pups, especially in the brain where AA and DHA are crucial for normal development. Whether there are benefits for incorporating CLA in the diets of pregnant and lactating mothers requires further investigation.

1.18 Sensitivity of Portable Personnel Portal Monitors: Potential Problems when Dealing with Contaminated Persons

G.H. Kramer¹, K. Capello¹, B.M. Hauck¹, and J.T. Brown²

¹ Human Monitoring Laboratory, Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

² Defence Research and Development Canada, National Defence, Ottawa, ON

OBJECTIVES: Health physicists are usually concerned with small amounts of radioactivity and strive to develop techniques to measure them; however, following a terrorist attack involving radioactive materials the converse might be the case, and exposed persons may be heavily contaminated. This work has determined the distance at which portal monitors will alarm at different levels of radioactive contamination on or in exposed persons following a terrorist attack that dispersed radioactive materials.

DESIGN: The Human Monitoring Laboratory (HML) has field tested its Portable Personnel Portal (P3) Monitors using sources up to 1700 MBq (47 mCi) to determine the alarm distance as a function of activity.

OUTPUT/RESULTS: The definition of the “circle of sensitivity” (radius equal to alarm distance) now allows the HML to better plan siting requirements in the event of a response to an incident.

IMPACTS/OUTCOMES/CONCLUSIONS: These results have shown that previous plans are not valid and must be abandoned as it is now clear that adjacent units must be separated in the open to avoid simultaneous alarms by as much as 70 m, although this distance will be greatly dependent on the levels of contamination of the affected persons. Building materials could shield the monitors allowing units to be placed closer together than in the open where there is no shielding; however, the attenuation may not be sufficient enough to allow monitors to be placed in adjacent rooms. Crowd control remains an issue that will require careful thought, as doorways and windows can provide an aperture for contaminated persons (or a crowd of contaminated persons) to alarm the monitors from a distance.

1.19 The Efficiency Curve: A New Function

G.H. Kramer¹

¹ Human Monitoring Laboratory, Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Simple efficiency equations are only accurate over a limited range (e.g., 160 keV to 1333 keV). Others, that cover a wider range, may involve the use of integral calculus to develop a set of semi-empirical equations that can well define the efficiency of point or extended sources over a wide energy range. However, most of these equations were developed independently of the physical process that occurs as photons travel through matter. This study was initiated to search for a relatively simple equation based on the physical properties of photon transport through various materials. The improved function is to be applied to the estimate of radioactivity that has been accidentally internalized by a person

DESIGN: Starting from first principles a series of fundamental equations were assembled that described the photon transport process. Combining these equations and making some simplifying assumptions yielded a simple difference of two exponentials that could be used to define the efficiency curve.

OUTPUTS/RESULTS: A new equation has been developed that fits counting efficiency as a function of photon energy based on physical interactions of radiation with matter. The function gives an excellent fit to the data, especially in the knee region (the region where the function's slope changes from positive to negative) where other functions often have problems.

IMPACTS/OUTCOMES/CONCLUSIONS: The function developed by the Human Monitoring Laboratory (HML) has been compared to a variety of other functions that have been developed and used by other authors. Compared with other published functions, the HML function gives a better fit to the data and its use will improve the accuracy of activity estimates resulting in more accurate dose estimates. As a result, any health risk (cancer at low doses, other symptoms at higher doses) estimate based on these data will also be more accurate.

1.20 Automation of Separation Protocols, a Tool to Improve Sample Throughput in Case of an Radiological/Nuclear Emergency

D. Lariviere, PhD¹, C. Li, PhD¹, S. Kiser¹, and J. Cornett, PhD¹

¹ Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: In the previous years, numerous analytical protocols using inductively coupled plasma mass spectrometry (ICP-MS) as a detection instruments have been developed for long-lived radioisotopes. Although these protocols are fast and permit detection of femtogram of actinides in environmental matrices, they nevertheless require skilled laboratory staff to perform them. The use of automated protocols could further enhance performances and rapidity while reducing the variability resulting from the user.

DESIGN: A high performance liquid chromatography (HPLC) unit was coupled to four automated switching valves to produce a system that can operate three different extraction resins (i.e., TEVA, UTEVA, DGA). Depending on the type of samples or the requested analyte(s), the system can be modified by simply selecting the appropriate protocol from the developed library. The system developed can be coupled to any commercially available ICP-MS, making it quite versatile.

OUTPUTS/RESULTS: The protocols (for urine, drinking water, air particulates, and swipe samples) provide validated analytical methods for rapid and sensitive assessment of actinides in field samples following an R/N emergency. The sample throughput is two to six samples per hour, and the sensitivity for the most interested nuclides is around 1-100 fg per ml or gram (e.g., for Pu-239, pg/L in urine).

IMPACTS/OUTCOMES/CONCLUSIONS: The protocols, now almost fully automated, are among the most sensitive to date. They provide the nuclear cluster laboratories in Canada technically standardized solutions for emergency preparedness and that, without a significant increase their need for additional staffing. Technologies developed throughout the project can be applied for other research and application projects, such as nuclear forensic.

1.21 Testicular Toxicant 2-Methoxyacetic Acid Causes Spermatocyte Apoptosis by Increasing Acetylation of Core Histones

M. Wade¹, A. Lee¹, A. Williams², C.L. Yauk³, and I. Chu¹

¹ Systemic Toxicity and Pharmacokinetics Section, Environmental Health Sciences Bureau, HECSB, Health Canada, Ottawa, ON

² Biostatistics and Epidemiology Division, Environmental Health Sciences Bureau, HECSB, Health Canada, Ottawa, ON

³ Mutagenesis Section, Environmental and Occupations Toxicology Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To evaluate the mechanisms by which the testicular toxicant 2-methoxyacetic acid (MAA) disrupts spermatogenesis.

DESIGN: Sexually mature male rats were exposed i.p. to saline (control) or MAA (650 mg/kg). Groups of 6 MAA-treated or concurrent controls were sacrificed at intervals post exposure (PE: 4, 8, 12 and 24 hours). Testis were removed and either snap frozen for gene and protein analyses or fixed for histological analyses. Using high-density microarrays (Agilent), steady state levels of mRNA transcripts were determined in total testis RNA from all MAA-treated and concurrent control animals. Germ cell apoptosis was examined in testis sections using in situ staining for DNA fragmentation. Also, acetylation of histone H4 was examined by Western blot and immunohistochemistry.

RESULTS: MAA treatment resulted in increased death of pachytene spermatocytes (PS) starting 8 hours PE and increasing dramatically at 12 and 24 hours PE. Microarray results indicated that at 4, 8, 12 and 24 hours PE steady state levels of 7, 6, 519 and 527 different RNA transcripts were significantly altered by MAA treatment. As the goal was to examine mechanisms of toxicant action, all genes changed at 4 hours PE were examined by literature search. One gene (histone H1(0)) showed significant (> 2 fold) upregulation at 4, 8, and 12 hours post exposure. As expression of this gene has been shown to indicate increased core histone acetylation we examined MAA-induced changes in histone H4 acetylation (acH4) in testis nuclear protein and found that acH4 immunoreactivity was increased at 4 hours and remained elevated up to 24 hours PE. At 4 hours PE, Immunohistochemical analyses indicate that PS nuclei stained intensely for acH4 while no staining was seen in concurrent control PS.

CONCLUSIONS: Intense acetylation of histone H4 precedes cell death in PS suggesting a causal relationship between core histone acetylation and induced death of meiotic germ cells.



1.22 The Mutagenic Hazards of Complex Mixtures of Polycyclic Aromatic Hydrocarbons (PAH) in Soil

C. Lemieux, BSc¹, I.B. Lambert, PhD^{1,2}, R. Gagné, BSc¹, M. Tysklind, PhD³, S. Lundstedt, PhD^{1,3}, G.R. Douglas, PhD¹, and P.A. White, PhD¹

¹ Mutagenesis Section, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

² Biology Department, Carleton University, Ottawa, ON

³ Department of Chemistry, University of Umea, Umea, Sweden

OBJECTIVES: To evaluate risk assessment methods currently employed to predict the mutagenic and carcinogenic hazards of complex PAH mixtures in contaminated soils.

DESIGN: Organic components of PAH-contaminated soils were extracted using pressurized fluid extraction, and were subsequently separated on silica gel into polar and non-polar fractions. Synthetic mixtures containing 16 priority PAHs were prepared to match the results of earlier chemical analyses. The mutagenic potencies of the complex soil extracts/fractions, synthetic PAH mixtures, and individual PAH constituents were evaluated using the *Salmonella* mutagenicity assay, and the lacZ mutation assay in FE1 Muta™ Mouse lung epithelial cells.

OUTPUT/RESULTS: Eight of 16 PAHs yielded a mutagenic response in the *Salmonella* assay, although only five induced a significant increase in lacZ mutations in FE1 cells. All reconstituted mixtures and PAH-containing soil fractions also elicited significant mutagenic responses in both assays. A significant response was also observed for the polar fraction in *Salmonella* YG1041, a strain that is sensitive to N-heterocyclic compounds and aromatic amines. The predicted mutagenic activity of the non-polar fraction, whether based on: 1) its synthetic mixture; or, 2) the sum of the effects expected from the identified PAH constituents, was significantly greater than the observed mutagenic activity of the PAH-containing fraction.

IMPACTS/OUTCOMES/CONCLUSIONS: The results indicate that the total mutagenic activity of a complex PAH mixture, such as that present in a contaminated soil, is less than that calculated under an assumption of complete additivity. Thus, a targeted risk assessment approach focusing on priority PAHs should provide useful, conservative assessments of mutagenic activity for the PAH-containing fraction of contaminated soils. However, such an approach cannot account for additional risks associated with unidentified compounds in other fractions, including aromatic amines or heterocyclic compounds. Exclusion of such fractions in an assessment may lead to significant underestimation of the actual total mutagenic (or carcinogenic) hazard.

1.23 Gerbils – Animal Model for *Enterobacter sakazakii* Infection

R. Lenati^{1,2}, M. Lin³, J.M. Farber^{1,2}, and F. Pagotto¹

¹ Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

² Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

³ Canadian Food Inspection Agency/Animal Diseases Research Institute, Ottawa, ON

OBJECTIVES: *Enterobacter sakazakii* (Es), an emerging opportunistic pathogen causing neonatal meningitis, is often associated with consumption of powdered infant formula (PIF). The mechanism(s) by which it causes disease in humans and its minimum infectious dose (MID) remain unknown. As such, it is difficult for regulatory agencies to set policies and for industry to develop control measures for this organism. Herein, we assessed six animal species to find a model that better mimicked human pathogenesis and clinical manifestations of Es infection.

DESIGN: Young (chicks, gerbils, guinea pigs, pigs, and rabbits) and neonatal (gerbils, rats) animal models were orally challenged with 10⁹cfu of clinical, environmental or food isolates of Es. The animals were observed up to day 14 post-inoculation (p.i.) and their blood, fecal specimens and organs (brain, heart, liver, spleen, mesentery, kidney, and intestines) examined for the presence of Es.

OUTPUTS/RESULTS: None of the young animals presented clinical symptoms observed in Es infections in humans. Some neonatal (6/36) gerbils died within 48 hours of infection. While Es was isolated from fecal samples of all animals challenged, it was only recovered from tissues, including the brain, of gerbils (young and neonatal). Future studies will consist of challenging the neonatal gerbils with a larger set of Es strains (n=30) in order to assess differences amongst them.

IMPACTS/OUTCOMES/CONCLUSIONS: Gerbils may be a suitable animal model to evaluate virulence of Es strains, and possibly its MID. A suitable animal model for the study of Es pathogenesis will be useful for extrapolation to what is observed in human infections, and to base policy development with respect to the presence and/or tolerance of Es in PIF and other foods on sound science.

1.24 Solubility Study of Uranium Oxide Particles in Simulated Lung Fluids

W. Li, PhD¹, C. Li, PhD¹, R. Skinner, MSc¹, S. Kiser¹, and J. Cornett, PhD¹

¹ Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: The overall goal of this project is to assess the effects of particle sizes, mechanism, and kinetics of the particle dissolution on solubility of uranium oxide particles in simulated lung fluid and indicate different biological effects.

DESIGNS: A batch method has been used to study solubility of uranium oxide particles. Particles were suspended in simulated lung fluid at 37°C. Different ranges of particle sizes were studied. Sub-samples were taken from the solutions and filtered through 0.45 µm filter membranes (Whatman), and then diluted for inductively coupled plasma mass spectrometry analysis.

OUTPUTS/RESULTS: Evaluation of biological effects of inhaled aerosol particles involves multi-tiered processes including dissolution of the particles and the transport of the dissolved particles. Solubility of UO₂ particles with different particle sizes were studied in simulated lung fluid at biological temperature. The particles were also studied by scanning electron microscope (SEM) to identify size; distribution and morphology; and by ICP-MS to identify uranium chemical forms of the particle.

IMPACT/CONCLUSIONS: This study showed that smaller particle sizes of uranium oxide dissolved significantly faster than larger ones in simulated lung fluid. The small particles therefore exert more biological impact on bodies when uranium aerosol is inhaled. These experiments provided an effective scientific tool to assess biological and chemical aerosol particle properties and also linked chemistry with biology to help understand biological effects of inhaled UO₂ particles.

1.25 Residue Analysis and Tissue Distribution of Complex Organochlorine Mixtures in Rats After Gestational and Lactational Exposure

N. Li¹, W.J. Bowers¹, J. Nakai¹, R. Strathern¹, D. Moir¹, A. Yagminas¹, and I. Chu¹

¹ Environmental and Occupational Toxicology Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: As part of a multi-disciplinary project to assess developmental effects of a complex organochlorine (OC) mixture (25 OC pesticides and polychlorinated biphenyls), this study investigated residue analysis and tissue distribution of this complex mixture in rats following gestational and lactational exposure.

METHODS: Serum was extracted with hexane, and cleaned up with a Florisil column chromatography. For liver, brain and adipose, samples were homogenized and extracted with a mixture of acetone and hexane (2:1). The extract was dried with a column of anhydrous Na₂SO₄, and cleaned up with a Florisil column chromatography. Instrumental analysis was carried out using gas chromatography with an electron capture detector. The method was evaluated for linearity of calibration and for analyte recoveries. The quality control for routine analysis was conducted by inclusion of two surrogate standards, benzene hexachloride (β -BHC) and 2,2',3,4,5,5'-Hexachlorobiphenyl (PCB141), in all samples being analyzed with an acceptable range of recovery of 70% to 130%.

RESULTS: Satisfactory recoveries were obtained for all individual OCs in the mixture from serum, liver, brain and adipose. Calibration with standard extract over a 80-fold concentration range shows good linearity, typically $R^2 > 0.999$. The detection limits were estimated to be between 0.02 to 0.05 pg. Over 1000 tissue samples were analyzed, and the tissue distribution of each chemical was determined.

CONCLUSION: The established method is efficient for analysis of OC and PCB residues in rat tissues. With only one clean-up step, the method is also simple. Quality control for routine analysis has been established.

1.26 A Comprehensive Congener-Specific Analysis of Polybrominated Diphenyl Ethers in Rat Tissues Dosed with Commerical DE-71™

N. Li¹, I. Chu¹, J. Nakai¹, F. Wu¹, R. Strathern¹, M. Wade¹, A. Yagminas¹, P. Wall¹, R. Mueller², O. Pulido², and W.J. Bowers¹

¹ Environmental and Occupational Toxicology Division, HECSB, Health Canada, Ottawa, ON
² Toxicology Research Division, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: 1. Develop a method for quantitative analysis of polybrominated diphenyl ether (PBDE) congeners in serum, liver and brain of experimental rats dosed with DE-71™ (Great Lakes Chemicals). 2. Investigate tissue distribution of major PBDE congeners of DE-71™ in serum, liver and brain. 3. Compare the concentration profile of PBDE congeners in rat tissues with that of commercial DE-71™.

METHODS: A total of 20 PBDE congeners were identified in DE-71™ that was used to dose rats to examine developmental neurotoxicity. All the 20 PBDE congeners were quantified with gas chromatography (GC) with electron capture detection (ECD). The analytes were extracted from rat tissue with a mixture of hexane and acetone. The extract was dried with anhydrous Na₂SO₄ and cleaned up with a Florisil column. 2,2',3,3',4,4',5,5',6-Nonachlorobiphenyl (PCB206) was used as internal standard for GC analysis, and 6-fluoro-2,2',4,4'-tetrabromodiphenyl ether (FBDE-47) was used as the surrogate standard for routine analytical quality control.

RESULTS: Good recoveries (typically over 80%) and linearity of calibration (over 0.999) were obtained for all the 20 PBDE congeners. Detection limits were between 0.01 to 0.05 pg. Over 1000 tissue samples (serum, liver and brain) from rat pups of various ages exposed gestationally and lactationally to four dose levels of DE-71™, as well as from rat dams, were analyzed. The concentration profile of the PBDE congeners in above tissues were obtained and compared with that of DE-71™. The tissue distribution and potential for bioaccumulation were established and compared with those of typical polychlorinated biphenyls (PCBs).

CONCLUSION: This is the first of a comprehensive quantification of PBDE congeners in rat tissues exposed to DE-71™. While most studies have focused on the major PBDE components, i.e., BDE47, BDE100, and BDE99, this work expands the analysis to 20 congeners found in DE-71™. In conjunction with the comprehensive behavioural, physiological, molecular and anatomical analysis of brain development conducted in these pups, these congener-specific residue data will provide insight into toxicology of PBDEs.



1.27 Tissue Distribution of Polychlorinated Biphenyls in Rats After Gestational and Lactational Exposure to Aroclor 1254: A Comprehensive Congener-Specific Quantitative Analysis Using Gas Chromatography

F. Wu¹, W.J. Bowers¹, N. Li¹, J. Nakai¹, D. Moir¹, A. Yagminas¹, and I. Chu¹

¹ Environmental and Occupational Toxicology Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: This project was designed to provide congener-specific analysis of polychlorinated biphenyls (PCBs) and establish the congener profiles in rat tissues in comparison to that of the dosing mixture, Aroclor 1254, and to compare tissue distribution and accumulation potential of individual PCB congener within the rat.

METHODS: A total of 112 PCB congeners were identified in the Aroclor 1254 mixture. Congener-specific quantification for all 112 PCB congeners was conducted with multiple gas chromatography (GC) analyses with electron capture detection (ECD) and four capillary columns. The tissue samples were extracted with a mixture of organic solvents, dried with anhydrous Na₂SO₄, and cleaned with a Florisil column. Working standard solution of all the 112 PCBs were prepared within two groups of mixture. Octachloronaphthalene (OCN) was selected as internal standard for GC analysis, and PCB30 and PCB199 were the surrogate standards for quality control of routine analysis.

RESULTS: Depending on the number and pattern of chlorine substitution, the instrumental detection limits for PCB congeners were estimated to be between 0.01-0.2 pg. Rat dams were dosed with 15 mg/kg/day and over 200 samples from the dams and their pups at various ages were analyzed. Most of the PCBs found in the Aroclor 1254 mixture were also detected in rat tissues. The concentration profiles of the PCB congeners in rat tissues were obtained and compared with the Aroclor 1254. The tissue distribution and accumulation of individual congeners in tissue were determined.

CONCLUSION: Although much research has been reported for a comprehensive congener-specific analysis of commercial PCB products, this is the first practical method for comprehensive congener-specific analysis of PCBs in tissues of rats exposed to a commercial PCB mixture. These results will aid in the interpretation of toxicity data.

1.28 Distinct Interactions of Metals in Air Particulate Matters with Modified Simulated Biological Media

D. Bérubé, PhD¹, and X. Liao, PhD¹

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

OBJECTIVES: Investigate the effect of experimental conditions on solubility of metals in particulate matter.

DESIGN: Inductively Coupled Plasma Mass Spectrometry (ICP-MS) was used for metal measurement. Particulate matter (PM) samples were completely digested through microwave energy for the determination of total metal composition. Time sequential leaching was used for solubility determination. The solutions primarily simulated biological fluids by including the main electrolytes and biological buffer. Other components of lung fluids, such as citric acid or glutathione, and chelation therapy agents, such as EDTA or dimercaptopropanesulfonic acid, were also added.

OUTPUTS/RESULTS: When examining PM emissions of a Nickel (Ni)/Copper (Cu) smelting process, samples collected at the plant and in the surrounding ambient air showed similar dissolution behaviour in simulated biological fluids. Ni and Cu showed continuous slow dissolution over a period of two weeks. The dissolutions remained partial, particularly for Ni (< 40%). Further investigations showed no significant change in dissolution behaviour after addition of chemicals increasing the complexation strength. No significant effect was also observed for other modifications of the leaching conditions, such as change in solid-to-liquid ratio or use of water alone. In comparison, samples from other sources showed large variations after the same experimental modifications. In the case of emissions from another Ni/Cu process, the dissolution of Cu was faster and more complete (> 80%) while the dissolution of Ni remained similarly slow and partial. Large differences were observed between experiments in water and in simulated biological fluid, especially for Cu. The dissolutions of both metals were affected by the complexation strength and solid-to-liquid ratio.

IMPACTS/OUTCOMES/CONCLUSIONS: The absence of effect from experimental modifications normally affecting solubility equilibria suggests that surface reactions control the dissolutions. These observations result in a better understanding of PM interactions with biological fluids, contributing to health effect studies and risk assessment/management of *Canadian Environmental Protection Act* (CEPA) priority substances.

1.29 Effects of Personal Exposure to Particulate Air Pollution on Diabetic Patients-Changes in Cardiovascular System and Biomarkers of Inflammation and Oxidative Stress

L. Liu, MMD, PhD¹, M. Szyszkowicz, PhD¹, M. Dalipaj², H. You, MSc¹, R. Poon, PhD³, T. Ruddy, MD², A. Wheeler, PhD¹, and R. Dales, MD¹

¹ Air Health Effects Division, SEP, HECSB, Health Canada, Ottawa, ON

² University of Ottawa Heart Institute, Ottawa, Ontario

³ Environmental Health Science Bureau, SEP, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: We investigated the personal acute exposure to particulate matter (PM) of diabetic subjects in Windsor Ontario and the relationship with cardiovascular function and blood biomarkers for inflammation and oxidative stress.

DESIGN: Non-smoking diabetics (n=25), age 27-67 years, were recruited. Each subject wore a personal monitor for PM at diameter <10 µm (PM₁₀) for 24 hours, followed by measurements of heart rate, blood pressure, brachial artery diameter, flow-mediated vasodilation (FMD), and blood C-reactive protein (CRP), thiobarbituric acid reactive substances (TBARS), tumour necrosis factor-α, endothelin-1 and interleukin-6. The procedure was repeated 2-14 (mean=7) times for each subject. Associations between exposure to PM₁₀ and markers of health were tested using mixed-effects models, adjusted for temperature, relative humidity and glucose. Subjects were stratified by the presence or absence of body mass index >29, vasoactive medication, hypertension and hypercholesterolemia.

RESULTS: The 24-hour median concentration of PM₁₀ was 25.5 µg/m³. For all subjects, an increase in PM₁₀ was significantly associated with an increase in FMD (lag 18 hours), an increase in basal artery diameter (lag 0-6 hours), a decrease in brachial artery flow and heart rate (lag 18 hours), a decrease in systolic blood pressure (lag 0-6 hours), and an increase in TBARS (lag 6 hours) and CRP (lag 18 hours). In subjects not taking vasoactive medication, most of these associations were more pronounced. In this sub-group of subjects, increased PM₁₀ was also significantly associated with a reduction in basal end-systolic artery diameter (lag 12 hours), and an increase in diastolic and systolic blood pressure (lag 12 hours).

IMPACTS/OUTCOMES/CONCLUSIONS: Results suggest that acute exposure to PM₁₀ may be linked to an imbalance of autonomous nervous system that regulates cardiovascular function in a time-dependent fashion. Particulate pollutants may contribute to the pathogenesis and progression of the cardiovascular complications of diabetes mellitus.



1.30 Sub-Chronic Exposure to Dietary Soy Isoflavones from Two Different Sources Enhances Cell Proliferation, but Reduces Apoptosis in Rat Liver

E. Lok, BSc¹, K. Kapal¹, M. Taylor¹, S. Gilani, PhD², and R. Mehta, PhD¹

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

² Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Current scientific evidence does not support health claims for potential beneficial effects of soy-rich diets on breast and prostate cancer. The safety of soy-based infant formulas are a further cause for concern. Our previous data suggested estrogenic and cancerous effects of isoflavones on rat mammary gland. The present study addresses a data gap concerning effects of dietary soy isoflavones on rat liver cancer biomarkers.

DESIGN: Weanling female Sprague-Dawley rats were fed for 16 weeks diets containing 0- 400 mg/kg diet of isoflavones from Novasoy®, or 200 mg/kg diet of isoflavones from a commercial soy-based infant formula. At necropsy, livers were fixed and processed for immunohistochemistry and in situ end-labeling of fragmented DNA to analyse for: proliferating cell nuclear antigen (PCNA), a cell proliferation biomarker; glutathione S-transferase placental form (GSTP), a hepatocyte preneoplasia biomarker, and apoptosis, or natural cell death. Hepatocyte biomarker labelling indices were quantified using a Northern Eclipse interactive image analysis system.

OUTPUTS/RESULTS: Statistically significant increases in PCNA labelling with 200 mg/kg diet infant formula compared to 0 and 200 mg/kg diet Novasoy® were observed. In contrast, the apoptotic indices were significantly reduced in all Novasoy® and infant formula fed rats compared to 0 mg/kg diet Novasoy® fed rats. GSTP expression did not differ significantly in any of the soy-based diet groups compared to the control group.

IMPACTS/OUTCOMES/CONCLUSIONS: Soy-based infant formula demonstrated a greater capacity to enhance liver cell proliferation, and reduce apoptosis in comparison to Novasoy®. While no effects were observed on GSTP, a preneoplasia marker, our data imply a potential for soy-based infant formula to alter the balance between normal cellular proliferation and death in rat liver. Our observations demand further investigations in the liver to verify any additional biological implications in relation to the estrogenic properties of soy isoflavones, and probable health risks in the developing infant associated with soy-based infant formulas.



1.31 Development of a Rapid Typing Method for *Campylobacter jejuni*, Based on Comparative Genomics

J. MacKinnon, BSc¹, E. Taboada, PhD¹, K. Rahn, MSc¹, J. Nash, PhD², C. Luebbert, MSc², M. Pearson, BSc¹, and J.M. Farber, PhD³

- ¹ Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Guelph, ON
² National Research Council, Ottawa, ON
³ Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Investigation of the suitability of using a subset of hypervariable genes as potential targets for a novel molecular typing scheme and development of a low cost easy multiplex PCR as a prototype for this typing scheme.

DESIGN: We have previously carried out a microarray-based Comparative Genomic Hybridization (CGH) analysis on 150 *C. jejuni* strains, which allowed us to identify 122 hypervariable genes in the *C. jejuni* genome. Previous comparative genomic analysis of *C. jejuni* has shown that approximately 80% of the genome is conserved across strains and thus only a small fraction of the genes contribute to meaningful data from a phylogenetic or typing perspective. We have subsequently investigated the suitability of using a subset of these genes as potential targets for a novel molecular typing scheme.

After extensive testing, we have selected 18 hypervariable genes for use as targets in a multiplex PCR-based system. Analysis of 45 *C. jejuni* strains, from human, animal and food sources was completed using CGH, MLST, and the new *C. jejuni* multiplex system for Hyper-Variable Gene Fingerprinting (HVGF).

RESULTS: Clustering results obtained from the HVGF analysis of 18 hypervariable genes yielded similar clustering patterns as those obtained by MLST and CGH. PCR analysis of hypervariable gene targets yields data that is consistent with MLST and whole genome CGH.

CONCLUSIONS: Although comparative genomics provides the most accurate data that can be used to infer strain relatedness, the considerable effort and cost to generate such data precludes its use in routine strain typing. The HVGF method provides a fast and cost-efficient method for investigating strain relationships for phylogenetic and epidemiological investigations.

1.32 Customization of the USDA Automated Multiple-Pass Method (AMPM) for 24-hour Recall Data Collection in the Canadian Community Health Survey

I. Massarelli, RD¹, M. Villeneuve, RD¹, P. Roach¹, and I. Rondeau, RD¹

¹ Nutrition Survey Section, Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To customize the USDA Automated Multiple-Pass Method (AMPM) for 24-hour recall data collection in the Canadian Community Health Survey - Nutrition (CCHS 2.2)

DESIGN: The USDA Automated Multiple-Pass Method (AMPM) for 24-hour recall data collection was modified and used for the Canadian Community Health Survey - Nutrition section (CCHS 2.2). The modifications included: the addition of Canadian brands and foods; the addition of metric measures; and, French translation. This collection exercise was then assessed against criteria of adaptability, language, costs and compatibility.

OUTPUTS/RESULTS: The AMPM provided too many choices in the look-up tables (LUT), resulting in wrong food selections. The Tri-gram search mechanism resulted in both languages appearing jointly in the main food list (MFL) and LUT. Interviewers were not sufficiently trained to navigate through difficult situations and some used the tool, for the first time, weeks after training.

IMPACTS/OUTCOMES: This software was chosen for many reasons: manual data collection was not a viable option due to the magnitude of the survey sample; the high cost of developing a data collection tool for similar populations; the type of interviewers utilized; and the high level of compatibility between the US and Canadian food composition databases.

CONCLUSION: Despite the proximity of the two countries many differences remain. Separating the French from English in the MFL and LUT, restoring the Tri-gram search, adapting questions in problematic categories and narrowing possibilities of answers in LUT will further reduce errors and improve adaptability of this valuable tool. Furthermore, the data from the CCHS 2.2 Nutrition survey is now available. It is the first national survey of Canadians' eating habits since the early 1970s addressing a 35-year gap on what Canadians are eating. The information collected with the AMPM tool will be most valuable to Health Canada, provincial governments and other stakeholders, in nutrition promotion, policy and program developments.

1.33 Monitoring the Human Intestinal Bacterial Community Using Universal 16S rRNA Primers: Effect of Antibiotics

M.L. Kalmokoff¹, M. McAllister², J. Kwan², C. Gourgue-Jeannot², C.W.C. Kendall³, D.J.A. Jenkins³, and S.P.J. Brooks²

- ¹ Atlantic Food and Horticulture Research Centre, Agriculture and Agri-Food Canada, Kentville, NS
² Bureau of Nutritional Research, Food Directorate, HPFB, Health Canada, Ottawa, ON
³ Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, ON

OBJECTIVES: Investigate the effect of antibiotics on the bacterial profile of the human gut.

DESIGN: This represents part of a larger study on the relationship between cardiovascular disease risk factors and oral antibiotics. Twenty-two men and women took antibiotics for 10 days (ciprofloxacin for 13 subjects or metronidazole for 10 subjects), with 10 days control in random order separated by two-week washout periods. Faecal samples were collected during the last three days of the test period and freeze-dried. Analysis was conducted on pooled samples by: 1) shotgun cloning of PCR-amplified DNA using universal primers directed against the full-length 16S rRNA gene as well as using primers directed against smaller hyper variable regions within this gene (V2-3 and the V6-8 regions); and, 2) by Denaturing Gradient Gel Electrophoresis (DGGE) of the V2-3 region.

OUTPUTS/RESULTS: Freeze-drying degraded the Gram negative DNA preferentially, necessitating the use of primers targeting smaller regions of the 16S rRNA gene (V2-3 and V6-8 regions). Using these primers gave a profile containing 23% Gram Negatives (16% Bacteroides-Cytophaga), 4% Bacilli, 13% Bifidobacteria, and 51% from the Clostridium super-family (35% *Clostridium coccooides* and 13% *Clostridium leptum*). Ciprofloxacin and metronidazole profoundly affect the population but in different ways. Individuals taking ciprofloxacin had 69% *Clostridium coccooides*, 22% Gram Negatives (17% Bacteroides), 3% Bacilli and 0% Bifidobacteria while those taking metronidazole had 16% *Clostridium coccooides*, 10% *Clostridium leptum*, 32% Gram Negatives (4% Bacteroides), 8% Bacilli and 28% Bifidobacteria. DGGE analysis showed large differences between the bacterial communities of the individuals. Antibiotics primarily affected the high G+C Gram positive bacteria, with several bands disappearing after antibiotic treatment although new bands were also observed in antibiotic-treated subjects.

IMPACTS/OUTCOMES/CONCLUSIONS: The present study indicates that the intestinal bacterial community is highly specific to individuals. In addition, Bifidobacteria may represent a significant proportion of the gut bacterial community, a result not previously found using 16S rRNA primers. Antibiotic feeding profoundly affected the bacterial community but this effect was individual-specific and antibiotic-specific.

1.34 Evaluation of Antibody Microarray Technology in Screening for New Biomarkers from *In Vitro* and *In Vivo* *Bacillus* Exposures

K.C. Nguyen¹, S. Popovic², D. Parks², V.L. Seligy¹, and A.F. Tayabali¹

¹ Safe Environments Program, HECSB, Health Canada, Ottawa, ON

² Animal Resources Division, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To evaluate and compare different commercially available protein binding slides and antibody micro-array kits and their assay protocols for capacity to provide high application (spot) quality, signal to noise (S/N), sensitivity, and reproducibility.

DESIGN: Six types of protein binding slides, with different surface coatings, used for constructing in-house antibody arrays, and three commercially available antibody array kits were evaluated and compared in their performance for detecting cytokines and new biomarkers. For this study, cell and tissue lysates were obtained from the 2-hour and 4-hour exposures of different *B. cereus* (Bc) and *B. thuringiensis* subsp. *kurstaki* (Btk) preparations to murine macrophage cells (J774A.1) and Balb/c mice. Multiplexed bead array, ELISA, and Western assays were used as validative references.

OUTPUTS/RESULTS: Hydrogel and Fast™ slides showed consistency in spot homogeneity and overall background, and good slide-to-slide reproducibility, compared to Path™, polymer-coated, Epoxy, and Poly-L-Lysine slides. Hydrogel and Path™ slides produced highest S/N compared to the others. Besides surface chemistry, the performance of slides in array assays depended greatly on antibody specificity, detection systems, and assay conditions. Clontech arrays produced low background with high S/N compared to Panorama and Spring arrays. With 2-hour exposures, Clontech and Panorama arrays failed to show changes in any biomarker. In contrast, 4-hour exposures resulted in all three types of arrays showing reproducible detection of new biomarkers. Due to the lack of specificity of their immobilized antibodies, Clontech and Spring arrays failed to detect cytokines known to be elevated using validation tests.

IMPACTS/OUTCOMES/CONCLUSIONS: This study evaluates the performance of protein and antibody microarray technology by testing current commercially available products. The data showed limitations of the technology, including surface-immobilization chemistries, antibody specificity, and assay sensitivity. The study also demonstrated the application of antibody arrays in screening protein markers from a complex sample in a high- throughput- manner.



Session D: Innovation: Application of Biotechnology Innovations to Toxicological Research, O'Connor Salon, October 30, 2006, at 10:15 a.m.

1.35 Development of an Oligonucleotide Microarray for Determination of the Five Most Prevalent *Salmonella* Serotypes in Canada

C. Yoshida¹, K. Franklin¹, P. Konczyk¹, J. McQuiston², K. Rahn¹, E. Taboada³, C. Clark⁴, P. Fields², C. Fitzgerald², J. Nash³, and F. Pagotto⁵

- ¹ Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Guelph, ON
- ² Centers for Disease Control and Prevention, Atlanta, GA, USA
- ³ National Research Council, Ottawa, ON
- ⁴ National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB
- ⁵ Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: The objective is to construct an oligonucleotide microarray, specific for the somatic (O) and flagellar (H) antigens to serotype *Salmonella* and to assess probe performance on two different microarray slide surfaces. The aim is to develop a microarray-based assay that would be consistent with the Kauffmann-White nomenclature but could be used to overcome the lengthy and cumbersome methods currently used to serotype the five most frequently isolated *Salmonellae* from humans in Canada and in the United States.

DESIGN: Short oligonucleotide probes (20-30 bp) were designed and synthesized based on bioinformatics analyses of publicly available sequences of gene targets. These targets included: antigen-specific sequences within the flagellin (H) antigen phase 1 (*fljC*) and phase 2 (*fljB*) genes and somatic (O) antigen biosynthesis within the *rfb* cluster (Groups B, C1, C2, D1) for the 5 most common *Salmonella* serotypes. Microarray targets were prepared by PCR amplification of entire *fljC* and *fljB* H antigen genes, and targeted somatic genes within the *rfb* cluster. Cy3 was directly incorporated into the PCR products, which were pooled and hybridized to the microarray.

RESULTS: A number of specific probes were identified for each of the O and H antigens in the five most common *Salmonella* serotypes, except for H:1,5 whose probes cross-react with the H:1,2 antigen. More specific probes were identified when printed on Epoxide slides as opposed to Aldehyde slides. A further generation of microarrays printed on Epoxide slides is being optimized by eliminating non-specific probes, and adding new probes that will accurately detect the H:1,2 antigen.

CONCLUSIONS: The prototype DNA-based typing microarray described here has the potential to be a rapid and automated alternative to the traditional antigen-antibody based serotyping scheme currently used for *Salmonella*. Further microarray designs of this type should allow the establishment of a standardized global surveillance system.

1.36 Understanding Bioaccessibility: An Investigation of Metal Speciation in House Dust

P. Rasmussen, PhD¹, S. Beauchemin, PhD², N. Hassan, PhD¹, M. Nugent, MSc¹, M. Lanouette¹, and M. Chénier¹

¹ Environmental Health Sciences Bureau, Safe Environments Program, HECSB, Health Canada, Ottawa, ON

² Mine Waste Management, Natural Resources Canada, Ottawa, ON

OBJECTIVES: The objective of this research is to understand why bioaccessible metal concentrations are commonly elevated in indoor settled dust samples compared to corresponding outdoor soil samples.

DESIGN: Novel analytical approaches are employed to investigate metal speciation in household dust, and to elucidate the influence of matrix composition on the bioaccessibility of particle-bound copper (Cu) and zinc (Zn). Metal speciation was investigated using synchrotron X-ray absorption spectroscopy (XAS). Inorganic and organic carbon species were determined by combustion at 900°C, followed by CO₂ absorption and thermal conductivity detection. The migratable metal fraction was extracted using simulated stomach acid. Total metal concentrations were determined using microwave-assisted digestion and a 4:1 mixture of concentrated nitric acid and hydrogen peroxide, followed by inductively coupled plasma mass spectrometry (ICP-MS).

OUTPUTS/RESULTS: Synchrotron XAS analysis indicates that about one-third of the Cu in the household dust samples is associated with organic-bound sulphides, while about half of the Zn in the dust samples is in the form of Zn hydroxyl carbonate. Characterization of metal distribution over a wide range of size fractions (from 57 nm to 150 microns) shows that total metal contents generally tend to decrease as particle size increases. The carbon analyses show that organic carbon content is elevated in house dust samples (median 28%; n = 58) compared to corresponding garden soil samples (median 5%; n = 66).

CONCLUSIONS: Metal speciation and particle size are key factors affecting metal bioaccessibility in household dust. Indoor/outdoor ratios of certain metals appear to be enhanced by the ability of the organic-rich indoor dust matrix to accumulate certain metals (irrespective of source) to higher concentrations than are found in soil.



1.37 Inter-Method Comparison for Analytical Quantification of Petroleum Hydrocarbons in Soil: Atlantic Risk-Based Corrective Action vs. Canada-Wide Standards

W.J. Dyck, MSc¹, F.N. Brodie, P. Eng², J.A. MacDonald, MSc³, N.M. Roest, MES⁴, and G.M. Richardson, PhD⁵

- 1 Conestoga-Rovers & Associates, Waterloo, ON
- 2 Conestoga-Rovers & Associates, Fredericton, NB
- 3 Maxxam Analytics, Bedford, NS
- 4 Safe Environments Programme, HECSB, Health Canada, Halifax, NS
- 5 Contaminated Sites Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVE: The comparability of analytical results for petroleum hydrocarbons (PHCs) in soil under Canada-Wide Standards (CWS) and Atlantic Risk-Based Corrective Action (RBCA) methods was investigated.

DESIGN: Soil samples were collected from nine contaminated sites with a wide range of PHC concentrations, and the samples were split for analysis by both CWS PHC and Atlantic RBCA methods. Both 'Tier 1' (screening) and 'Tier 2' (more detailed fractions) methods were considered. For CWS PHC analysis, a Tier 2 method was developed based on Atlantic RBCA separation of PHC sub-fractions (aromatic and aliphatic), since the CWS does not define a specific Tier 2 analytical procedure. PHC fraction concentrations in soils studied ranged over two to five orders of magnitude.

OUTPUTS/RESULTS: Atlantic RBCA methods yielded higher concentrations on average compared to the CWS PHC for Tier 1 analysis of benzene, toluene and xylenes, light-chain and heavy-chain PHCs. These findings were reversed in the Tier 2 analyses, although the Atlantic RBCA method did yield higher concentrations for medium-chain length PHC sub-fractions. However, these inter-method differences were of similar magnitude to those found due to sampling matrix and intra-lab variability.

IMPACTS/OUTCOMES/CONCLUSIONS: Overall, the Atlantic RBCA Tier 2 extraction, sub-fractionation and analysis procedures, followed by summation of sub-fractions to report results analogous to the CWS PHC F1, F2 and F3 fractions, can be used conservatively to quantify PHCs within Tier 1 of the CWS (i.e., for screening-level comparisons to guidelines). Therefore, the two analytical methods (CWS PHC and Atlantic RBCA) are concluded to be comparable for the investigation of PHCs in soil at contaminated sites.

The data obtained also indicate that the CWS PHC extraction steps appear to be more efficient (yielding higher analyte concentrations) than the Atlantic RBCA extraction steps. In contrast, the Atlantic RBCA Tier 2 analysis procedure appears more sensitive than the CWS PHC analysis procedure. An overall more superior method (yielding the most conservative assessment, i.e., highest PHC concentrations) may be obtained by combining the CWS PHC Tier 1 extraction and preparation steps with the Atlantic RBCA Tier 2 sub-fractionation and analysis procedures.

1.38 Reduced Expression of Abcg5/Abcg8 is Associated with Increased Retention of Dietary Plant Sterols and Stanols in Diabetic BB Rats

K.A. Scoggan, PhD^{1,2}, H. Gruber, MSc¹, L.J. Plouffe¹, J.M. Lefebvre, BSc³, H. Rocheleau, MSc¹, B. Wang, PhD¹, J. Bertinato, PhD¹, M.R. L'Abbé, PhD¹, and W.M.N. Ratnayake, PhD¹

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

² Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

³ Department of Biochemistry, Carleton University, Ottawa, ON

OBJECTIVES: Type 1 diabetes is associated with low synthesis and high absorption of cholesterol, which also characterizes the disorder, sitosterolemia. Mutations in either Abcg5 or Abcg8 cause sitosterolemia and result in increased retention of dietary plant sterols and stanols (PSS) and premature heart disease. We have previously determined that insulin-treated diabetic BB rats (BBdt), a model for type 1 diabetes, have lower hepatic expression of Abcg5/8 and incorporate elevated levels of PSS in aorta and red blood cells. The objectives of this study were to confirm our previous results by measuring hepatic PSS incorporation as well as intestinal Abcg5/8 expression in BBdt rats and to determine if increased PSS incorporation was due to mutations in either Abcg5 or Abcg8 transporters.

DESIGN: BBdt and non-diabetic control (BBc) rats were fed a control diet or diets supplemented with plant sterols or stanols (5 mg/g diet) for four weeks. Liver tissue levels of PSS were measured by gas chromatography. Expression of Abcg5/Abcg8 in intestine was assessed by realtime qPCR. The coding region of Abcg5 and Abcg8 genes were also investigated for mutations.

OUTPUTS/RESULTS: Confirming our previous results, BBdt rats showed increased accumulation of PSS, especially plant sterols, in liver compared to control rats when fed diets supplemented with plant sterols or stanols, respectively. In addition, intestinal Abcg5/8 mRNA expression was lower in BBdt versus BBc rats fed the control diet. Several SNPs were identified in Abcg5 and Abcg8 genes, however, none of these sequence variations resulted in amino acid changes.

IMPACTS/OUTCOMES/CONCLUSIONS: Decreased basal levels of Abcg5/8 in BBdt rats may account for the increased retention of plant sterols in tissues on these rats. The reduced levels of Abcg5/8 in BBdt rats were not due to mutations in the coding region of either Abcg5 or Abcg8 genes. These results warrant studies to investigate the cause and potential health effects of increased incorporation of PSS in diabetic individuals, as these studies may impact food safety assessments of PSS.



1.39 Characterization of the Physical Properties of Murine Norovirus-1 (MNV-1)

A.H. Shukla¹, K. Mattison¹, S. Bidawid¹, and J.M. Farber¹

¹ Microbial Research Division, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: The purpose of this study is to determine whether Murine Norovirus-1 (MNV-1), is a better surrogate for the study of Human Norovirus (NoV) than Feline Calicivirus (FCV). NoV cannot be cultured and so a surrogate system is necessary to study NoV biology. The discovery of MNV-1 provides the potential for a new, and possibly more appropriate, surrogate. In contrast to the current surrogate, FCV, MNV-1 displays a more similar nucleotide and protein sequence to NoV.

DESIGN: MNV-1, FCV and NoV were subjected to a range of temperature and pH conditions that are physiologically relevant to virus survival. Infectivity assays were used to measure MNV-1 and FCV PFU after treatment in RAW 264.7 murine macrophages and CRFK feline kidney cortex epithelial cells, respectively. Additionally, the presence of viral RNA was tested by reverse transcription - polymerase chain reaction (RT-PCR) and followed the same trend.

OUTPUTS/RESULTS: Standardized infectivity and RT-PCR methods have been developed for FCV and MNV-1 and testing of the effects of temperature and pH on FCV, MNV-1 and NoV has begun. Preliminary findings indicate that NoV and MNV-1 are more pH resistant than FCV. The temperature survival profiles of the three viruses are similar. Together, these results indicate that the survival profile of MNV-1 is more similar to NoV, than FCV.

IMPACTS/OUTCOMES/CONCLUSIONS: MNV-1 was recently discovered and may prove to be a suitable surrogate to study the biology of noroviruses because it replicates in cell culture, has been shown to infect mouse models, and here, has been shown to have a similar survival profile to NoV. This is a significant improvement over the current FCV surrogate.

1.40 Uranium Speciation and Diffusion Through Bi-Layer Lipid Membranes

R. Skinner, MSc¹, W. Li, PhD¹, D. Lariviere, PhD¹, S. Kiser¹, C. Li, PhD¹, and J. Cornett, PhD¹

¹ Radiation Surveillance and Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Characterize uranium speciation and mass transport rates through planar bi-layer lipid membranes (BLMs) in simulated body fluids.

DESIGN: Planar bi-layer lipid membranes were formed spanning a small aperture in a Teflon film that divided two compartments of a diffusion cell. Once the membrane was stable, UO₂²⁺ was added to one chamber and, its concentration in another chamber was monitored by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Phospholipid content of BLMs were altered to mimic the desired biological ratio for lung alveolar, red blood and renal cells. The appropriate simulated body fluids were used accordingly. Uranium speciation before and after diffusion was determined by CE-MS.

RESULTS: The BLMs in these experiments were the first formed using fluid volumes as large as 100mL, according to the literature. Uranium diffusion rates are being determined for each type of BLM and simulated body fluid. Preliminary measurements indicate speciation of uranyl anions concurred with computer-generated models under identical conditions.

CONCLUSIONS: Knowing *in vitro* diffusion rates and speciation is only the first step for this work. *In vivo* studies will have to confirm these results. Furthermore, having speciation data on biologically relevant radionuclides is important, as it is the first step for decorporation studies. If the exact species that form when a radionuclide dissolves in a given body fluid is known, then specific drugs or chelators can be designed to decrease their retention rates in the body.

1.41 Simulating Nutritional Profiles for the Canada Food Guide Revision

M. Vigneault¹, and B. Junkins¹

¹ Bureau of Biostatistics and Computer Applications, HPFB, Health Canada, Ottawa, ON

OBJECTIVE: The objective was to assess potential recommended patterns of food intake by simulating nutritional profiles in populations with intakes consistent with the patterns, but reflecting current food supply and food preferences in the population. In the context of the Canada Food Guide Revision project, this allowed examination of the differential impact of potential food patterns in subpopulations with different food preferences or access: age, sex, and income.

DESIGN: Detailed food records from Federal-Provincial food and nutrition surveys were compiled into “popularity lists”, reflecting the food choices made within each subpopulation of interest. Then nutritional profiles expected from potential Food Guide food intake patterns were developed by simulating a large number (500) of diets consistent with the proposed patterns and with the preferences for the subpopulations. Individual foods were selected to populate the patterns within each of the food groups or subgroups separately, with probability of selection proportional to current preferences. Subpopulations of particular interest were 14 DRI age-sex groups as well as low-income populations.

OUTPUTS: The distribution of expected nutrient intakes associated with each Food Guide pattern was estimated for each age-sex group. The percent was examined relative to chosen DRI benchmarks such as Estimated Average Requirements (EAR), Adequate Intakes (AI), Tolerable Upper Intake Levels (UL) and Acceptable Macronutrient Distribution Ranges (AMDR).

CONCLUSIONS: The outputs provided evidence for use by the Food Guide Revision team to assess the different risk of nutritional inadequacy and excess in different subpopulations of potential intake patterns. This evidence was based on the current food supply and the different subpopulation preferences rather than idealized food records.

1.42 Modelling Drinking Water Quality in the Distribution System: City of Gatineau

S. Wasay, PhD¹, B. Koudjonou, PhD¹, and L. Dabeka¹

¹ Chemistry Research Division, HECSB, Health Canada, Ottawa, ON

INTRODUCTION: Maintaining residual disinfectant in water distribution systems (DS) is always a priority for water suppliers. For example, chlorine, the most used disinfectant is well known to react with organic matter present in water to form the trihalomethanes (THMs) and other disinfectant by-products (DBPs). The formation of DBPs in the DS depends on various parameters including the source water quality, treatment strategies, pipe materials and the complexity of the distribution system. Developing computer-based models will offer a promising tool to predict temporal and spatial variations of residual chlorine and THMs in the DS. However, effective and reliable water quality models require properly defined parameters like the hydraulics and the mechanisms of disinfectant decay and THMs formation.

OBJECTIVE: The objective of this study is to model chlorine residual and THM formation in a selected drinking water DS, and to validate the model using field data collected during winter and summer.

RESULTS AND DISCUSSIONS: Data obtained on water samples collected in the DS of City of Gatineau in winter 2006 (available) and summer (June - August 2006) will be presented. Chlorine decay and THM formation coefficients are important model input parameters. They were determined on treated water at controlled laboratory temperature (4°C for winter). Results indicated that chlorine decay and THMs formation were first order reactions. THMs formation was very slow; the maximum formation potential was not reached even after a 144 hour contact time. Field measurements conducted at 30 different locations in the DS are being compared with simulation results. In order to fine-tune the mathematical predictive model, a series of simulations will be performed using alternative decay and formation kinetic models. The appropriate coefficients will be calculated to help correlate water quality to various parameters including pipe material and size.

RELEVANCE: Findings of this study will provide drinking water plants and distribution systems managers with a tool to predict chlorine residual and THM levels at any location in the distribution system. This information is essential in complying with the Canadian drinking water guideline, and thus in protecting the health of Canadians.

1.43 Identification of Differentially Expressed or Modified Hepatic Proteins Induced by Dietary Soy Proteins in Rats Using Proteomic Approaches

C.W. Xiao, PhD¹, C. Wood, MSc¹, D. Weber, PhD², M.R. L'Abbé, PhD¹, and G.S. Gilani, PhD¹

¹ Nutrition Research Division, Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON

² Food Research Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Consumption of soy-based products such as soy milk, tofu and soy infant formula is increasing in Canada. However, our knowledge on the health safety and potential benefits of soy components are limited and inconsistent. This study aimed to identify proteins differentially expressed or modified by dietary soy proteins in rat liver.

DESIGN: Sprague-Dawley male rats at 50 days of age were fed diets containing either 20% casein or alcohol-washed soy protein isolate (SPI), the sole protein source of soy infant formula, for 70 days. Liver total proteins (200 µg) pooled from 3 rats fed the same diets were separated by two-dimensional gel electrophoresis and stained with Coomassie blue. Proteins differentially expressed or modified between the dietary groups were identified using a LC/MS/MS technique.

OUTPUTS/RESULTS: A total of 38 diet-related protein spots (23 from casein and 15 from SPI) were identified. Among them, four proteins [ATP synthase (ATPS), carnitine palmitoyltransferase-2, methylmalonate semialdehyde dehydrogenase, glucose regulated protein] are related to fatty acid metabolism, and 8 [phenylalanine hydroxylase, S-adenosylhomocysteine hydrolase, 4-trimethylaminobutyraldehyde dehydrogenase, lactate dehydrogenase A, dihydrolipoamide acetyltransferase, ornithine carbamoyltransferase, arginase 1, glutathione S-transferase (GST)] to amino acid metabolism. Interestingly, the isoelectric points (pI) of some of these proteins such as ATPS, β-actin, GST-µ2, GST-8 were changed by diets, indicating the differences in protein modifications.

IMPACTS/OUTCOMES/CONCLUSIONS: These results suggest that different sources of dietary proteins (casein and soy proteins) may affect lipid and protein metabolism differently through regulation of the enzymes involved. The techniques established in this study can be used in the extensive screening of disease or nutrient-specific gene expression, which will contribute to the safety assessment and determination of nutritional quality of food products.

1.44 Phthalates in Ottawa Residential House Dust

J. Zhu, PhD¹, X. Yang¹, P. White, PhD², and R. Gagne²

¹ Chemistry Research Division, Bureau of Environmental Health Research, HECSB, Health Canada, Ottawa, ON

² Mutagenesis Section, Bureau of Environmental Health Research, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Phthalates are widely distributed in the environment, and have been detected in many different matrices as well as human body tissues and fluids. However, levels of phthalates in house dust in Canada have not been determined. The aim of the present study is to measure phthalate concentrations in house dust that is representative of a residence in Ottawa.

DESIGN: House dust samples from vacuum bags or the reservoirs of a central vacuuming device were collected during the Ottawa Indoor Air Study (winter of 2002/2003). The dust (0.3 grams, sieved down to 150 µm) was extracted with organic solvents and cleaned-up using a Gel Permeation Chromatographic column. The phthalate fraction was concentrated to 1 mL and analyzed by gas chromatography - mass spectrometry.

OUTPUTS/RESULTS: The mean and median values of the total phthalates were 989 and 950 µg/g, respectively; with a maximum value of 3452 µg/g. Levels of phthalates in the samples exhibit a near log-normal distribution. Of the phthalates measured, di(2-ethylhexyl) phthalate was the predominant compound detected in samples with the mean and median values of 521 and 406 µg/g respectively. The other major phthalates included benzylbutyl phthalate and didecyl phthalate. Some unknown phthalate peaks were also observed.

IMPACTS/OUTCOMES/CONCLUSIONS: Phthalates are generally considered to be endocrine disrupting chemicals. However, the effects of chronic exposure and the health impact of phthalates on humans, particularly to fetus growth and infant development, are not well understood. Information on the levels of individual phthalates in house dust is an important contribution to the growing body of scientific knowledge on the prevalence of these pollutants in the environment. It is particularly important for estimating phthalate exposures of children that ingest settled house dust via hand-to-mouth behaviour. The observations of several phthalate congeners not observed in earlier studies would provide direction for future phthalate monitoring programs.



2.01 Identification and Control of Hazards of Non-Oxidative Hair Dye Shampoo: How Science Drives Policy in Health Canada's Cosmetic Program

D. Koniecki¹, L. Carter-Phillips¹, P. Chantal², N. Ritchot², M. Gvildys³, and C. Messier⁴

¹ Cosmetics Division, Product Safety Programme, HECSB, Health Canada, Ottawa, ON

² Product Safety Laboratory, HECSB, Health Canada, Ottawa, ON

³ Product Safety Regional Office-Ontario & Nunavut, HECSB, Health Canada, Toronto, ON

⁴ Product Safety Regional Office-Quebec, HECSB, Health Canada, Longueuil, PQ

OBJECTIVES: The objectives of the investigation were to minimize public health risks from the use of non-oxidative hair dye shampoo containing p-phenylenediamine (PPD). This is one example of how science is integrated into policy in Health Canada's Cosmetics Program, from initial consumer complaint to its ultimate control as an ingredient in cosmetics.

DESIGN: We applied the HC Decision Making Framework, which drives the decisions that affect the acceptability of a cosmetic product. An investigation into the chemistry and safety of the hair dye shampoo was restricted to the activities that provided the scientific information to be used in the decision-making process. The quantitative and qualitative analyses of the product were conducted using the GC-MS method.

OUTPUTS/RESULTS: We found that complaints about the product were a rare combination of irritation and contact allergy from PPD. The elevated PPD level was due to the absence of an oxidizing agent, normally found in dark permanent hair dyes on the market. Based on our findings, the product posed a risk of injury and was therefore in violation of section 16(a) of the *Food and Drugs Act*. We recommended that the product be either removed from sale or reformulated to meet the Canadian safety standards for cosmetics.

IMPACTS/OUTCOMES/CONCLUSIONS: The utilization of an integrated Decision Making Framework with policy making and the support of scientific evidence resulted in changes to the policy and ultimately regulations on PPD's use in hair dyes and removal of the product of concern from sale. Limiting PPD to oxidative hair dyes protects consumers from undue risks.

2.02 Accuracy of Toxicological Information on Material Safety Data Sheets for Respiratory Tract Sensitizers and Asthmagens Used in Workplaces in Canada

G.M. Liss, MD, MS, FRCPC^{1,2}, L. El Bilali, PhD³, and M. Nicholas, PhD³

- ¹ Gage Occupational and Environmental Health Unit, University of Toronto, Toronto, ON
² Occupation Health and Safety Branch, Ontario Ministry of Labour, Toronto, ON
³ Public Awareness, Surveillance and National Compliance Coordination, National Office of WHMIS, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Material Safety Data Sheets (MSDSs) are one of the primary means of hazard communication that allow workers to safely use, handle, and dispose of hazardous chemicals. MSDSs in Canada, solely a Workplace Hazardous Materials Information System (WHMIS) requirement, are established under the *Hazardous Products Act (HPA)* and the *Controlled Products Regulations (CPR)*. In the province of Ontario, guidelines and best practices on the investigation of occupational asthma (OA) recommend that clinicians who are investigating adult-onset asthma or possible OA review patients' exposures including relevant MSDSs. Using the example of toluene diisocyanate (TDI; a well-recognized sensitizer), which production in Canada, along with other isocyanates, increased by 10.7%/year since 2002 due mainly the high demand and use in the construction, automotive and furniture sectors, this presentation investigates the accuracy of the toxicological information disclosed on MSDSs and its impact on Canadian workers' health.

METHODS: We examined results of recent studies commissioned by the National Office of WHMIS where MSDSs for products containing TDI sold to Canadian workplaces were audited, and assessed the impact of inaccurate MSDSs on worker health and safety and diagnosis.

RESULTS: Audit reports of MSDSs for TDI containing products sold to Canadian workplaces reveal serious discrepancies that may adversely affect the health and safety of Canadian workers. For example, asthma, wheeze, and sensitizer were omitted by 83, 184 and 127 of 203 MSDSs, respectively.

CONCLUSIONS/IMPLICATIONS: Omission or non-disclosure of these agents in MSDSs may limit physicians in making an effective diagnosis of work-related asthma. Therefore, MSDS compliance with WHMIS (i.e., *HPA/CPR*) requirements is essential to ensure the safe use/handling of respiratory tract sensitizers and asthmagens in Canadian workplaces. Nationally coordinated enforcement, surveillance, and education of suppliers and physicians are needed to address the discrepancies in MSDSs. Such actions will consequently result in safer workplaces in Canada.

2.03 CD Ligand Significantly Enhances Specific Cellular Immune Response but Substantially Suppresses Mucosal Antibody Response in Balb/c Mice

D. Huang¹, A.V. Pereboev², N. Korokhov³, R. He², B. Jaentschke¹, L. Larocque¹, C. Gravel¹, W. Casley¹, M. Lemieux¹, D. Curiel³, R. He³, W. Chen⁴, and X. (Sean) Li^{1,5*}

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

² Gene Therapy Centre, University of Alabama at Birmingham, USA

³ National Microbiology Lab, PHAC, Winnipeg, MB

⁴ Institute of Biological Sciences, National Research Council, Ottawa, ON

⁵ Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON

OBJECTIVES: CD40 ligation has been suggested to promote the activation and antigen-presenting functions of dendritic cells (DC), which express CD40 receptor and are known to play a critical role in orchestrating immune response. However, the feasibility of CD40 ligand as an adjuvant for vaccination is yet to be defined, especially with immunization using live viral vectors such as adenovirus (Ad).

METHODS: Here, we presented the first report that involves comparison of wt Ad (wAd) with modified Ad (mAd), engineered for selective targeting to CD40(+) DCs, in terms of tissue distribution, toxicity and immunogenicity in Balb/c mice.

RESULTS: We observed the mAd was more rapidly captured by the liver following intravenous administration while subcutaneous injection saw mAd being mainly processed in CD40(+) cells near the injection site. Furthermore, intranasal administration of wild type Ad expressing the nucleocapsid proteins of SARS coronavirus, used here as model vaccine (denoted as mAd-NP), resulted in significant damages to the lung tissues and the infection of the brain by the viruses. Yet, such undesirable reactions were completely abolished with the use of mAd vector.

Administration of mAd not only resulted in drastic increase (>1000 fold) in the uptake of the viruses by the dendritic cells but also strongly enhance Th1 (cellular) immune response (up to 17-fold) against SARS-CoV NP. Interestingly, Th2 (humoral) immune response against SARS-CoV NP vectored by mAd was drastically suppressed, with a more pronounced reduction of mucosal IgA and IgG levels than that from the sera, an observation differing from other reports with protein-based vaccines in conjunction of soluble CD40 ligand as adjuvant.

CONCLUSIONS: These data suggest that CD40 ligation could be considered for induction of immunity against certain intracellular pathogens or cancers where cellular immune response play predominant roles, but argue against this approach when the induction of humoral responses is crucial, i.e., generation of neutralizing antibodies against viral surface proteins. Overall, these novel findings should provide important scientific guidance for the assessment of the safety and efficacy of related products at Health Canada, given that over 100 clinical trials of adenovirus vectored vaccine or gene therapy are ongoing.

2.04 Climate Change Impacts and Adaptation in First Nations Communities

S. Bediako-Cra¹, D. McClymont-Peace¹, and P. Berry²

¹ Environmental Research Division, FNIHB, Health Canada, Ottawa, ON

² Climate Change Office, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Climate change impacts are predicted to be greatest on vulnerable populations, especially in Northern communities. Increasing evidence suggests unpredictable weather patterns and attendant changes in lifestyles of First Nations people. In the absence of scientific frameworks, the objective of this review is to highlight the networking, current tools and practices used in assessing and mitigating human health impacts of climate change in First Nations communities.

DESIGN: Health Canada's Climate Change and Health Office (CCHO) and many networks are exploring the need to start using climate projections in planning. The CCHO has developed a toolkit, *Your Health and a Changing Climate: A Risk Management Toolkit for Public Health Professionals 2005* containing timely, credible information about the health impacts of climate change for use by public health decision-makers across Canada. CCHO and First Nations and Inuit Health Branch (FNIHB) are currently developing a backgrounder and factsheet on climate change and health risks for Canadians living in northern communities to be added to the toolkit. Research projects on climate change health impacts in Canada's North are being undertaken.

RESULTS/OUTPUT: The toolkits will be provided to health officials. Many residents in the North have already begun changing behaviours to adapt. For example, communities in the region of Nunatsiavut Labrador are taking, or have recommended taking the following actions: forming search-and-rescue teams; performing ice track tests and notifying people about the safety of travel routes; coordinating and distributing food to communities affected by changed caribou migration routes; wearing sunscreen, hats and sunglasses to protect themselves against increased ultraviolet radiation. etc., a number of which are directly or indirectly supportive of health and well-being.

IMPACTS/OUTCOMES/CONCLUSIONS: This exercise will keep policy makers and scientific research community better informed about what networks, initiatives and decision making processes are available, paving the way for the adoption and application of optimal strategies and integrated frameworks in adapting to climate change in First Nations communities.



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2.05 Federal Science eLibrary Pilot Project

M. McConnell, MLS¹, D. Speevak, MLS², B. Dumouchel, MLS³, P. MacDonald, MLS⁴, J. Patterson, MLS⁵, E. Daniel, MLS⁶, C. Found, MLS³

- 1 Science Library Network, HPFB, Health Canada, Ottawa, ON
- 2 Canadian Agriculture Library, Agriculture and Agri-Food Canada, Ottawa, ON
- 3 Canada Institute for Scientific and Technical Information, National Research Council of Canada, Ottawa, ON
- 4 Earth Sciences Information Centre, Natural Resources Canada, Ottawa, ON
- 5 Environment Canada Library, Environment Canada, Gatineau, QC
- 6 Fisheries and Oceans Library, Fisheries and Oceans Canada, Ottawa, ON

In 2003 the Strategic Alliance of Federal Science and Technology Libraries, with the support of Health Canada's Chief Scientist, funded a study to assess the feasibility of delivering electronic content government-wide. The study recommended that the Strategic Alliance sponsor a request for \$45 million over five years to build a Federal Science eLibrary. In 2005 the Strategic Alliance initiated a pilot project to demonstrate the value of an e-Library.

The project was managed by the Canada Institute for Scientific and Technical Information (CISTI) on behalf of the Strategic Alliance. Three regional sites in two departments were given customized access to CISTI's digital repository from November 2005 to January 2006. The pilot's purpose was to act as a proof of concept and strengthen the case for investing in an e-Library by evaluating: 1) the impact on pilot users of easy desktop access to a core collection of e-journals; 2) the impact on the pilot libraries of delivering increased access to e-journals using the pilot infostructure; and 3) whether CISTI's existing infostructure could reliably deliver an e-Library service.

The pilot project increased desktop access to a core body of e-journals in science, technology and medicine for three sites where researchers have limited access. Questionnaires, teleconferences, usage statistics and email were used to gather and measure researchers' response and show impacts.

Pilot groups reported significantly reduced time finding and verifying information. Time that was saved was redirected into critical activities, e.g., manuscript preparation, peer review activities, professional reading and other research and laboratory activities. Participating librarians found that it helped them serve their clients better. The results showed that CISTI's current infostructure provided secure and reliable access.

The pilot results provided proof of the feasibility of offering an e-Library and clearly showed how investment in increased access would benefit government researchers' work.



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2.06 Human Exposure to Perchlorate in the Canadian Environment

K. McKendry, BSc¹

¹ Contaminated Site Division, Health Impact Bureau, HECSB, Health Canada, Halifax, NS

Perchlorate (ClO₄⁻) is an anion, which is produced most often from its salt form as ammonium perchlorate. It is an excellent oxidizing agent at high temperatures; this property makes it an outstanding choice as an additive to explosive compounds, such as rocket fuel. Most perchlorate in the environment is of man-made origin, however, recent research is uncovering natural occurrences of perchlorate, especially in very arid regions.

Perchlorate is a widespread contaminant in the United States, yet little is known of its occurrence outside North America. Few countries have guidelines for perchlorate in the environment. The determination of a Drinking Water Equivalency Level of 24.5 ppb by the USEPA was a long and controversial process. Because of this controversy, the National Academy of Sciences was asked to do an independent review of the USEPA's work on perchlorate. Many US states are now determining their acceptable levels of perchlorate in drinking water, ranging from 1ppb to 18ppb. The extent of perchlorate contamination in Canada is presently unknown, but some contamination as a result of weapons testing, military training, and industrial processes is likely.

This project is the first attempt to describe and quantify the risks associated with environmental perchlorate exposure in Canada. A detailed literature review was conducted, and, in conjunction with data and advice from many experts familiar with the contaminant, was used to formulate an estimate of environmental exposure for Canadians. Exposure pathways are described, and an estimate of multi-media exposure to perchlorate is provided, based on Health Canada human health risk assessment guidance for contaminated sites. This poster will provide an estimate of exposure to perchlorate for Canadians by using estimates of concentrations in environmental media, including recent data from Canadian sources. It will raise awareness about perchlorate as a potential contaminant of concern in Canada, but takes important first steps in putting the issue in a Canadian context.

2.07 Waterborne Illness Events and Recommended Procedures in First Nations Communities on Reserves

M. Nestic¹, and A. La Prairie¹

¹ Office of Community Medicine, FNIHB, Health Canada, Ottawa, ON

OBJECTIVES: The purpose of this study is to identify risks and corrective procedures related to the occurrence of waterborne illness events in First Nations (FN) communities on reserves.

DESIGN: The study is based on data obtained from Regional Medical Officers Council as well as from relevant full-length articles, published in peer-reviewed Canadian journals, quoted by PubMed.

OUTPUTS: The most frequent risks associated that might lead to waterborne illness events in FN communities on reserves are:

- a) insufficient amount of water for hand washing due to a lack of indoor water taps;
- b) the use of indoor pails for toilets due to a lack of indoor flushing toilets;
- c) overcrowded population per housing unit; and
- d) insufficient health education.

Risk management goals could be divided into three groups:

- a) short term goals
 - issuance of drinking water advisories for the FN communities on reserves
 - isolation and/or evacuation
- b) medium term goals
 - adequate equipment
 - scientific expertise
- c) long term goals
 - improvement of housing conditions on reserves
 - health care education of the population on reserves

OUTCOMES: The achievement of risk management goals would result in the following outcomes:

- a) decreased rate of water-borne diseases as the result of bottled water supply
- b) parameters of drinking water safety and quality in water treatment facilities as the result of increased number of treatment operators
- c) accessibility to safe drinking water as the result of increased number of portable water purification systems
- d) better drinking water quality as the result of better monitoring
- e) decreased rate of water contamination in households as the result of better housing
- f) decreased rate of water-borne diseases and complications as the result of more health care professionals in FN communities on reserves

2.08 A Micro-Simulation Model to Evaluate Hypothetical Drug Plans

L. Nguyen¹

¹ Microsimulation Modelling and Data Analysis, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: The Pharmasim micro-simulation model has two closely related objectives. The first is to estimate the benefit that a Canadian family/individual would receive as a consequence of implementing various hypothetical national drug insurance plans (pharmacare). The second is to estimate the federal and provincial costs associated with implementing such drug plans. We demonstrate the capability of the model through a specific example.

DESIGN: We have developed a micro-simulation model with a synthesized micro database. The required database was created by statistically merging the Survey of Household Spending to the Survey of Labour and Income Dynamics for health related expenditures information. Imputed variables containing information on drug coverage, drug utilization and tax deduction/credit variables from the National Population Health Survey, private Brogan data, Régie de l'Assurance Maladie du Québec data and Ontario Drug Benefit data further enhance this merged database. Assembling these disparate data sources involves various statistical techniques such as statistical matching, logistic regression and Monte Carlo simulation. The federal/provincial tax routines and provincial drug programs are also incorporated. The model operates on this unique and comprehensive database to analyze the impact of new drug policies on households and government expenditures.

OUTPUTS/RESULTS: This micro-simulation model is applied to drug expenditure data to evaluate possible drug insurance schemes. The model allows estimating the revenue impacts of a suite of possible proposals and also assessing the distributional impacts on households from policy changes, including winner/loser analysis.

IMPACTS/OUTCOMES/CONCLUSIONS: The Pharmasim model provides information to better inform policy makers in selecting optimal national and/or provincial pharmacare plans.



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2.09 Metals in Windsor Indoor Dust: A Spatial Study

M. Nugent, MSc^{1,2}, P. Rasmussen, PhD^{1,2}, M. Chénier², A. Wheeler, PhD^{2,3},
and M. Smith-Doiron³

¹ Department of Earth Sciences, University of Ottawa, Ottawa, ON

² Environmental and Occupational Toxicology Division, Health Canada, Ottawa, ON

³ Air Health Effects Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: The purpose of this project was to investigate spatial relationships between settled indoor dust metal content and known sources of metals. Specific goals were to: 1) determine elemental associations in settled indoor dust; 2) confirm presence or absence of elemental spatial trends in indoor dust; and, 3) investigate the potential influences of industrial sources of metals, major roads, highways and/or expressway.

DESIGN: Settled dust from 45 indoor environments was sampled in the city of Windsor, Ontario. The dust was collected using an ASTM vacuum method, sieved to 150µm and analyzed for total metal concentrations using ICP-MS. MS Excel was used to manage the dust metal data and calculate correlation coefficients. ArcGIS (version 9.1) was used to analyze and visualize the data.

OUTPUTS: Some metals (Fe, Mn, Al and Tl) are strongly associated to one another, which could indicate a common indoor or outdoor source or could be the result of natural associations between these metals. Inverse Distance Weighted (IDW) surfaces display spatial trends as clusters of sampling points with similar concentrations. In the present study, such clusters exist in areas of low concentration for Pb, Zn and Ni. No clusters exist in sample areas of higher metal concentration. No correlations were observed between metal concentrations in indoor settled indoor dust and distance to the nearest industrial source, or major roads and highways/expressway.

SUMMARY: Windsor settled indoor dust metal content does not appear to be influenced by a proximity to known outdoor sources of metals, based on the present data set. It is acknowledged that spatial trends in the metal content of indoor dust may exist, but further detailed survey information is required. A soil survey will be undertaken to more fully characterize relationships between metal content of indoor particulate matter and the outdoor soil metal content in Windsor, Ontario.

2.10 Metal Concentrations in Indoor Dust: Integration of Research Findings into Health Canada Guidance for Contaminated Site Risk Assessment

D. Schoen, MPH¹, and P. Rasmussen, PhD²

¹ Safe Environments Program, Quebec Region, Health Canada, Longueuil, QC

² Environmental and Occupational Toxicology Division, Safe Environments Program, Health Canada, Ottawa, ON

Health Canada, as an Expert Support Department for the *Federal Contaminated Sites Action Plan* (FCSAP), provides guidance, training, and tools for assessing the human health risks of contaminated sites. One of Health Canada's FCSAP-sponsored research projects investigates indoor exposures to toxic metals commonly found in contaminated soils, and the ability to predict indoor exposures from outdoor geochemistry. Specifically, this research will allow us to refine estimations of background exposure to selected metals, to examine our assumptions in regard to indoor dust/outdoor soil ratios, and to better evaluate the factors influencing bioavailability of metals in indoor dust and outdoor soil.

A recent Health Canada study examined 48 homes in the Ottawa area, evaluated indoor/outdoor ratios in the concentrations of lead, cadmium, and nickel. Indoor dust elemental concentrations were not spatially correlated with outdoor (garden soil) elemental concentrations. Moreover, indoor/outdoor ratios of total metal concentration were consistently higher than unity: 5.5 for Pb, 16.4 for Cd, and 3.4 for Ni. Considering only the migratable fraction, the indoor/outdoor ratios were found to be 24.8 for Pb, 20.7 for Cd, and 40.4 for Ni. Relative bioavailability factors (migratable/total metal) were also found to be higher in indoor dust as compared to outdoor soil. The high values appear to be related to the ability of the organic-rich indoor dust matrix to accumulate metals.

2.11

[Withdrawn]

2.12

[Withdrawn]

2.13 Examination of Traditional Food Consumption Patterns on the Basis of Community-Based Research Undertaken by Selected First Nations in Canada

C. Tikhonov, MD¹, and K. Lydon-Hassen, BSc¹

¹ Environmental Research Division, FNIHB, Health Canada, Ottawa, ON

OBJECTIVES: To assess dietary studies undertaken in the process of community-exposure assessments and community-based research projects with First Nations across Canada between 2000 and 2006.

DESIGN: Results of 24-hour recall and/or food frequency questionnaires were analyzed to assess levels of wild game/fish and other country food consumption by selected First Nations communities to estimate the level of risk presented by environmental contaminants in country foods. Integration of dietary information has not been previously done and could allow for comparison with historical data and the development of understanding about current levels of reliance on country foods by selected First Nations.

OUTPUTS/RESULTS: The preliminary analysis of consumption practices in ten First Nations in different regions of Canada suggests that there may be decreasing reliance on traditional foods among First Nations on-reserve.

IMPACTS/OUTCOMES/CONCLUSIONS: The analysis is focused on a series of case studies and the results should be interpreted with caution. Despite this, the new information on the rates of country food consumption among First Nations could be applied to projects involving risk assessments on reserve.

3.01 Sexually Transmitted Infections (STIs) in Aboriginal Street Youth: Results from Enhanced Surveillance of Canadian Street Youth (E-SYS)

O. Agboola, MSc¹, M. Gully, MSc¹, T. Wong, MD, FRCPC¹, U. Auguste, MD, MSc², M. Lem, MD, MHSc, FRCPC², and T. Mersereau, MSc, BScN²

¹ Community Acquired Infections Division, CIDPC, Public Health Agency of Canada, Ottawa, ON

² Communicable Disease Control Division, FNIHB, Health Canada, Ottawa, ON

OBJECTIVES: To describe the epidemiology of sexually transmitted infections and sexual risk behaviours among Aboriginal Street Youth (SY) population in selected cities across Canada.

DESIGN: The Enhanced Surveillance of Canadian Street Youth (E-SYS) is a repeated cross-sectional survey carried out in 1999, 2001 and 2003. SY aged 15-24 years inclusive, who had spent at least three consecutive nights away from home, were recruited in seven cities across Canada. Information was collected in a nurse-administered questionnaire; blood and/or urine samples were also collected for STIs/HIV testing.

RESULTS: 1656 SY were recruited in 2003; 601 (36.3%) were Aboriginal youth. Of these 601, 60% were male and 40% were female; the average age was 19 years with 59% younger (15-19 years) and 41% older (20-24 years) youth.

The prevalence rates of STIs were significantly higher in Aboriginal SY than in general population youth of the same age range - chlamydia (14% vs. <1%), gonorrhoea (4.7% vs. 0.09%) and infectious syphilis (0.4 vs. <.01%).

Approximately half (50%) reported not using any form of protection at their last sexual encounter. The average number of sex partners in the past three months was 4; most reported high-risk partners who trade sex (10%), are injected drug users (9%), and were high on drugs during sex (40%). Compared with non-Aboriginal SY, more Aboriginal SY reported having traded sex ever (24% vs. 22.6%), and in the past 3 months (41.3% vs. 35.6%).

CONCLUSIONS: High-risk behaviours are common among SY and increase the risk of contracting and transmitting STIs. These findings show that there is an urgent need to develop intensive and long-term services that provide alternatives to the sex trade as means of meeting economic needs among the Aboriginal SY population. Knowing the factors that put SY at risk for STIs/HIV is imperative in identifying areas for intervention and establishing harm reduction measures.

3.02 Analysis, Stability and Fate of Disinfection By-Products in Canadian Drinking Water Systems

R. Aranda-Rodriguez¹, B. Koudjonou¹, C. Kubwabo¹, B. Jay¹, B. Stewart¹, and J. Harvie¹

¹ Chemistry Research Division, Environmental Health Science Bureau, Health Canada, Ottawa, ON

OBJECTIVES: Health Canada has been conducting research studies focussing on disinfection by-products (DBPs) produced by drinking water (DW) treatment plants across Canada. Research focuses on method development, stability of compounds, seasonal and spatial variations in the distribution systems.

DESIGN: Five methods have been developed at the Chemistry Research Division (CRD) to include up to 40 drinking water contaminants. Surveys have been conducted at various drinking water facilities using different source waters and purification strategies to gather information on the occurrence of DPBs in the distribution systems.

OUTPUTS/RESULTS

Neutral-extractable DBPs: The consolidated approach developed at the CRD (derived from US EPA 551.1 method) allows for the determination of 25 target compounds including trihalomethanes (THMs), haloacetonitriles (HAN), haloacetaldehydes (HAs), halonitromethanes (HNMs).

THMs: Findings -from surveys, in-house and inter-laboratory studies- support the need to standardize sample collection procedures for THM analysis. For some systems, the Purge-and-Trap technique overestimates THMs, partly due to conversion of some DBPs.

HAs highly contribute to the pool of DBPs (HA/THM: 10-45% w/w) and may degrade to corresponding THMs at typical DW conditions.

HNMs are stable in water at our sampling conditions (pH 4.5, 4°C); however, brominated HNMs readily degrade to less brominated HNMs.

Acid-extractable DBPs: *Haloacetic acids.* The method developed for HAA allows the detection of eight haloacetic acids. Tribromoacetic acid is unstable in water and was not found in Canadian DW. In general, HAAs contributes more than THMs to the DBPs.

Other DBPs

n-Nitrosodimethylamine (NDMA): The method adapted at the CRD allows the detection of NDMA at 0.5 ng/L. Levels lower than 2.5 ng/L (below the Ontario Drinking Water Objective, 9 ng/L) were found in selected samples collected in 2005.

Mutagen X (MX) or 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone. The method adapted at the CRD allows the detection of MX at 7.7 ng/L. A pilot study

conducted in the Ottawa region revealed the presence of MX in DW samples at an average concentration of 31.1 ng/L.

IMPACTS/OUTCOMES/CONCLUSION: The CRD research findings have been instrumental in the derivation of drinking water DBPs guidelines. In the new Canadian Guideline for Drinking Water, released in May 2006, the maximum acceptable concentration for THMs is set at 0.1 mg/L, including 0.016 mg/L for bromodichloromethane. The guidelines for chloral hydrate and haloacetic acids are in preparation.

3.03 Physician's Care at Home: Who Receives it and Who Provides it?

K. Basu¹

¹ Microsimulation Modelling and Data Analysis, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVE: To analyze the characteristics of family physicians (FPs) offering home visits and the circumstances of their patients.

DESIGN: The physicians' supply of services is modeled using a negative binomial regression where the number of home visits is the dependent variable and physician's age groups, practice settings, sex, and payment modes are the independent variables.

For the purpose of analyzing the patients who required home visits, we estimated a Logit Model where home visit (yes/no) is considered as a dependent variable and the dummies for age group, sex, location (rural/urban), the most responsible diagnosis, and years as the explanatory variables.

OUTPUTS/RESULTS: The study shows that 10% of the FPs provide over 50% of the total home visit services. Patients who received home visits are predominantly elderly female living in the rural areas with terminal or chronic diseases. Services in the rural areas have a higher likelihood of receiving a home visit. The physicians who made home visits are more likely to be male, older, under fee-for-service pay mode, and in solo practice setting.

IMPACTS/OUTCOMES/CONCLUSIONS: The FP home visit is drawing more attention today as a complement to home care services. In the first four decades of the twentieth century, home visits by physicians were more commonplace. Over time, the introduction of technology, the growth of third party payers, the intrusiveness of treatments in general, favoured the controlled context of office based or hospital care. However, there is still a large number of home visits needed by patients who are likely to be old and suffering from severe chronic diseases and unable to go to the FP office on their own.

Integration of home care and primary care should be considered by policy makers.

3.04 Benzene in Soft Drinks and Other Beverage Products from the Canadian Market: A Survey and Formation Study

X.-L. Cao¹, V. Casey¹, B. Tague¹, S. Seaman¹, and A. Becalski¹

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

OBJECTIVES: To investigate: 1) the levels of benzene in beverages containing benzoate salts on the Canadian market; and, 2) the formation of benzene from the possible precursors - benzoate salts and ascorbic acid.

DESIGN: Beverage samples spanned a wide range of domestic and imported products and consisted of carbonated and non-carbonated drinks, cocktail mixes, low alcohol (0.5% alcohol vol.) drinks, sports/energy drinks and which were packaged in a variety of glass, plastic and aluminum containers. The majority of the drinks were selected because benzoate salt and/or ascorbic acid were listed on their product labels. A few cranberry drink products were also included since they are known to contain benzoic acid as a natural constituent.

A simple and rugged method based on isotope dilution headspace gas chromatography-mass spectrometry (GC-MS) in a selected ion monitoring (SIM) mode was developed. Model experiments on solutions containing benzoate and ascorbic acid were performed. Formation of benzene in soft drink products under extreme environmental conditions during transportation and storage was also investigated.

OUTPUTS/RESULTS: Of the 124 soft drink products tested (samples of two products were purchased in two different lots), more than 80% did not contain benzene or its levels were below method reporting limit of 1 µg/L. There were six products (< 5%) with benzene levels close to or above the Canadian maximum contaminant level (MCL) of 5 µg/L for benzene in drinking water, and four products (~3%) with benzene levels close to or above the World Health Organization (WHO) guideline for benzene in drinking water (10 µg/L). The highest concentration of benzene, 23 µg/L, was found in a soft drink product for children. The formation of benzene from precursors was positively correlated with temperature in model reactions.

IMPACTS/OUTCOMES/CONCLUSIONS: Our findings were disseminated to manufacturers and stakeholders, to assist in reformulations of products to avoid excessive formation of benzene and to confirm the effectiveness of their mitigation strategies.

3.05 Overexpression of Copper Transporter 2 Increases Copper Content and Downregulates Copper Chaperone for Cu/Zn Superoxide Dismutase Expression in COS-7 Cells

J. Bertinato, PhD¹, E. Swist¹, and M.R. L'Abbé, PhD¹

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

OBJECTIVES: Marginal copper (Cu) deficiency from consuming diets low in copper or high in zinc (Zn) (zinc reduces copper absorption) may be more prevalent than previously thought. A better understanding of the intracellular trafficking of copper is necessary to accurately assess health risks associated with marginal copper deficiency and set precise Dietary Reference Intakes for copper and zinc. To date, a number of copper transporters and chaperones have been shown to play important roles in maintaining copper balance within cells when copper is in excess or scarce. The primary objective of this study was to begin to elucidate the function of human copper transporter 2 (Ctr2).

DESIGN: Ctr2 expression in rat and human tissues was determined by Western blot. Human Ctr2 was expressed in COS-7 cells (monkey kidney) as a green fluorescent protein (GFP) fusion protein (GFP-Ctr2) by transient transfection. GFP-Ctr2 localization was determined by direct fluorescence in live cells. Copper content and copper chaperone for Cu/Zn superoxide dismutase (CCS) expression in GFP or GFP-Ctr2 expressing cells was determined by graphite furnace atomic absorption spectrometry and Western blot, respectively.

OUTPUTS/RESULTS: In rat tissues, Ctr2 was abundantly expressed in placenta and heart, while in human tissues Ctr2 was highly expressed in ovary, pancreas, small intestine and heart. GFP-Ctr2 localized to the membrane of large vesicles reminiscent of vacuoles. Cos-7 cells expressing GFP-Ctr2 accumulated 2-3-fold more copper than cells transfected to express GFP alone. Increased copper content in GFP-Ctr2 expressing cells was inversely correlated with CCS expression level.

IMPACT/OUTCOMES/CONCLUSIONS: Together, these data suggest that Ctr2 activity influences cellular copper levels in COS-7 cells and Ctr2 functions to deliver copper to CCS. These are the first data demonstrating a role for Ctr2 in copper trafficking in mammalian cells.

3.06 Immunomodulatory Effects of Perfluorooctanesulfonate in Rats

G. Bondy, PhD¹, I. Curran, PhD¹, L. Coady¹, C. Armstrong¹, M. Parenteau², M. Barker, DVM, MSc¹, V. Liston¹, L. Hierlihy¹, and J. Shenton, PhD¹

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

² Animal Resources Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Perfluorooctanesulfonate (PFOS) has numerous industrial applications and is widely disseminated in the environment. Although the structurally related contaminant perfluorooctanoic acid (PFOA) has been shown to be immunomodulatory in laboratory animals, similar studies have not been conducted with PFOS. To address this gap, rats were exposed to PFOS in feed and changes in immune parameters were assessed.

DESIGN: Rats were exposed to PFOS for 28 days at levels ranging from 2 to 100 mg/kg in feed. The following endpoints were measured post-necropsy: spleen and thymus weights, blood lymphocyte phenotype, total immunoglobulins, spleen lymphocyte proliferation, histopathology of immune tissues.

RESULTS: At the highest PFOS dose, thymus weights were lower in male and female rats and spleen weights were lower in female rats. In male rats, circulating T and Thelper (TH) lymphocytes (expressed as % of total lymphocytes) increased with dose, while % B lymphocytes decreased. In female rats total white blood cell numbers were elevated along with elevated total T, TH and TSuppressor (TS) cells; % T and TH lymphocytes increased and % B lymphocytes decreased with increasing PFOS in diet. Lymphocyte proliferative responses to the T cell mitogen Con A and the B cell mitogen LPS were not altered. Serum IgG levels were elevated in male rats, while serum IgM levels were elevated in females. Increased incidence of thymic lymphocyte apoptosis was more prevalent in male than female rats in the highest PFOS dose group.

CONCLUSIONS: While splenic and thymic atrophy and decreased B lymphocytes in PFOS-treated rats were indicative of immunosuppression, elevated T lymphocytes and increased serum immunoglobulins were indicative of immunostimulation. To determine the functional significance of these changes, an immune challenge assay has recently been completed to assess the effects of PFOS on cellular and immune responses to keyhole limpet hemocyanin. When analyses are completed, these studies will indicate whether human exposure to PFOS may influence immune function. In the longer term, the data will contribute to hazard assessments for PFOS in foods and other matrices.

3.07 Human Health Risk Assessment of Chemicals in Air

R.M. Wilson, MSc¹, S. Petrovic, MSc², and O. Bose³

¹ SNC-Lavalin Morrow Environmental, Burnaby, BC

² Contaminated Sites Division, HECSB, Health Canada, Burnaby, BC

³ Safe Environments Programme, HECSB, Health Canada, Edmonton, AB

OBJECTIVES: Human health risk assessment (HHRA) of chemicals in air presents separate challenges as opposed to the assessment of chemicals in food, water, soil and other sources. Consequently, an approach for HHRA of chemicals in air is developed according to Health Canada policy. This air quality HHRA approach will provide guidance for new developments or risk management/remediation for contaminated sites under federal jurisdiction in Canada. In addition, the purpose of this project is to develop screening level air concentrations for the protection of human health for a list of chemicals composed in Health Canada's Federal Contaminated Site Risk Assessment in Canada (2004) Part II Guidance.

DESIGN: The risk assessment approach used to achieve the objectives of this project is primarily based on the standard Preliminary Quantitative Risk Assessment (PQRA) approach described by Health Canada (2004) for contaminated sites but modified for assessment of chemicals in air. The steps that are used to develop Air Screening Concentrations for the protection of human health include:

1. Determine a risk-based air concentration (RBAC) considered to be acceptable on a continuous basis
2. Adjust RBAC for time spent at site
3. Apply allocation factor to time-adjusted RBAC

OUTPUTS/RESULTS: Screening level air concentrations for the protection of human health are developed for 95 chemicals. Information on key issues and methods related to guidance on HHRA of chemicals in air are also provided.

IMPACTS/OUTCOMES/CONCLUSIONS: The guidance for information developed through this project should help standardize air quality assessments for federal sites through prescribing standard exposure pathways, receptor characteristics, toxicological reference values, and other parameters required to quantitatively assess the potential chemical exposures and risks from chemicals that may occur in air. It will also help to ensure all relevant data are presented in air quality HHRA reports.

3.08 Effects of Respirable Particles on the Respiratory Burst of Rat Alveolar Macrophages

D. Breznán, MSc^{1,2}, V. Chauhan, PhD^{1,3}, P. Goegan, MSc¹, J.R. Brook, PhD⁴, and R. Vincent, PhD^{1,2}

¹ Inhalation Toxicology and Aerobiology Section, HECSB, Health Canada, Ottawa, ON

² University of Ottawa, Faculty of Medicine, Department of BMI, Ottawa, ON

³ Consumer and Clinical Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

⁴ Atmospheric Environment Service, Environment Canada, Downsview, ON

OBJECTIVES: To examine the effects of respirable particles on the respiratory burst of primary rat alveolar macrophages.

DESIGN: Alveolar macrophages were isolated from rat lungs by bronchoalveolar lavage and incubated (2h) with aqueous suspensions of urban particles (Ottawa, EHC-93; St-Louis, SRM-1648; Washington, SRM-1649), fine PM_{2.5} (southern Ontario, VERP), minerals (titanium dioxide, silicon dioxide) and metals [iron(III)oxide, iron (II/III)oxide, nickel(II)oxide, copper(II)oxide]. The cells were stimulated with phorbol 12-myristate 13-acetate (PMA, 40 minutes), yeast cell fragments (zymosan, 5 hours), or bacterial cell wall lipopolysaccharide (*S. typhimurium*) plus interferon-gamma (LPS+IFN, 5 hours). The respiratory burst during exposure to particles and during stimulation was determined from luminol-enhanced chemiluminescence.

RESULTS: EHC-93 and silicone dioxide initiated a respiratory burst, while VERP and the soluble fraction of EHC-93 (EHC-93*sol*) decreased baseline production of reactive oxygen species. Overall, pre-exposure of the macrophages to particles suppressed the respiratory burst induced by PMA, zymosan, or LPS+IFN. VERP, EHC-93*sol* and metals including iron oxides and copper(II)oxide were potent suppressors of the effects of the burst inducers. Using the XTT reduction assay, concentration-dependent decreases in cell viability were detected in cells exposed to the urban particles and to most metals, copper(II)oxide being most toxic. VERP and EHC-93*sol* had no effect on cell viability despite their pronounced effect on the respiratory burst. Inhibition by particles of the respiratory burst in response to agents that mimic pathogens indicates that the effect is not through direct cytotoxicity of the particles.

CONCLUSIONS: Macrophages undergo a differential respiratory burst upon exposure to respirable particles of varying composition and origin, illustrating a role for the physico-chemical characteristics of particles as modulators of the respiratory burst in primary rat alveolar macrophages. Subsequent challenge of the cells with compounds that mimic contact with pathogens reveals that particles can compromise the functional integrity of the cells, rendering them potentially less competent with respect to microbial clearance. This provides an insight into potential detrimental effects of particles to human health due to perturbation of normal immune responses, for example in individuals undergoing infection.

3.09 The Biological Effects of Radiofrequency Fields Emitted by Mobile Phones

V. Chauhan, PhD¹, A. Mariampillai, BSc¹, G.B. Gajda, PhD¹, A. Thansandote, PhD¹, and J.P. McNamee, PhD¹

¹ Consumer and Clinical Radiation Protection, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: With the rapid expansion of mobile telephones, the possible health risks of exposure to radiofrequency (RF) fields has become a great public concern. Although the majority of the research conducted to date suggests that mobile phones pose no risk towards carcinogenesis, there are still concerns that RF field exposure may induce stress responses and alter cellular functions. Several studies involving either animals or cell cultures have reported no biological consequences attributable to RF fields. The current study was undertaken to evaluate gene expression changes in three human immune cell-lines following RF field exposure.

DESIGN: HL-60, TK6 and Mono-Mac-6 (MM6) cells were exposed to intermittent (5 minutes on, 10 minutes off) 1.9 GHz pulse-modulated RF fields at average specific absorption rates (SARs) of 1 and 10 W/kg at $37 \pm 0.5^\circ\text{C}$ for 6 hours. Concurrent negative and positive (heat-shock for 1 hour at 43°C) controls were conducted with each experiment. Immediately following RF field exposure (T=6 hours) and 18 hours post-exposure (T=24 hours), cell pellets were collected from each of the culture dishes and analyzed for transcript levels of proto-oncogenes (c-jun, c-myc and c-fos) and the stress-related genes (heat shock proteins (HSP) HSP27 and HSP70B) by quantitative RT-PCR.

RESULTS: No significant effects were observed in mRNA expression of HSP27, HSP70, c-jun, c-myc or c-fos between the sham and RF-exposed groups, in either of the two cell-lines at either 6 hours or 18 hours post-exposure. However, the positive control group displayed a significant elevation in the expression of HSP27, HSP70, c-fos and c-jun in both cell-lines at T=6 hours and 24 hours, relative to the sham and negative control groups.

CONCLUSIONS: This study found no evidence that exposure of cells to non-thermalizing levels 1.9 GHz pulse-modulated RF fields can cause any detectable change in stress-related gene expression. This knowledge will strengthen the scientific justification for risk assessment decisions for existing and future Health Canada radiation safety guidelines.

3.10 The Development of a Radon Map on Canada

J. Chen, PhD¹, B.L. Tracy, PhD¹, and D. Moir, PhD¹

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

OBJECTIVE: Recent studies on the link between lung cancer and residential exposure to radon gas have lead Health Canada to recommend that the Canadian radon guideline for dwellings be lowered from 800 to 200 Bq/m³. This project seeks to development a set of radon maps of Canada for effective communication of radon risk.

DESIGN: All available measurements of radon in homes and public buildings are being combined through GIS software to develop maps of varying scales and levels of detail to address the needs of a national radon program. Other types of data (e.g., geological formations, soil types, and aerial radiation surveys) are being utilized to fill in blank spaces in the maps.

OUTPUTS/RESULTS: The following maps have already been produced:

- radon concentrations for major cities in Canada
- estimated percentage of homes with radon levels above 200 Bq/m³
- radon concentrations in Indian Reserves across Canada
- radon concentrations in Saskatchewan schools and hospitals
- a detailed radon map for the city of Winnipeg

IMPACTS/OUTCOMES/CONCLUSIONS: These maps will aid government planners in deciding where to focus resources in a nation-wide radon testing and mitigation program. They will also serve as a guide to homeowners on the likelihood of a radon hazard in their locality and on the degree of importance they should assign to radon testing of their homes.

3.11 Characterization of CEPA 1999 Domestic Substance List Micro-Organisms by Profiling Fatty Acid Composition and Antibiotic Resistance (Minimum Inhibitory Concentration)

G. Coleman, BSc¹, P.S. Shwed, PhD¹, A.F. Tayabali, PhD¹, G. Arvanitakis, BSc², D. Johnston, PhD², and V.L. Seligy, PhD¹

¹ Safe Environments Program, HECSB, Health Canada, Ottawa, ON

² Product Safety Program, HECSB, Health Canada, Ottawa, ON

OBJECTIVE: The Domestic Substance List (DSL) of the *Canadian Environmental Protection Act* (CEPA 1999) includes micro-organisms (MOs) which are considered "existing" and therefore do not require notification and assessment before manufacturing or importing into Canada. Because many DSL MOs have not undergone a screening-level risk assessment (SLRA), and in several cases even lack details about their identity and virulence potential, we have characterized them for key traits deemed to be important for input into risk assessment models and monitoring their release.

DESIGN: Only DSL bacteria available from the American Type Culture Collection (ATCC) were tested. Replica tests on them included: purity and taxon assignment by colony and cell type morphology and Gram staining, fatty acid methyl ester (FAME) profiling by MIDI-Sherlock Microbial Identification system (Agilent Technology), and screens for expression of enterotoxin, hemolysin-cytotoxin-like activity using mammalian cells, and resistance to antibiotics (10 classes), and growth preference for mammalian cell physiologic conditions.

RESULTS: Cytotoxic, enterotoxic, and hemolytic assays identified the same DSL MOs, enabling a ranking of 'toxic' potential relative to *Bacillus cereus*14579. A FAME library was developed and refined using DSL strains grown on clinical and environmental selection media to link data with proprietary databases (MIDI). Power to resolve identity, heterogeneity (in some DSL MOs) and virulence hierarchy of strains was further enhanced by linking to MIC antibiotic data and multi-variate analysis. Only DSL *B.cereus*14579 and Bt13367 killed mucosal cells (HT29) and macrophage cells (J774A.1). However, the latter exhibited normal phagocytic and killing activity with all other DSL MOs.

CONCLUSIONS/IMPLICATIONS: The multi-indicator screen provides a comprehensive package of data for SLRA of 19, ATCC available DSL bacteria. Only a few merit the highest priority for further assessment by *in vivo* tests. However, some others need further investigation because they elicit unusual responses in our immune cell model.

3.12

[Withdrawn]

3.13 Characterization of Virulence Genes Within *Bacillus Cereus* Group Organisms by Comparative and Functional Genomics

J. Crosthwait, BSc¹, P.S. Shwed, PhD¹, A.F. Tayabali, PhD¹, and V.L. Seligy, PhD¹

¹ Safe Environments Program, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: *Bacillus thuringiensis* (Bt) is considered a genetic member of a group containing *B. cereus* (Bc) and *B. anthracis* (Ba). We are characterizing Bt strains of biotechnology interest using microarray-based technology and have detected by DNA hybridization several virulence factors characteristic of Bc or Ba strains. The current study involves the validation of these observations by isolating and cloning different virulence genes, in particular hemolysins, and characterizing their expression in Bt commercial products derived from Bt *israelensis* (Bti) and Bt *kurstaki* (Btk) strains.

DESIGN: Microarray hybridizations of Bs, Bc, Bti and Btk genomic DNAs were performed on oligonucleotide arrays designed from the *B. anthracis* A2012 genome and validated with those from Bc14579. PCR primers to screen Bt strains were for Bc genes [hemolysin II (*hlyII*) and hemolysin BL (*hbl*) enterotoxin operon (*hblA*, *hblC*, *hblD*)]. Amplified products were cloned into plasmid vectors for sequencing and expression. To identify other potential virulence genes, genomic libraries were made using Bti and Btk. Blood agar plates were used to screen for hemolytic activity in all clones.

RESULTS: Putative sequences for different classes of virulence factors, including several different hemolysins, lipases and toxins were identified by scoring Bti and Btk microarrays. PCR amplification from Bti and Btk showed that the Bc *hblA-hblC-hblD* operon is conserved on a 5.7kb amplicon and nucleotide sequencing evidence indicated >97% identity. An amplicon of 1.7kb, homologous to Bc *hlyII* was also obtained from Bti. When cloned into *E. coli*, transformants showed hemolytic activity.

OUTCOMES: The identification of Bt virulence factors related to Bc and Ba, by functional cloning (hemolytic expression), enables analysis of virulence genes and their elimination in new commercial Bt strains. Also, the build of antibody-based probes will allow for rapid screening and quantification of toxicity/pathogenicity potential of these and other related microbes and their by-products, including new commercial formulations.

3.14 Perfluorooctanesulfonate (PFOS) Toxicity in the Rat: A 28-Day Feeding Study

I. Curran, PhD¹, G. Bondy, PhD¹, V. Liston¹, L. Hierlihy¹, L. Coady¹, and S. Gurofsky¹

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

OBJECTIVES: Perfluorooctanesulfonate is a widely disseminated environmental contaminant due to its usage in commercial fluorochemical applications. Analyses of wildlife at different trophic levels of the food chain indicate that PFOS is bioaccumulative. PFOS is the dominant fluorochemical compound found to bioaccumulate in northern biota. To address potential health effects, rats were exposed to PFOS in feed and clinical and toxicological endpoints were monitored and assessed.

DESIGN: Male and female rats were exposed for 28 days to PFOS in feed ranging from 2 to 100 mg/kg feed. The following endpoints were measured post-necropsy: weights of liver, kidney, brain, thymus, spleen, adrenals, heart and in males testes; histopathology of liver, kidney, brain and heart; 26 clinical chemistry endpoints were performed on serum and basic hematology on whole blood. Hepatic gene expression was evaluated, as this is a known target organ.

OUTPUTS/RESULTS: At necropsy liver weights were significantly increased while heart and kidney weights were significantly decreased in a dose-dependent manner. Clinical changes included significantly decreased serum cholesterol and triglyceride levels in males and females, consistent with the known hypolipodemic effects of PFOS. Hematological changes were observed several endpoints for female rats but not males. Analyses of hepatic gene expression indicated that there were significant dose-related increases in markers of peroxisome expression in males and females.

IMPACTS/OUTCOMES/CONCLUSIONS: Comparison of hepatic gene expression between livers from PFOS treated male rats and archived samples treated with ciprofibrate (a known peroxisome proliferator used as a positive control) found significant differences. Weight changes in heart were also not typical of other reported hypolipodemic compounds. PFOS does induce peroxisome proliferation typically observed in rats, but also indicates a distinct mode of action from other peroxisome proliferators. Upon completion, these studies will be used to assess whether human exposure to PFOS in foods or other matrices will influence human health.

3.15 Repair-Related Gene Knockdown Increases Tandem Repeat Mutations Induced by Toxicants in C3H 10T1/2 Murine Cell Line

G. Zhou¹, C. Parfett¹, C. Healy¹, M. Wade², and A. McMahon²

¹ Mutagenesis Section, Bureau of Environmental Health Research, HECSB, Health Canada, Ottawa, ON

² Systemic Toxicology and Pharmacokinetics Section, Bureau of Environmental Health Research, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: In previous microarray studies, we examined three promoters (nongenotoxic/epigenotoxic carcinogens) of morphological transformation in pluripotent mesenchymal C3H/10T1/2 cell cultures: xanthine substrate with xanthine oxidase (XXO); 12-O-tetradecanoylphorbol-13-acetate (TPA), benzoyl peroxide (BPO). Many operative and checkpoint genes in the pathway of DNA replication and DNA repair (mismatch, recombinational) were found down-regulated significantly. In this investigation, we conducted RNA interference to observe whether physiologically-relevant cause-and-effect relationships exist between DNA repair-related gene knockdown and DNA instability.

DESIGN: C3H 10T 1/2 cells were transfected with DsRed reporter plasmids. The DsRed constructs have tandem repeat sequences inserted upstream of the DsRed coding sequence that put the DsRed sequence out of frame.

Chemically synthesized small interference RNAs (siRNA) were transfected into cultures. Time course and dose-responses of gene silencing were performed using RT-PCR. The knockdown cultures were subsequently exposed to 9-amino-acridine (9AA). Frame-shift mutations that resulted in red fluorescent revertants were determined by flow cytometry.

OUTPUTS/RESULTS: Mre11 was examined as a representative of DNA repair genes. Efficient mRNA knockdown (50% ~ 90%) was detected with different gene-specific sequence siRNAs. The chemical treatments induced a statistically significant, dose-dependent response in both siRNA-silenced cells and negative control cells. Mutation rates observed, however, were significantly greater in cells transfected with gene-specific siRNA than in cells transfected with the negative control oligo.

IMPACTS/OUTCOMES/CONCLUSIONS: Results from the experiments reveal that the decreased expression of DNA repair-related genes such as Mre11 might lead DNA instability. Nongenotoxic/epigenotoxic carcinogens may act (at least in part) by eliciting changes to expression of many genes, which create disruption to metabolic and regulatory pathways controlling DNA structure, synthesis and repair thereby resulting in decreased genomic stability.

3.16 Characterization of *Giardia Duodenalis* and *Cryptosporidium spp.* in Swine

B. Dixon¹, L. Parrington¹, T. Coklin¹, A. Cook², F. Pollari², R. Friendship³, and J.M. Farber¹

¹ Microbiology Research Division, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

² C-EnterNet, Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Guelph, ON

³ Department of Population Medicine, University of Guelph, ON

OBJECTIVES: To determine the presence and genotypes of *Giardia duodenalis* and *Cryptosporidium* spp. in Canadian swine.

DESIGN:

- 122 faecal (pooled manure and pit) samples were collected from 10 swine farms in southern Ontario, between September 2005 and May 2006.
- *Giardia* cysts and *Cryptosporidium* oocysts were concentrated from the faecal samples using sucrose flotation.
- The presence of cysts and oocysts was determined by staining with FITC-labelled monoclonal antibodies and examining by epifluorescence microscopy.
- DNA was extracted from the concentrates, and fragments of the SS rRNA and β -giardin genes (*Giardia*), and SS rRNA and HSP-70 genes (*Cryptosporidium*) were amplified by nested PCR.
- Samples found to be PCR positive were sequenced to determine species and genotypes.

OUTPUTS/RESULTS: 64/122 (52.5%) of the swine manure samples were found to be PCR positive for *Giardia*. Similarly, 67/122 (54.9%) were PCR positive for *Cryptosporidium*. Slightly lower positive rates were determined by epifluorescence microscopy. Sequencing data demonstrated the presence of the zoonotic genotypes, *Giardia duodenalis* Assemblage A and *Cryptosporidium parvum* (bovine).

IMPACTS/OUTCOMES/CONCLUSIONS: While the prevalence of both *Giardia* and *Cryptosporidium* was relatively high in the pooled swine manure, and zoonotic genotypes were identified, further study will be required to demonstrate a risk of transmission to humans. It is anticipated that human stool samples submitted to public health laboratories in the same area will be made available in the future for similar molecular characterization.

3.17 Why do People Living in Rural Areas Have a Higher Incidence of Cardiovascular Disease (CVD)?

M. Ducharme¹, and M. Connolly¹

¹ Health Supply and Demand Analysis Division, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: To understand why incidence rates of CVD are higher in rural areas of Canada.

DESIGN: In a previous study, we found that incidence rates of AMI and stroke tend to be higher in rural areas than in urban areas in Ontario and British Columbia, contrary to the popular belief that it is healthier to live in rural areas. We found no articles in the literature that explicitly explained why CVD rates are higher in rural areas in Canada. Therefore, in this study, we build a framework of potential factors (e.g., risk factors, access issues, service delivery, etc.) to explain the differences. We identify empirical evidence for each factor and compile the results to produce a potential explanation for the higher rural CVD rates. These results can serve as a basis for later studies.

RESULTS: Our preliminary results indicate that some factors are specific to CVD and other factors apply to all diseases and are a function of rurality (e.g., access issues). For example, we find that there is a higher prevalence of CVD risk factors, such as smoking and obesity, in rural areas than in urban areas. We also find that people in rural areas do not have the same access to health services as those in urban areas, affecting the prevention and treatment of CVD. There are fewer physicians, longer distances to hospitals and specialists, and different practice and referral patterns.

CONCLUSIONS: Because rural areas face higher levels of both CVD and its risk factors, health promotion and prevention programs could be designed to address these differences. Rural areas also face unique difficulties in accessing care and appropriate treatments in a timely fashion. This could be improved with different health human resource allocation and innovative service delivery methods, such as telehealth.

3.18 Sub-PPB Multi-Residue Determination of Quinolone, Fluoroquinolone and Sulfonamides Antibacterials in Fish and Shrimp by LC-MSMS

G. Dufresne¹, A. Fouquet¹, and A. Robichaud¹

¹ Food Directorate, Québec Region Laboratory, HPFB, Health Canada, Longueuil, PQ

OBJECTIVES: Develop a specific, sensitive and multi-residues quantitative method for the determination of sulfonamide, quinolone (QN) and fluoroquinolone (FQ) antibacterials in fish and shrimp. Limit of detection are between 0.1 and 0.8 ppb in tissue.

DESIGN: Tissues are extracted in Ethyl alcohol-acetic acid solvent. The extract is diluted in aqueous HCl, defatted with hexane and passed on a cation-exchange SPE cartridge to retain the analytes. Analytes are eluted using NH₄OH/methanol and concentrated before injection. Measurement is carried out using a capillary HPLC system with a 1.0 x 150 mm phenyl-hexyl column, coupled to a triple-quad mass spectrometer operating in ESI+ mode. Two injection runs are performed; one for FQs+QNs, and one for sulfas. Surrogate-recovery compounds and internal standards are used. Calibration is made by matrix-matched standards.

OUTPUT/RESULTS: Eight FQ compounds, four QN, 18 sulfonamides (sulfas) and two potentiators of sulfas, trimethoprim and ormethoprim were determined. The method has been validated for shrimp tissues at 1.25, 3.0 and 10 ng/g (ppb). It has been validated for FQs and QNs in salmon and trout, and showed to work for sulfas in those commodities using incurred samples. Recovery ranges from 50% (sulfacetamide) to 100 % (flumequine) with RSD ranging from 3 to 20%. Limit of detections are from 0.1 to 0.8 ppb. Shrimp from Asia are most often found positive; the compounds found (always below 10 ppb) are: enrofloxacin, flumequin, sulfadimethoxine, sulfamethazine, and sulfamethoxazole.

IMPACTS/OUTPUT/CONCLUSIONS: Although concentrations found are very low, many of the compounds found in imported fish are not permitted for use on animals in Canada.

3.19

[Withdrawn]

3.20 Evaluating the Evidence of Replacing Trans Fatty Acids (TFAs) with Alternative Fatty Acids on Cardiovascular Disease Outcomes

S. Farnworth, MSc¹, M.J. Cooper, PhD¹, L. Dumais, DtP¹, W.M.N. Ratnayake, PhD², and B.E. McDonald, PhD³

¹ Nutrition Evaluation Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

² Nutrition Research Division, Food Directorate, HPFB, Health Canada, Ottawa, ON

³ University of Manitoba, Winnipeg, MB

OBJECTIVES: Recently there has been significant interest surrounding TFAs in Canada since they have been negatively associated with cardiovascular disease (CVD). Part of the mandate of a joint Health Canada and Heart and Stroke Foundation of Canada Task Force was to develop recommendations and strategies for reducing TFAs in foods to the lowest levels possible. As part of the process, a focused literature review was undertaken to assess the strength of the scientific evidence regarding the replacement of TFAs with various alternatives. Thus, our objective was to evaluate the evidence on the impact of replacing TFAs with different types of fatty acids including monounsaturated, polyunsaturated, saturated (SFA), and specific SFAs on CVD outcomes.

DESIGN: We conducted focussed literature searches in Medline and Current Contents databases to identify primary research articles published between 1999 and 2005. Additionally, studies had to be published in English and conducted in adult human subjects (age > 17 years). Key search terms included: dietary fat, fatty acids, and cholesterol. All eligible studies were then assessed for methodological quality.

RESULTS: There were 491 titles and abstracts that were screened from the database searches and from articles suggested by Task Force members. Upon further screening, 144 of these articles were reviewed for their relevancy to the topic, of which 42 were deemed appropriate. Studies were then evaluated for methodological quality and grouped according to the research question(s) they were answering, i.e., which fatty acids were being compared. Although there is general agreement that TFAs in the diet should be limited due to the adverse effects on the risk factors for CVD, results from this focussed review did not identify a specific SFA that could be used as a possible replacement for TFAs.

CONCLUSIONS: This focused review provides the foundation for continued investigation on the impact of replacing TFAs with alternatives such as monounsaturated, polyunsaturated, and saturated fatty acids on CVD outcomes.

3.21 Bisphenol A (BPA) Content of Commercial Polycarbonate (PC) Baby Bottles

D. Page¹, G. Lacroix¹, P.J. Lalonde², and M. Feeley³

¹ Food Research Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON (ret'd)

² Product Safety Programme, HECSB, Health Canada, Ottawa, ON

³ Chemical Health Hazard Assessment Division, Bureau of Chemical Safety, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To measure the extractable BPA content in a random sample of PC baby bottles. Following detection of BPA, bottles will be subjected to standard migration simulations in order to quantify possible leaching of BPA.

DESIGN: 1 cm² sections of baby bottle (thread and main body) were completely dissolved in dichloromethane and then extracted into a methanol fraction. Following filtration, the BPA content was analyzed using a HPLC fitted with a UV detector. For the leaching experiments, baby bottles were filled with a 50% ethanol solution (milk simulant) and subjected to various combinations of time periods at room temperature (22°C), refrigeration (4°C) or in an oven (70°C).

OUTPUTS/RESULTS: BPA could be detected at concentrations ranging from 4.2-60.5 µg/g following organic solvent extraction of the PC bottles. Only blank amounts of BPA were detected during leaching studies at either room temperature and/or refrigeration. However, when the bottles were subjected to temperatures of 70°C, time dependent increases in BPA could be detected in the ethanol solution, but at much lower amounts (ppb) than with the extraction studies.

IMPACTS/OUTCOMES/CONCLUSIONS: Results from the extraction studies indicate that BPA could be detected in PC bottles. This was as expected considering BPA and carbonyl chloride are the main reaction materials used in the production of various polycarbonate plastics and synthetic resins. Leaching studies indicated that low concentrations of BPA could migrate into a milk simulant but only under conditions of extreme use. Under normal conditions, it is estimated that the daily intake of BPA from PC baby bottles would be in the range of 1-10 ng/kg bw/day or 1000-fold lower than the current most conservative tolerable daily intake. Overall, these results suggest there are no BPA-safety concerns with PC baby bottles.

3.22 Street Youth and Their Use of Substances

J. Flight, MA¹, and S. Racine, M.Ps.¹

¹ Drug Strategy and Controlled Substances Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Youth are a focus of Canada's Drug Strategy. Street youth, in particular, are at high risk of harms due to a myriad of factors of which substance use is an important one. In this presentation, street youth's substance use and associated risk factors are examined.

DESIGN: Results are based on the Public Health Agency of Canada's Enhanced Surveillance of Canadian Street Youth (E-SYS), a comprehensive study monitoring street youth, aged 15 to 24 years of age, since 1999. Various outreach means were used to recruit 4728 street youth over three phases of data collection (1999, 2001, 2003). In-person interviews covered demographics, lifestyle, substance use, sexual practices, attitudes and knowledge of risk behaviours and family history. Results are contrasted with those of general population youth (Canadian Addiction Survey, Canadian Tobacco Use Monitoring Survey).

OUTPUTS/RESULTS: When examining alcohol, street youth presented similar rates and patterns of use as general population youth, but comparability is weak across surveys. Street youth had higher rates of use of non-injection drugs (including cannabis) as well as higher rates of daily use of tobacco (average 80% vs. 30%). About 20% of street youth reported injection drug use, while this behaviour is too low to be reportable in general population youth.

IMPACTS/OUTCOMES/CONCLUSIONS: Street youth are different from general population youth. This study increases our knowledge about this population, which is not reached through standard monitoring activities. Furthermore, it provides social workers and other care providers with an enhanced knowledge about street youth's substance involvement and associated risks and harms and enables improvements to programs and services aimed at them.

3.23 Evaluating the Toxicity of Diesel Emissions Generated Using Different Fuel and Engine Technologies

M.L. Gagnon, BSc¹, M. Meier¹, and P.A. White, PhD¹

¹ Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: The objectives of this study are to employ *in vitro* bioassays including the *Salmonella* mutagenicity test, as well as the DR- and ER-CALUX assays, to assess the comparative toxicological properties of diesel engine emissions.

DESIGN: Diesel emissions were collected by Environment Canada's Emission Research and Measurement Division using specialized facilities and equipment. Particulate material generated under different test conditions was collected on 70mm Pallflex® filters upstream of a polyurethane foam (PUF) plug. The soluble organic material was extracted from the filters and the PUF plugs using pressurized fluid extraction and separated into polar aromatics and non-polar neutral fractions. (Geno)toxicity of the individual fractions was evaluated using the *Salmonella* mutagenicity assay as well as the DR- and ER-CALUX assays.

OUTPUT/RESULTS: Standard reference material (SRM 2975) generated by a heavy-duty forklift, was used to validate the performance of the three assays. Both fractions of this material yielded significant positive results in the *Salmonella* mutagenicity assay, and are currently being evaluated with the DR- and ER-CALUX assays. Archived material of delivery vehicle emissions generated using a variety of fuels and driving cycles have been extracted and fractionated and testing is currently underway. Additional emission samples, representing heavy-duty trucks operated with alternative fuels, are currently being collected.

IMPACTS/OUTCOMES/CONCLUSIONS: Research has clearly demonstrated that traffic related air pollution contributes to an enhanced risk of adverse health effects including renal failure and pulmonary diseases. Because mobile sources are the leading cause of air pollution in many urban areas, it is imperative to develop strategies that minimize human exposure and risk. The results obtained to date indicate that diesel emissions contain substances that are mutagenic and have the potential to induce dioxin- and estrogen-like responses. The results of current and future analyses will provide an ability to evaluate diesel combustion technology, and identify scenarios that minimize exposure and the risk of adverse health effects.

3.24 Effects of Spirituality on Self-Rated Health Status

J. Grose, BSc, BA¹, and K. Basu, PhD²

¹ Health Accountability and Performance Reporting Division, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

² Microsimulation Modelling and Data Analysis Division, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: Study the effects on self-rated health status of spiritual values and participating in religious activity. Do spiritual/religious people live happier lives? Is it necessary to be religiously active to enjoy this effect, if any, or is being spiritual in and of itself sufficient? In future research, should spirituality or religiosity be treated as control variables, just as significant as the standard age, sex, income, education, marital status and province variables?

METHODS: Using the Canadian Community Health Survey (CCHS) 2002 1.2 Mental Health and Well-being, study the relationships between mental health, physical health, religious activities and being spiritual.

The independent variables used were:

SPVB_1: Spiritual values play an important role: “Do spiritual values play an important role in your life?” (Yes/No)

SPVB_7: The self-perception of being very or somewhat religious: “In general, would you say that you are very religious, religious, not very religious, not religious at all?” This was collapsed to very religious or religious vs. not very religious or not at all religious.

The dependent variables used were:

SCRBDPHY: Self-rated physical health: “In general, would you say your health is (excellent, very good, good, fair, poor)?” This was collapsed to excellent or very good vs. good, fair or poor.

SCRBDMEN: Self-rated mental health: “In general, would you say your mental health is (excellent, very good, good, fair, poor)?” This was collapsed to excellent or very good vs. good, fair or poor.

RESULTS: Logistic regressions revealed that, after controlling for age, sex, income, education, marital status and province:

- Those who are **spiritual** are more likely to be in very good or excellent self-rated
 - **physical** health (OR = 1.12 (1.04, 1.21), p <0.01).
 - **mental** health (OR = 1.12 (1.04, 1.21), p <0.01).
- Those who are **religious** are more likely to be in very good or excellent self-rated
 - **physical** health (OR = 1.13 (1.05, 1.21), p <0.001).
 - **mental** health (OR = 1.17 (1.08, 1.26), p <0.001).

CONCLUSIONS:

Those who are religious are more likely to be both physically and mentally healthy.

Those who are spiritual are more likely to be both physically and mentally healthy.

Policy Implications and Next Steps

Clearly in our pluralistic society the Government of Canada has no business urging people to be more religious or spiritual. However in future studies of health, whether physical or mental, investigators may wish to consider including religiosity and/or spirituality with standard control variables.

Still to be explored is the cause and effect relationship, if any, between spirituality/religiosity and self-rated physical/mental health. Does being spiritual or religious lead to an improvement in one's physical and mental health? Does being physically and mentally healthy lead to an increased level of spirituality or religiosity? Is there a confounding variable? A longitudinal study following the spirituality/religiosity and physical/mental health of subjects might help answer these questions.

3.25

[Withdrawn]

3.26 Determinations of Vitamin D Via High Pressure Liquid Chromatography and Radioimmunoassay in Biological Samples

N. Hidioglou¹, and K. Sarafin¹

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

INTRODUCTION: Vitamin D is receiving considerable interest in both the scientific and public arena in its role in health and chronic disease outcomes. Vitamin D status including deficiency and insufficiency is an emerging issue in many parts of the world including Canada. Vitamin D has been suggested to play a role in health/disease beyond its classical function in bone health. Some emerging areas include its potential role in autoimmune disease, cardiovascular disease and cancer.

OBJECTIVES: Health Canada Laboratories (Ottawa) are re-establishing their analytical capabilities to quantify Vitamin D and its metabolites in biological samples by: 1) High Pressure Liquid Chromatography and; 2) Radioimmunoassay technique in biological samples.

METHODOLOGY: The best marker for vitamin D status is serum 25 (OH-D) and thus was used in the analytical methodology work up.

For the HPLC method, 25-OH Vitamin D was extracted from serum by a liquid-liquid organic solvent extraction. Extract was removed and cleaned by passing through a solid phase extraction cartridge. The eluent was dried and re-dissolved into the HPLC mobile phase for analysis by HPLC-PDA (photodiode array detection). The HPLC analysis was done isocratically with acetonitrile on a reverse-phase column.

For the RIA, total Vitamin D status was measured for comparison by radioimmunoassay (RIA) utilizing a commercial kit (Diasorin Inc). The RIA is based on an antibody with specificity to 25-OH-Vitamin D.

OUTPUT/RESULTS: A high correlation coefficient (r value > 0.95) was found between the HPLC and RIA method for serum vitamin D (25-OH-D). Serum vitamin D (25-OH-D) recovery data obtained from HPLC analysis was in the range of 80-105%. To further validate the HPLC and RIA vitamin D techniques, quality control serum samples are routinely obtained from DEQAS (International Vitamin D Quality Control Assessment Scheme, based in the UK) for vitamin D analysis. Our data obtained to date are well within the targeted vitamin D levels.

IMPACTS/OUTCOMES/CONCLUSIONS: This technical capacity will allow for in-house and external collaborations on vitamin D nutrition regulatory research issues such as food fortification practices, bioavailability, nutritional status, safety and health/disease issues. In addition, with the development of these assays will directly support the Nutrition Research Division (NRD's) participation in the upcoming Canadian National Health Measures Survey (Fall 2006). The NRD will provide analytical and scientific expertise related to various markers of nutritional status including vitamin D.

3.27 Human Health Risk Assessment of Fluorotelomer Based Substances: Basis for Assessment Conclusions, Regulatory Implications, International Cooperation, and Consideration of an Action Plan to Address PFCA Precursors from Fluorotelomer Sources

M. Hill¹, R. Gandia¹, G. White¹, and G. Hammond²

¹ New Substances Assessment and Control Bureau, HECSB, Health Canada, Ottawa, ON
² New Substances Programme, Environment Canada, Ottawa, ON

OBJECTIVES: Develop an integrated approach for the management of perfluorinated carboxylic acids (PFCAs) and their precursors in order to protect human health and the environment from adverse effects of PFCAs.

DESIGN: In 2004, four fluorotelomer-based substances intended for use as stain/water repellants for textiles, carpets, stone and tile, as sizing agents for paper products with food contact applications, and as levelling agents in coatings, were notified pursuant to subsection 81(1) of the *Canadian Environmental Protection Act* (CEPA), 1999. The assessments were based upon information submitted by the notifiers, studies published in the scientific literature, and information otherwise available to the Departments of Health and Environment.

OUTPUTS/RESULTS: The substances were suspected of being toxic under section 64 of CEPA, 1999, and were subject to temporary prohibitions. The assessment conclusions were based upon information indicating the substances would ultimately be a source of PFCAs. Members of the PFCA class are known to be persistent and suspected to be bioaccumulative, subject to long-range transport and associated with adverse effects in laboratory animals. Particular concern exists for PFCAs with longer chain lengths, as these have shown greater potential for bioaccumulation. A literature review in 2006 corroborated the occurrence of PFCAs in environmental compartments that directly impact human exposure such as indoor air, dust, food and drinking water. Biomonitoring clearly demonstrates the presence of PFCAs in human blood globally. Detection of PFCAs in seminal plasma, breast milk and umbilical cord blood raises new concerns regarding routes of human exposure and potential effects.

IMPACTS/OUTCOMES/CONCLUSIONS: An Action Plan is being considered to address PFCAs and precursors. The plan includes an approach to address the substances currently prohibited and similar new substances in the future, as well as members of this class already in commerce. It encourages engagement of the research community and international regulators in contributing to assessment and management issues.

3.28 Sensitivity Analysis on Estimating Nutrient Inadequacy

R. Huang¹, B. Junkins¹, and M. Vigneault¹

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

OBJECTIVE: An important indicator in the development of nutrition focused health policies is the proportion of a targeted population whose usual intakes of a nutrient fail to meet their individual requirements. While this proportion is simple to define in principle, an accurate calculation requires a comprehensive understanding of the joint distribution of individual usual intakes and requirements for each nutrient. Such detailed information is usually missing, so that approximate methods must be employed. This study aims to compare the sensitivity to underlying assumptions of two different approaches to estimating nutrient inadequacy, namely the full probability approach and the Estimated Average Requirement (EAR) cut-point method.

DESIGN: This analysis is based on data derived from the Federal / Provincial Food and Nutrition Surveys (1990 - 1999) which encompasses a total of 20 373 respondents. We analyzed five nutrients - Magnesium, Vitamin C, Vitamin B12, Riboflavin and Thiamin. These nutrients provided a sufficiently varied challenge to the assumption estimation procedures to form a basis for sensitivity analysis. For each nutrient, a distribution of usual intakes was derived and combined with information on requirements consistent with the full probability approach. Next, nutrient inadequacy was calculated based on the two proposed approaches and differences were analyzed, accounting for uncertainties in estimation.

OUTPUTS/RESULTS: The EAR cut-point method is the simpler method but requires rather strict conditions on the underlying joint distribution of usual intakes and requirements. While the full probability approach uses a more detailed analysis, it too incorporates a number of important assumptions. This analysis demonstrates the deviation of the distribution of usual intakes from the assumptions inherent in the EAR cut-point method have important impacts on the resulting estimated levels of nutrient inadequacy.

IMPACTS/OUTCOMES/CONCLUSIONS: This study shows the importance of establishing an appropriate methodology in estimating the key health related measures in establishing effective policy.

3.29 Effects of Selenium Plus Vitamin E on Methylmercury-Induced Changes in Physiology, Hematology, Biochemistry, and Oxidative Stress in Male Sprague Dawley (SD) Rats

X. Jin, PhD¹, E. Lok, BSc¹, S. Gill, PhD¹, D. Caldwell, DVM¹, M. Taylor¹, K. Kapal¹, L.M.H. Chan, PhD², and R. Mehta, PhD¹

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

OBJECTIVES: Human exposure to methylmercury through consumption of contaminated fish and marine mammals has become an increasing concern in the Arctic. Fish and marine mammals as important components of Northern traditional diet are rich in protein, polyunsaturated fatty acids, selenium (Se), vitamin E (VE) and fiber. This study was conducted to investigate the effects of dietary Se plus VE ([Se+VE]) on acute toxicity of methylmercury in male SD rats.

DESIGN: Male SD rats were fed starch-based casein diet alone, or casein diet supplemented with a high level of Se (3 mg/kg diet) plus a low level of VE (250 mg/kg diet) for 28 days. The rats were then gavaged with 0, or 3 mg MeHg/kg body weight (BW) for 14 consecutive days. Body weights were recorded. At necropsy, target organs were weighed, and blood and urine samples were collected and analyzed for hematology, biochemistry, and oxidative stress endpoints.

RESULTS: MeHg significantly decreased body weight, red blood cell counts, hematocrit, and hemoglobin concentration, and increased relative kidney weight, to a similar degree with or without [Se+VE] supplementation. However, MeHg significantly increased relative spleen weight and monocyte counts, and decreased relative liver weight to a greater degree in the rats fed casein diet alone than casein plus [Se+VE] diet. MeHg significantly increased serum lipase and creatinine and urinary 8-hydroxydeoxyguanosine in rats fed casein diet alone, but not in rats fed casein plus [Se+VE] diet.

CONCLUSIONS: Dietary supplementation with a high level of Se plus a low level of VE improved performance of some toxicological endpoints in rats, but did not attenuate the effects of MeHg on other endpoints. Results of this study will contribute towards characterizing the beneficial effects of dietary constituents in managing health risks associated with mercury exposure.

3.30 The Development and Application of Probabilistic Methods in the Derivation of Estimated Daily Intakes for Canadian Populations

E.A. Sigal¹, J.A. Archbold², G.M. Ferguson¹, C.E. Bacigalupo¹, D.R.J. Moore¹, G.M. Richardson³, and H. Jones-Otazo⁴

¹ Cantox Environmental Inc., Mississauga, ON

² Environmental Protection Office, Toronto Public Health, Toronto, ON

³ Contaminated Sites Division, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

⁴ Safe Environments Programme, HECSB, Health Canada, Toronto, ON

OBJECTIVES: This research explores the development and application of probabilistic Estimated Daily Intakes (EDI) for use in the derivation of *Canadian Soil Quality Guidelines*. Probabilistic methods may be used to account for and communicate uncertainty and variability in estimates of exposure to provide more useful information to the risk manager. Probabilistic EDI distributions of nickel (Ni), vanadium (V) and beryllium (Be) were developed to characterize inter-individual variability expected within the Canadian population.

DESIGN: Probability density functions (PDFs) were developed using a 1-Dimensional Monte Carlo Analysis (MCA) approach. This approach combined point estimate values (i.e., the 95% upper confidence limit on the arithmetic mean for media concentration) with log normal PDFs (describing the inter-individual variability among Canadian receptor characteristics and intake rates) to estimate the EDI distributions for Ni, V and Be.

OUTPUTS/RESULTS: With the exception of infants, the EDI rates of Ni, V and Be for all Canadian receptor age classes were driven by the daily consumption of general food stuffs. The infant EDIs were driven by the consumption of human breast milk or infant formula. The incidental soil ingestion pathways appear significant to the overall EDI of V for the toddler, and to the overall EDI of Be for the infant and toddler.

IMPACTS/OUTCOMES/CONCLUSIONS: This research highlights the pathways and assumptions that appear to shape the EDI PDFs, and provides a discussion of some of the general observations, conclusions and recommendations with regards to the derivation and application of probabilistic analyses that were used to estimate EDI rates of Ni, V and Be. The methods and discussion presented are applicable to other types of chemicals in the Health Canada database.

3.31 Corrosion, Biocompatibility and Wear of Orthopaedic Alloys — Literature Review

C. Jary¹, and J. Karov, PhD²

¹ Department of Biochemistry, University of Waterloo, Waterloo, ON

² Department of Biochemistry, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To review the recent scientific publications on corrosion, biocompatibility and wear of three orthopaedic alloys.

DESIGN: More than seventy scientific publications were reviewed. The corrosion, biocompatibility and wear topics were summarized, outlining the current understanding from the available data.

OUTPUTS/RESULTS: The results of this review were presented to Health Canada evaluators of medical devices. Also, the information will be formatted and posted on a corrosion intranet site to assist in pre-market evaluation of orthopaedic implants. Some examples of the information for biocompatibility are: Cr⁶⁺, which is released from stainless steel prostheses, is highly toxic and may inhibit a number of metabolic processes. Both chromium and its compounds, and nickel and its compounds are potent carcinogens in animals. Titanium has low toxicity and accumulates in tissues adjacent to the implant in giant cells and is not excreted.

IMPACT/CONCLUSIONS: Safety and efficacy of medical devices used in Canada depend heavily on the pre-market review process. The results of the scientific literature review provide the evaluators with an up to date knowledge on the corrosion, biocompatibility and wear of orthopaedic implants.

3.32 The Effect of UHMWPE Articulation on the Corrosion Characteristics of Three Orthopaedic Alloys

L. Fishman¹, and J. Karov, PhD²

¹ Department of Mechanical Engineering, University of Ottawa, Ottawa, ON

² Department of Biochemistry, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: To assess the effect of High Molecular Weight Polyethylene (UHMWPE) articulation against orthopaedic implants on the corrosion of orthopaedic implants.

DESIGN: Fifteen samples were prepared from three main orthopaedic implants: stainless steel, Co -Cr-Mo alloy and Ti-Al-V alloys (five samples for each alloy). Corrosion experiments were carried out on a Gamry 105 corrosion system coupled with in-house built wear apparatus. Each sample was subjected to several corrosion tests under base (no articulation) and wear (UHMWPE articulation) conditions that simulate the electrolytic environment and the stresses found *in vivo*. One sample from each alloy group was also tested under wear with a ceramic pin to simulate third body wear and to provide reference.

OUTPUTS/RESULTS: Articulation of UHMWPE against Stainless Steel alloy had the following effects: The corrosion potential E_o increased (-364mV to -287mV), the corrosion current was not affected. The Tafel slope of anodic polarization was steeper, indicating the presence of a more effective passive layer. In cycling experiments, the articulation of UHMWPE shifted E_b (the breakdown potential) and E_p (the protection potential) to higher values (922mV and -173mV to 1033mV and -105 mV respectively). Articulation of UHMWPE against Co-Cr -Mo alloy lowered the E_o to a more active level and reduced the corrosion current (-238mV to -428mV, 0.76 μ A to 0.25 μ A). The Tafel slope of anodic polarization was steeper indicating the presence of a more effective passive layer. In cyclic experiments the break down potential (E_b) was lowered from 622mV to 444mV while E_p the protection potential was not affected. UHMWPE articulation against Ti alloy increased the E_o to more noble values (-295mV to -183mV). The corrosion current increased by more than two orders of magnitude under UHMWPE articulation (0.254 μ A to 67 μ A).

IMPACT/CONCLUSIONS: Biocompatibility of orthopaedic implants is strongly dependent on their corrosion characteristics. The relatively small change in corrosion parameters suggest that the articulation does not remove the passive layer but may modify it possibly by compressing locally the oxide layer and/ or depositing a thin layer of UHMWPE. Our results help to estimate the UHMWPE articulation effect on the implant biocompatibility.

3.33 Revision of Canada's Food Guide: An Innovative Evidence-Based Approach to Dietary Guidance Development

S. Katamay¹, K. Esslinger¹, I. Sirois¹, E. Jones-McLean¹, C. Martineau¹, B. Junkins², M. Vigneault², L. Robbins³, A. Kennedy³, and J. Johnston⁴

- ¹ Office of Nutrition Policy and Promotion, HPFB, Health Canada, Ottawa, ON
- ² Bureau of Biostatistics and Computer Applications, Food Directorate, HPFB, Health Canada, Ottawa, ON
- ³ Cross-Sectoral Food Industry Affairs Division, Food Value Chain Bureau, Agriculture and Agri-Food Canada
- ⁴ Nutrition Evaluation Division, Bureau of Nutritional Sciences, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Develop a dietary pattern applicable to the Canadian population that will result in acceptable nutrient outcomes and likely contribute to reduced risk of chronic diseases.

DESIGN: To develop the dietary pattern a statistical modelling approach was employed. Food composites were used to provide a first estimate of the number of servings of each food group required to meet defined nutrient outcomes across 16 age and sex groups. The number of servings of each food composite group was then used to inform the creation of 500 test diets using foods reported in four Federal - Provincial nutrition surveys. These test diets yielded distributions of nutrient content, which were then assessed for adequacy using methods recommended in *Dietary Reference Intakes: Applications in Dietary Assessment*. Adjustments to the dietary pattern were made as necessary to achieve a low prevalence of inadequate nutrient content. The pattern was also assessed using lower income and vegetarian food choices.

The summary of two large systematic reviews provided additional information to the developed pattern to ensure it was consistent with epidemiological evidence around chronic disease prevention and foods, in particular.

OUTPUTS/RESULTS: This innovative evidence-based approach resulted in a final pattern that achieves satisfactory results across most nutrients assessed and is consistent with evidence linking diet to reduced risk of chronic diseases. Any person following the food intake pattern has a high probability of meeting their nutrient requirements as well as a low probability of nutrient excess. This approach provides rationale for specific messaging on whole grains, orange vegetables, dark green vegetables, fluid milk, lower-fat meat and dairy, unsaturated oils and fat, and fish.

IMPACTS/OUTCOMES/CONCLUSIONS: This integrated approach builds on enhanced assessment methods recommended through Dietary Reference Intakes and goes beyond consideration of nutrients alone.

3.34 Estimation of Pesticide Transformation Rates Across Environmental Media

I. Kennedy, PhD¹, L. Avon, MSc¹, and G. Malis, MSc¹

¹ Environmental Assessment Division, PMRA, Health Canada, Ottawa, ON

OBJECTIVES: Estimating concentrations of pesticides in water is an integral part of the risk assessment process conducted by the Pest Management Regulatory Agency (PMRA). The transformation rates of those pesticides in soil, water and sediment are key parameters for the PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modelling System) models used for calculating concentration estimates. In cases where data are not available in one of these media, PMRA currently assumes the pesticide does not transform in that medium. To provide more realistic concentration estimates, it is desirable to estimate a transformation rate from the rates measured in other media. For example, in the United States, the US Environmental Protection Agency (EPA) estimates the water transformation rate as half the soil transformation rate. Here we aim to provide guidance on estimating transformation rates from the rates in other media.

DESIGN: Evaluation of pesticides for registration in Canada requires measurements of pesticide transformation in soil, water and sediment. The PMRA thus has a database of measured values for transformation rates in these three media for a large number of pesticides. We compiled and compared measurements of transformation rates in all three media and calculated distributions of rates given the rates in other media.

OUTPUTS/RESULTS: The analysis indicates there is no consistent ratio between transformation rates in different media to allow accurate extrapolations across the media. However, it is possible to estimate bounds on the unknown rates, and these bounds can be used to choose defensible values for transformation rates to be used in modeling.

IMPACTS/OUTCOMES/CONCLUSIONS: The results are used to provide estimated transformation rates to use where data is missing, with the intention to produce values that are conservative but within a range we would expect given available data.

3.35 Proposed Framework for Aquatic Risk Assessments of Pesticides

S. Kirby, MSc¹, L. Avon, MSc¹, D. François, MSc¹, C. Hart, PhD¹, H. Mulye, PhD¹, T. Kuchnicki, PhD¹, H. Simmons, MSc¹, R. Sebastien, PhD¹, J. Villeneuve, MSc¹, J.D. Whall, MSc¹, and P. Delorme, PhD¹

¹ Environmental Assessment Division, PMRA, Health Canada, Ottawa, ON

OBJECTIVE: Like all science, risk assessment methods and approaches must reflect current knowledge and available methods. In the case of environmental risk assessments of pesticides, approaches to aquatic assessments have not changed significantly in the past 15 years. In order to incorporate advances in knowledge on the fate, effects and risk characterization the Pest Management Regulatory Agency (PMRA) is revising the approach it uses for aquatic assessments and is proposing a new framework.

DESIGN: The proposed framework uses a science-based tiered approach that considers both the inherent toxicity of the pesticide as well as the potential for exposure to that pesticide. Initial tiers (screening levels) use a deterministic approach with conservative exposure scenarios and using conservative effects endpoints. This approach allows those uses that do not pose any significant risk to the environment to be screened out in an efficient manner. The screening level also allows for the identification of taxonomic groups not at risk. Subsequent tiers of the risk assessment focus on refining exposure estimates using more sophisticated fate models with specific regional scenarios. Further refinements for higher tiers are considered on a cases by case basis and can include refinement of model inputs, considerations of additional effects data when available, or the use of probabilistic assessment methods.

OUTPUTS/RESULTS: Results of these changes provide a more scientifically sound risk characterization, reflecting a more modern approach.

OUTCOMES: Efficiency in the risk assessment process can be gained through the early identification uses or taxonomic groups with little or negligible risk. The approach also allows for greater flexibility in risk characterization as needed for specific products.

3.36 The Prediction of Toxicities for Indoor Relevant Mycotoxins

S.A. Kulkarni, PhD¹, J.C.C. Yu, PhD², J. Zhu, PhD¹

¹ Chemistry Research Division, HECSB, Health Canada, Ottawa, ON

² Department of Chemistry, Sam Houston State University, Texas, USA

OBJECTIVES: Investigation of toxicological properties of selected indoor mycotoxins using *in silico* predictions.

DESIGN: Numerous mycotoxins can be produced by molds under certain conditions. In indoor environment mycotoxins have been found from molds growing on building materials. Our project focused on the prediction of potential toxic effects of approximately fifteen known indoor relevant mycotoxins. QSAR models such as TOPKAT, MCASE and DEREK were run on each of these mycotoxins to obtain information on various toxicological endpoints including carcinogenicity and mutagenicity. Since limited experimental toxicity data are available for comparative assessments therefore, the model predictions were interpreted on the basis of the domains of applicability of individual models with respect to the individual mycotoxins. The indoor relevant mycotoxins will be ranked by their potential toxicity in order to elucidate the major group of hazardous compounds produced by indoor molds.

OUTPUTS/RESULTS: The present study included indoor mycotoxins such as Sterigmatocystin, T-2 toxin, Satratoxin G and H, Diacetoxyscirpenol, Deoxynivalenol, Verrucarol, T-2 tetraol, Citrinine, Fumagillin, Verruculogen, Penitrem A, Roquefortine C, Gliotoxin, Malformins, Mycophenolic acid, etc. CASETOX carcinogenicity model predicts high probabilities for mycotoxins such as Sterigmatocystin, T-2 toxin, Satratoxin G and H, and low probabilities for Roquefortine C, Gliotoxin, Malformins, Mycophenolic acid. On the other hand, the Ames mutagenicity models of both CASETOX and TOPKAT predict higher probability for Sterigmatocystin and lower probabilities for Penitrem, Diacetoxyscirpenol, Citrinine, Fumagillin and Mycophenolic acid. Predictions for some of the mycotoxins are found to be in agreement with the experimental data.

IMPACTS/OUTCOMES/CONCLUSIONS: The presence of mycotoxins is believed to be responsible for some of the adverse health effects including both acute and chronic. The experimental results of toxicities of indoor related mycotoxins are however, sporadically reported. Whereas the guidelines for monitoring highly toxic compounds occurring in the indoor setting would be the most relevant and of great interest to general public and indoor hygienists, our model prediction of toxicities of indoor-relevant mycotoxins will not only provide the likelihood of their health impacts in the event of exposure but also serve as a reference for the development of guidelines in monitoring indoor air quality. The model prediction of toxicities would also contribute to the establishment of investigation guidelines for the researchers working in the area of indoor air quality. Additionally, this study will help evaluate the predictability of the QSAR models for mycotoxins.

3.37 Alterations in the Faecal Population of Rats as a Function of Dietary Fructooligosaccharide

C. Gourgue-Jeannot¹, M.L. Kalmokoff², J. Kwan¹, M. McAllister¹, E. Kheradpir³, B.J. Lampi¹, and S.P.J. Brooks¹

¹ Bureau of Nutritional Research, Food Directorate, HPFB, Health Canada, Ottawa, ON

² Atlantic Food and Horticulture Research Centre, Agriculture and Agri-Food Canada, Kentville, NS

³ Bureau of Microbial Hazards, Food Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Determine the effect of dietary fructooligosaccharides (FOS) on faecal bacterial populations using a combination of molecular biology and culturing methods.

DESIGN: Two groups of seven 28-42 days old control BB rats were fed either Purina 5001 rat chow (control) or chow containing 5% w/w FOS. Fresh faecal samples were collected, pooled and homogenized at different time points. Analysis was conducted by: 1) culturing on specific media; 2) PCR amplifying DNA using universal primers directed against the full 16S rRNA gene, shotgun cloning and sequencing; or, 3) Denaturing Gradient Gel Electrophoresis (DGGE) after amplification of the 16S gene V2-3 region.

OUTPUTS/RESULTS: A greater diversity of inulin-utilising bacterial species in FOS-fed (vs. controls) was observed when bacteria were cultured using chicory inulin as the sole carbohydrate source, although inulin-utilizing species were identified in controls and experimental rats. The majority of species fell within the *Clostridium coccooides* group and *Clostridium leptum* subgroup and some were related to butyrate producing bacteria isolated from other animals. No Bifidobacteria were isolated. Shotgun cloning and DGGE analysis revealed a profound change in the faecal population that took approximately 12 days to stabilize. The final population contained only 12% of the clones found in control rats. The greatest change occurred in the low G + C Gram-positive bacteria where only three phylotypes were identical with those previously identified in the control. Estimates of species diversity in control and FOS-fed rats suggested FOS induced a reduction of about 50%.

IMPACTS/OUTCOMES/CONCLUSIONS: These results show that fermentable carbohydrates can exert a profound effect on the bacterial community of the lower bowel and that FOS does not stimulate Bifidobacteria exclusively but provides substrate for a wide variety of bacteria. This result is hardly surprising, given the diversity of bacteria in the gut and the niche that these bacteria occupy.

3.38 Youth Smoking Survey 2004-05: Results and Comparisons to 2002

M.W. Latendresse, MA¹, A. Diener, PhD¹, J. Snider, MSc¹, and M.J. Kaiserman, PhD, MBA¹

¹ Office of Research, Surveillance and Evaluation, Tobacco Control Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVE: To assess tobacco use and smoking related behaviours of school aged children in grades five through nine using the Youth Smoking Survey (YSS). It is generally recognized that this is the population most at risk for trying tobacco products.

METHODS: The YSS is a national survey sponsored by Health Canada and conducted by the Centre for Behavioural Research and Program Evaluation and their consortium of pan-Canadian researchers and students. This classroom-based survey was first conducted in 1994 and again in 2002. The most recent implementation of the YSS provided data for 2004-05. The YSS utilized a two-stage stratified clustered design with schools as the primary sampling units and classes as the secondary units. In 2004-05 data from a total of 29 243 students located in all 10 Canadian provinces was collected. The total response rate for Canadian school boards approached for participation in the YSS 2004/05 remained elevated at 73.8.

RESULTS: In 2002, there was a significant decline in the percentage of ever cigarette smokers (23%) among youth in grades five to nine, compared to 1994 (40%). YSS 2002 data indicated that smoking prevalence increases with grade (7% in grade five to 42% in grade nine). YSS 2004-05 data is embargoed until September 6, 2006 and results from this survey will be presented at the conference.

CONCLUSIONS/IMPLICATIONS: The YSS is an essential component of Canada's tobacco control monitoring system and provides a backdrop for making evidence based decisions on federal and provincial smoking policies as well as government based programs targeting the reduction of youth smoking. This project is used to monitor the success of the Federal Tobacco Control Strategy to reduce smoking prevalence from 25% to 20% by monitoring the knowledge, attitudes, and behaviours of youth who are at most at risk of trying cigarettes.

3.39 Monitoring Environmental, Nutritional and Immunoprotective Analytes in Canadian Human Milk

M. Legrand, PhD¹, and R. Dabeka, PhD¹

¹ Food Research Division, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Surveys of selected persistent organic pollutants (POPs) in Canadian human milk were undertaken in 1967, 1975, 1981, 1986, and 1992.

DESIGN: The cross sectional surveys recruited between 100 and 500 Canadian mothers from rural and urban centres within five designated regions (Atlantic, Quebec, Ontario, Prairies and British Columbia).

RESULTS: The data served as an indicator of the mother's body burden and infant's dietary exposure, and allowed an assessment of temporal trends. Since 1967, there has been a steady decline in the human milk levels of DDT, dieldrin and heptachlor epoxide. The concentrations of PCBs and hexachlorocyclohexane showed a general downward trend except for a sharp peak in 1982. Dioxins and furans were incorporated in the analysis as of 1981. Between 1981 and 1986, the levels dropped by half and remained constant through 1992.

DISCUSSION AND CONCLUSION: Despite the detection of these POPs in mother's milk, it was recommended that the nutritional, psychological and immunological benefits provided from the milk to the child outweigh the health risks from exposure to these contaminants. In its continual role of safeguarding the health of infants, the Health Products and Food Branch of Health Canada is planning the sixth national human milk survey for environmental, nutritional and immunoprotective analytes to take place in 2007/2008 with a pilot in 2006/2007. National human milk surveys strengthen health risk assessments in infants (including promotion of breastfeeding) and support measures to reduce exposure to environmental contaminants.

3.40 Rapid Estimation of the Smoker Exposure to Tobacco Smoke Emissions Using a Colour Scale

G. Levasseur¹, J. Fillion¹, and M.J. Kaiserman¹

¹ Tobacco Control Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVE: The objective is to provide the smoker with a personalized and visual way to estimate immediate intake of smoke emissions.

In this study, an exposure wheel using a colour scale is developed. When matched to the smoker's cigarette filter, the colour scale allows for the estimation of tar exposure per cigarette. Then, using the exposure wheel, intake of nicotine and other toxic compounds can be predicted.

DESIGN: The development of the colour scale is based on the assumption that the tar delivered to the smoker is directly linked to the colour of the cigarette filter. Toxic emissions of eight Canadian cigarettes were determined applying different non-standard smoking conditions. Their filter colours in relation with nicotine and tar levels were then studied to develop a colour scale.

Given that the Canadian market is quite homogeneous, consisting mainly of flue-cured tobacco grown in the same geographic area, a mathematical relationship between tar and other toxic emissions present in the smoke can be established.

OUTPUTS/RESULTS: Using the colour scale developed and a chart of 40 toxic emissions, a smoker can compare cigarette filter colour to the colour scale in order to estimate exposure to tobacco toxic emissions.

IMPACTS/OUTCOMES/CONCLUSIONS: Transferred to a handy wheel, it provides an educational tool to reach the smoker, help identify health hazards associated with smoking and make an informed choice.

3.41 PH and Nicotine Delivery of Different Tobacco Products on the Canadian Market

G. Levasseur¹, and M.J. Kaiserman¹

¹ Tobacco Control Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: The objective of this study is to determine the relationship between pH and nicotine of different tobacco products available on the Canadian market. Knowing that the pH of tobacco can influence the bio-availability of nicotine (higher pH more bio-available nicotine), the pH and nicotine content of different tobacco products are compared to establish their comparative efficiency in terms of nicotine delivery.

DESIGN: pH and alkaloid levels of different tobacco products were measured and compared in whole tobacco using tests mandated by the Tobacco Reporting Regulations (TRR). Tobacco products available on the Canadian market include; Canadian and imported cigarettes, fine cut tobacco, cigar, pipe tobacco and smokeless tobacco.

OUTPUTS/RESULTS: Products from two smokeless tobacco manufacturers were evaluated. It was shown that smokeless tobacco brands from the United State have high pH, between 6 and 8.5, and high nicotine content, 25-30 mg/g. In contrast, chewing tobacco from Sweden have a low pH 5.5 and low nicotine; 10 mg/g. Cigarettes and fine cut tobaccos cluster around a pH of 5 with average nicotine levels between 15 and 20 mg/g. Pipe tobaccos have the lowest observed pHs between 4.7 and 4.9, while nicotine content averaged around 17 mg/g. Cigars have pH levels between 6 and 7 while nicotine contents are low, between 7 and 12 mg/g.

IMPACTS/OUTCOMES/CONCLUSION: Smokeless tobacco products from the United States have a higher nicotine content at a higher pH than the Swedish product. While cigars have low nicotine content, its availability to the smoker is reinforced by a higher pH. Cigarette, fine cut and pipe tobacco present the lowest pH while their nicotine content seems to be at an average level.

3.42 Extended-Spectrum Beta-Lactamase-Producing Bacteria from Food and Companion Animals: An Emerging Issue

X.-Z. Li, PhD¹, M. Mehrotra, PhD¹, S. Ghimire, PhD¹, and L. Adewoye, PhD¹

¹ Human Safety Division, Veterinary Drugs Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Assess resistance to beta-lactams and the distribution of beta-lactamases, particularly extended-spectrum beta-lactamases (ESBLs), in animal-derived bacteria in order to identify potential issues of public health concern.

DESIGN: Analyze published antimicrobial resistance surveillance and literature data with an emphasis on identification of resistance to extended-spectrum beta-lactams via genotypic and phenotypic approaches (e.g., reported sequences and substrate/inhibitor profiles of beta-lactamases).

OUTPUTS/RESULTS: Beta-lactams are among the most important antimicrobials in human and veterinary medicine. Bacterial resistance to beta-lactams has been increasingly observed in bacteria, including those from animals. Over 400 beta-lactamases have been reported to date and these enzymes contribute predominantly to beta-lactam resistance in gram-negative bacteria such as *Escherichia coli* and *Salmonella* spp. A variety of beta-lactamases have been identified in bacteria from food and companion animals. The plasmid-encoded AmpC-like CMY beta-lactamases, which do not belong to ESBLs but mediate resistance to extended-spectrum beta-lactams, are significantly distributed in *E. coli* and *Salmonella* spp. from animals worldwide including in Canada and are mainly responsible for the increasing rates of resistance to third generation cephalosporins. Plasmid-encoded ESBLs, once rarely detected in animal-derived bacteria, are increasingly being observed in Asia and Europe, but so far not in Canada. The dominant ESBLs reported in animals are the CTX-M family, which is also increasingly being identified in bacteria from humans. The genes encoding CMY and CTX-M enzymes often coexist with other resistance determinants and can be associated with transposons/integrations, highlighting the potential enrichment of multi-drug resistant bacteria by multiple antimicrobial agents and dissemination of the resistance determinants among bacterial species.

IMPACT/OUTCOMES/CONCLUSIONS: Studies on beta-lactamases from animal-derived bacteria are somewhat an ignored field. The occurrence of ESBLs in animals is an emerging public health and animal health issue. Characterization of the animal-derived beta-lactamase-producing bacteria warrants further investigation of the type and distribution of beta-lactamases of animal origin and their potential impact on human medicine.

3.43 Environmental Contaminants and Traditional Foods Workshop Focus Groups: Applicability to Qualitative Research?

K. Lydon-Hassen¹, and C. Tikhonov¹

¹ Environmental Research Division, FNIHB, Health Canada, Ottawa, ON

OBJECTIVES: To qualitatively assess focus group information from First Nations community representatives from six regions across Canada who attended Environmental Contaminants and Traditional Foods Workshops (ECTFWs) between 2002 and 2005.

DESIGN: Results of focus group sessions conducted during six ECTFWs were compiled and analyzed independently by two evaluators to assess commonalities and disparities with respect to consumption of traditional foods and perceptions related to environmental contaminants in First Nations in six regions across Canada. Open ended questions asked about: traditional foods most often consumed; perceived changes in rates of traditional foods consumption over time; accessibility to traditional foods; environmental contaminant concerns; means of addressing concerns and improving risk communication. Reported responses were categorized under these themes as well as additional themes that emerged from each workshop. Evaluators ranked responses from 1-6; 1 indicating an issue cited in 1 workshop and 6 indicating an issue cited in all six workshops. The resulting datasets from each evaluator were compared to enhance reliability. The presentation/poster will report on commonly reported (highest ranked) themes in all regions as well as issues that may be more specific to a region.

OUTPUTS/RESULTS: Over 380 First Nations in six regions were invited to participate in the workshops and 73.5% of these agreed to participate. A total of 392 workshop attendees participated in two focus groups per workshop. There were expected regional and geographical variations in types of traditional foods consumed. A decrease in traditional food consumption in favour of market foods; decreased interest among youth in traditional harvesting; and increasing inaccessibility to traditional foods were commonly reported themes. Identified environmental concerns also varied by region and were often related to local industrial activities. Some additional reported concerns included: waste management sites; water quality; mercury and pesticide contamination.

IMPACTS/OUTCOMES/CONCLUSIONS: This analysis highlighted regional differences as well as several similarities with respect traditional foods consumption rates and environmental concerns among First Nations communities in six regions in Canada. The study has several major limitations and therefore the results should be interpreted with caution. Despite this, given the general lack of current information on these issues, this analysis sheds some light on the importance and perceived factors affecting the consumption of traditional foods among First Nations people across Canada.



Session A: Information: Exposure Hazards from Environmental Contaminants, Albert Salon, October 31, 2006, at 9:15 a.m.

3.44 The Relative Toxicity, Mutagenic Activity and Chemical Composition of Tobacco and Cannabis Smoke

R.M. Maertens, MSc¹, P.A. White, PhD¹, D. Moir, PhD¹, W.S. Rickert, PhD², G. Levasseur, MSc³, G.R. Douglas, PhD¹, and S. Desjardins, PhD⁴

¹ Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

² Labstat International Inc., Kitchener, ON

³ Tobacco Control Program, HECSB, Health Canada, Ottawa, ON

⁴ Drug Strategy and Controlled Substances Program, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Although the prevalence of tobacco use has decreased over the last decade, cannabis use has increased, particularly among youth. In addition, the use of cannabis for medical purposes is currently permitted under certain circumstances in Canada. Smoking cannabis is often perceived as less harmful than smoking tobacco, but solid scientific evidence regarding the comparative risk of adverse effects is lacking. This study examined the toxicological properties of cannabis smoke and Canadian flue-cured tobacco smoke.

DESIGN: Condensates of main- and side-stream smoke from hand-rolled cannabis and tobacco cigarettes were prepared using standard (i.e., ISO) conditions, as well as “extreme” conditions designed to reflect cannabis smoking habits. Biological analyses included cytotoxicity assessment via the Neutral Red Uptake Assay, and mutagenicity testing via the *Salmonella* Mutagenicity Assay. Chemical analyses included measurements of cannabinoids, tar, TPM, PAHs, and other chemicals commonly tracked in tobacco smoke.

OUTPUTS/RESULT: Cytotoxicity analyses showed a 2-fold lower IC50 value for cannabis smoke condensate, thus indicating greater cytotoxicity than tobacco. Cannabis smoke condensates consistently displayed higher mutagenic activity (1.2-7.5 fold) than the matched tobacco smoke condensates for all smoking conditions. Within the respective tobacco and cannabis results, the side-stream samples demonstrated greater mutagenic activity (1.1-5.0 fold) than the main-stream samples, and no significant differences were observed between the standard and extreme smoking conditions. Chemical analyses indicate that many analytes were more abundant in main-stream tobacco smoke than cannabis smoke. Total PAHs in tobacco smoke are approximately 1.6-fold higher than levels in cannabis smoke. However, cannabis smoke contained higher levels of pyridine, acrylonitrile, 1,3-butadiene, aminonaphthalenes and aminobiphenyls.

OUTCOMES: Epidemiological studies have thus far been inconclusive in demonstrating a link between cannabis smoking and cancer. However, the cytotoxicity and mutagenicity analyses in this study show that the particulate phase of cannabis smoke condensate is potentially more hazardous than tobacco smoke generated under the same conditions. Furthermore, cannabis and tobacco smoke contain qualitatively the same toxic chemicals. Until there is a better understanding of the mechanisms involved and the overall significance of *in vitro* data with respect to human health and cancer, this information should be taken into account when considering the potential harms associated with smoking cannabis.

3.45 Benzo[a]Pyrene: Emissions from Canadian Cigarettes

B. Marchand¹, M. Kaiserman¹, and J. Fillion¹

¹ Tobacco Control Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Polycyclic aromatic hydrocarbons (PAHs) formed during incomplete combustion of tobacco are considered to be one of the most carcinogenic groups of compounds in tobacco smoke. Data from the chemical analysis of benzo[a]pyrene (B[a]P) in smoke were evaluated for 34 brands sold in Canada in order to estimate the mean daily exposure of Canadian smokers to B[a]P .

DESIGN: The data were extracted from reports submitted by the industry under the *Tobacco Reporting Regulations* covering the 2004 reporting period including ISO smoking conditions and Canadian Modified conditions. The 34 selected Canadian brands represented over 40% of the sales volume for 2004.

RESULTS: B[a]P ranged between 0.44 ng/cig and 17.9 ng/cig in unburned tobacco, between 1.25 and 12.2 ng/cig in MS smoke (ISO smoking conditions), between 11.7 ng/cig and 23.7 ng/cig in MS (modified smoking conditions) and between 91.5 ng/cig and 163 ng/cig in SS smoke. Based on a smoking rate of 15.2 cig/day, the B[a]P mean daily exposure varied from 0.13 :g/day in MS smoke using ISO conditions to 0.29 :g/day in MS smoke using modified conditions.

CONCLUSIONS: The daily exposure of B[a]P in cigarette smoke is higher than the no significant risk level of the California state and lower than the permitted occupational exposure recommended by the Occupational Safety and Health Administration (OSHA). Tobacco smoke constitutes a non-negligible source of PAHs such as B[a]P. Tobacco smoke is also a complex mixture containing over 4000 chemicals including over 50 carcinogens and B[a]P represents only one of these carcinogens which have a serious impact on individual/population health.

3.46 Characterization of Norovirus Isolates from Healthy Swine

K. Mattison¹, M. Plante¹, A. Cook², F. Pollari², R. Friendship³, K. Karthikeyan¹, S. Bidawid¹, and J.M. Farber¹

¹ Microbial Research Division, Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

² C-EnterNet, Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Guelph, ON

³ Department of Population Medicine, Ontario Veterinary College, University of Guelph, ON

OBJECTIVES: To determine the presence and types of norovirus in swine.

DESIGN:

- 122 fecal (pooled manure and pit) samples were obtained from 10 Canadian swine farms over the months of September 2005 - May 2006.
- Manure was subjected to viral extraction procedures, and the resulting samples were tested for the presence of noroviral RNA by reverse-transcription polymerase chain reaction (RT-PCR).
- Presumptive positive samples by RT-PCR were sequenced to confirm norovirus isolation.
- A larger fragment of the noroviral genome from confirmed isolates was amplified and sequenced for genotyping purposes.

OUTPUTS/RESULTS: 60/122 (49%) swine manure samples were found to be presumptively positive for norovirus. To date, 3 and 17 of these have been confirmed to be human and swine genotypes, respectively. Testing will continue for the remaining samples. All confirmed isolates belong to genogroup II. Several of the swine isolates are novel sequences that have not previously been reported.

IMPACTS/OUTCOMES/CONCLUSIONS: The potential implications for public health remain uncertain. However, some of the norovirus isolated from healthy domestic swine fall into the same genogroup as strains that infect humans. Therefore, there is the potential for zoonotic transmission of noroviral disease if these truly are human pathogens. Continued and expanded active surveillance with full genetic comparison with human isolates will clarify this link. Additionally, both human and swine norovirus genotypes were found in these pooled fecal samples. There is the potential for recombination between these genogroup II strains, resulting in novel viruses. Once again, continuing and expanding the active surveillance of gastrointestinal disease in the Canadian population will enable quantification of this risk.

3.47 Dietary Soy Protein Isolate Inhibits Retinoic Acid-Induced Increase of Acetyl-CoA Carboxylase mRNA in Cultured Rat Liver Explants

J. Mei¹, C. Wood¹, and C.W. Xiao¹

¹ Nutrition Research Division, Bureau of Nutritional Sciences, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Retinoic acid (RA) is a metabolite of vitamin A and plays important roles in controlling cell growth, differentiation, lipid metabolism and carcinogenesis. Its effects are mediated mainly through its nuclear receptors (RAR). Our previous study had shown that consumption of soy protein isolate (SPI) affected the function of hepatic RAR in rats. However, the potential physiological impact of this intracellular response to SPI remains unclear. This study has examined the effect of dietary SPI on RAR-mediated gene expression of acetyl-CoA carboxylase (ACC), a rate-limiting enzyme involved in the synthesis of fatty acids, in *ex vivo* cultured rat liver explants.

DESIGN: Weaning Sprague-Dawley rats were fed diets containing either 20% casein or 20% alcohol-washed SPI for 60 days. Livers were isolated and rapidly cut into approximately 1-mm cubes and cultured in media containing 0, 1, 2.5 or 4 μ M RA for 2 hours. ACC α and ACC β mRNA abundances in the explants were measured by relative semi-quantitative RT-PCR.

OUTPUTS/RESULTS: Incubation with RA increased ACC α mRNA steady-state levels dose-dependently, but had no effect on ACC β mRNA levels in the liver explants of female rats fed casein. Higher dose of RA (4 μ M) significantly attenuated the mRNA abundances of both ACC α (0.66 ± 0.19 vs. 1.49 ± 0.56 , $p < 0.05$) and ACC β (1.13 ± 0.48 vs. 0.08 ± 0.05 , $p < 0.05$) in the explants of female rats fed SPI compared to the rats fed casein. However, RA had no significant effect on either ACC α or ACC β mRNA expression in the liver explants of male rats fed casein or SPI.

IMPACTS/OUTCOMES/CONCLUSIONS: These results suggest that consumption of soy-based products such as soy milk and soy infant formula may have different impact on the physiological functions of vitamin A and its metabolites compared to ingestion of bovine milk proteins. This information is important for the Food Directorate of Health Canada in the evaluation of health safety and nutritional quality of soy products.

3.48 Risk of Occupational Exposure to Ionizing Radiation Among Medical Workers in Canada

J.M. Zielinski, PhD^{1,2}, M.J. Garner, M Sc³, P.R. Band, MD¹, D. Krewski, PhD⁴, H. Jiang, PhD⁴, J.P. Ashmore, PhD⁴, W.N. Sont, PhD^{1,4}, M.E. Fair, MSc⁵, E.G. Letourneau, MD¹, and R. Semenciw, MSc⁶

- ¹ Safe Environments Programme, HECSB, Health Canada, Ottawa, ON
- ² Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON
- ³ Carlington Community and Health Services, Ottawa, ON
- ⁴ McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, Ottawa, ON
- ⁵ Health Statistics Division, Statistics Canada, Ottawa, ON
- ⁶ Public Health Agency of Canada, Ottawa, ON

OBJECTIVES: Medical workers are exposed to chronic low dose ionizing radiation from a variety of sources. Potential cancer risks associated with such exposures have been derived from cohorts experiencing acute high intensity exposure, most notably the Japanese atomic bomb survivors. Since such extrapolations are subject to uncertainty, direct information on the risk associated with chronic low dose occupational exposure to ionizing radiation is needed. We examined possible associations with cancer incidence and mortality in a cohort of medical workers ascertained by the National Dose Registry of Canada (NDR).

DESIGN: Data from the NDR were used to assess the exposure to ionizing radiation incurred between 1951 to 1987 inclusive in a cohort of 67 562 subjects classified as medical workers. Standardized mortality (SMRs) and incidence (SIRs) ratios were ascertained by linking NDR data with those from the Canadian Mortality and the Canadian Cancer Databases respectively. Dosimetry information was obtained from the National Dosimetry Services of the Radiation Protection Bureau of Health Canada. Individual doses were combined to obtain annual doses for each member of the cohort.

OUTPUTS/RESULTS: There were 23 580 male and 43 982 female medical workers in the cohort. During the follow-up period, 1309 incident cases of cancer (509 in males, 800 in females) and 1325 deaths (823 in males, 502 in females) were observed. Mortality from cancer and non-cancer causes was generally below expected compared to the Canadian population. Thyroid cancer incidence was significantly elevated in both males and females, with a combined SIR of 1.74 (90% CI: 1.40-2.10).

IMPACT/OUTCOMES/CONCLUSIONS: Our result of an increased risk of thyroid cancer among medical workers occupationally exposed to ionizing radiation confirms previous reports. Over the last 50 years, radiation protection measures have been effective in reducing occupational exposures of medical workers to ionizing radiation to current very low levels.



Session B: International: Research Advances in Support of International Environmental Monitoring, York Salon, October 30, 2006, at 10:15 a.m.

3.49 Canadian Cigarette Toxic Emissions Trends

M.-C. Nolet¹, J. Fillion¹, G. Levasseur¹, and M.J. Kaiserman¹

¹ Tobacco Control Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Evaluate the trends of the Canadian cigarette emissions over the last six years.

DESIGN: The Canadian *Tobacco Reporting Regulations* (TRR) requires the manufacturers to report every year the levels of 40 emissions under two smoking conditions. TRR allow manufacturers to request a reporting exemption by demonstrating a functional relationship between tar, nicotine and the other emissions (Benchmark) and submits data on various brands to support this request. In addition, Health Canada performs emissions testing on various cigarette brands in order to have additional data. The emissions levels of six brands selected from these two data sets were compared for a period of six years to determine whether there were any trends over time in emissions.

OUTPUTS/RESULTS: A major reduction in tobacco specific nitrosamines (TSNAs) levels is observed. This reduction can be explained by the change in curing process performed by the Canadian tobacco producers. The results indicate that overall, despite this decrease in TSNA, all other emissions show very little change over time. The reasons for this consistency, including source of tobaccos, cigarette engineering and product quality control will be discussed.

CONCLUSIONS/IMPACTS: Any changes in products profile may signal the need to investigate further the impacts on health. It is expected that this analysis will enhance evidence-based decision-making capability in connection with the regulation of tobacco products in Canada.

3.50 Ginger (*Zingiber Officinale Roscoe*) – A Hopeful Plant for Health Promotion

L. Ntezurubanza, PhD¹, V. Assinewe, PhD¹, and R. Marles, PhD¹

¹ Bureau of Clinical Trials and Health Science, Natural Health Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVE: To illustrate the potential roles for ginger containing health natural products in health promotion.

DESIGN: A review of ethnobotanical, chemical and pharmacological studies on ginger.

RESULTS: Today, ginger, *Zingiber officinale* Roscoe, is an ingredient in more than 50% of traditional herbal remedies described in Eastern and Western pharmacopoeias. There are many naturally occurring varieties of ginger and approximately 50 in India alone. There are striking differences in the essential oil and the oleoresin composition within *Zingiber officinale* chemotypes. Differing growing conditions and cultivation techniques result in each variety having its own unique aroma, flavour and pharmacological activities. For instance, milder examples tend to be found in China and more pungent ones in Africa. Jamaican ginger, which is used as a spice and a medicine, is one of the most highly valued commercial gingers worldwide.

This variability within rhizome composition may explain its different pharmacological activities, which have included gastrointestinal, cardiovascular, antiarthritic and antirheumatic, antimigraine, antinausea, antipyretic and analgesic, and serotonin-antagonist effects. Ginger has also shown antitumorogenic, antiparasitic and antiviral activities, mutagenicity and thermogenic action.

More recent results indicate the use of ginger for the prevention of nausea and vomiting associated with motion sickness and seasickness, the prevention of pregnancy-induced nausea and vomiting and the prevention of postoperative nausea and vomiting. Other recent results have shown that powdered root ginger could be as effective as an adjuvant to chemotherapy for treating ovarian cancer.

CONCLUSION: Ginger plays a role in the treatment of many ailments.

3.51 Reaching Through Cognitive Noise: Communicating Technical Health Risk Information to Stakeholders

R. Leblanc¹, T. Topolnisky¹, B. Pichette^{1,2}, and F. Valcin¹

¹ Ron Breecher, Golbaltox International. TrevorDiggins-Smith, Frontline Communications
² Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To educate GOC staff to develop an effective model that can be utilized to communicate technical health risk information to stakeholders in a way that enhances understanding of complex concepts while addressing stakeholder concerns.

DESIGN: The approach was based on an instructional design model. Best practices in risk communication were reviewed in addition to an environmental analysis of GOC stakeholders in the Contaminated Sites program. The stakeholder analysis included: factors influencing public perceptions of risk; communication challenges regarding technical information; risk communication principles; stakeholder expectations in terms of research dissemination and building capacity for effective communication.

OUTPUTS/RESULTS: The main findings or essential details in support of the impacts/outcomes/conclusions.

Stakeholder demand for effective communication of health risk information from Health Canada has increased significantly. In addition, stakeholder perception and understanding of risk are influenced by many factors, including their capacity to understand scientific concepts; the effects of the risk on individuals' well-being and on that of their community; the type of information they are looking for; and the extent to which stakeholders believe the source of risk information is credible, open and transparent. Risk assessment terminology can be highly technical and inaccessible to stakeholders if the communication model does not take these factors into consideration. Ineffective health risk communication may result in increased stakeholder frustration, and distrust of credible health risk information.

IMPACTS/OUTCOMES/CONCLUSIONS: A summary of the outcomes supported by the results and linked to specific health-related issues where relevant.

The utilization of a health risk communication model based on stakeholder analysis, which identifies that their capacities can enhance the stakeholders ability to understand complicated health risk information as that presented in a health risk assessment. Stakeholder analysis indicates that stakeholders perceive health risk through a filter of psychosocial, emotional and cultural factors.

3.52

[Withdrawn]

3.53 Quantification of Low Levels of Transgenic Fish DNA with the Use of Quantitative Reference Genes and the Delta-Delta Ct Method in Real-Time PCR

K.H. Poon¹, S.W. Dai¹, and R. H. Devlin²

¹ Western Region Laboratory, HPFB, Health Canada, BC/Alberta Region, Burnaby, BC
² West Vancouver Laboratory, Department of Fisheries and Oceans, West Vancouver, BC

OBJECTIVES: Develop a reliable method to quantify as low as 1% of DNA from transgenic fish in a mixed-DNA pool, consisting mainly of wild-type conspecific DNA.

DESIGN: Individuals from one specific line (M77) of the genetically modified coho developed by the West Vancouver Laboratory of the Department of Fisheries and Oceans were used in this study. The transgene construct onMTGH1 (comprising of the metallothionein-B promoter and the type-1 growth hormone gene from sockeye salmon) has been stably incorporated into its genome for several generations. Various amounts of its DNA were mixed into a larger pool of DNA from wild-type coho, and their levels measured by real-time PCR using Taqman chemistry in conjunction with the Delta-Delta Ct method. Primers and probes were carefully designed for three endogenous nuclear genes (RNase P, beta-actin, and 18S rRNA) to serve as candidate reference genes, and their suitability as reference genes for the relative quantification of onMTGH1 assessed.

OUTPUTS/RESULTS: The Delta-Delta Ct method that is conventionally used to study gene expression (i.e., messenger RNA level) by real-time PCR has been successfully adapted for use in the quantification of DNA levels of a transgenic fish in a pool of DNA of its conspecifics. Detailed analysis of the real-time PCR data of the three endogenous genes revealed the significant degree of genetic diversity among the several coho individuals studied, rendering their usefulness as quantitative reference genes limited. However, by carefully matching the genotypes of individual transgenic and wild coho and the adopting the appropriate reference gene sequences, it is possible to accurately measure as low as 1% of DNA of transgenic coho that has been mixed with a pool of wild coho DNA.

IMPACTS/OUTCOMES/CONCLUSIONS: The limit of quantification established in this study meets the labeling threshold levels set by any country in the world, the most stringent being 0.9% by the European Union. This study provides some useful data from a transgenic animal for discussing the practicality and scientific validity of the "labeling threshold" legislation, which has so far been analyzed only from the perspective of GM crops.

3.54 Insights from the Canadian Addiction Survey: Public Opinion, Attitudes and Knowledge of Canadians About Alcohol and Other Drugs Issues

S. Racine, M.Ps.¹, J. Flight, M.A.¹, and E. Sawka, M.A.²

¹ Office of Research and Surveillance, DSCS, HECSB, Health Canada, Ottawa, ON
² Alberta Alcohol and Drug Abuse Commission, Calgary, AB

OBJECTIVES: The presentation will focus on the results concerning public opinion attitudes and knowledge of Canadians about drugs issues. The themes covered include the following: perceived seriousness of the issue; perceived harms from substance use; and, opinions about cannabis or other illicit drugs.

METHODS: The Canadian Addiction Survey (CAS 2004) is a random digit dialing telephone survey of 13 909 Canadians aged 15 years old and over covering the 10 provinces (the Territories are not included) conducted between December 2003 and April 2004. Results were examined using logistic regressions.

RESULTS: The findings suggest that Canadians agree to a national response to substance use issues that favours a social/medical approach using treatment and prevention but not to the exclusion of enforcement and which is international in scope. However, they seem ambiguous with regards to cannabis, requesting less recourse to the criminal system but still agreeing to other legal actions and associated penalties such as fines.

CONCLUSIONS/IMPLICATIONS: In May 2003, the Government of Canada announced the renewal of Canada's Drug Strategy. One of the priorities identified was the conduct of a general population survey to determine the prevalence and harms associated with alcohol and other drugs use and abuse. In addition to updating our evidence-base on prevalence and harms, this survey allowed Health Canada to query the opinions of Canadians regarding their perception, attitudes and knowledge on these issues and to examine the correspondence with the recommended investments of *Canada's Drug Strategy* and of the *National Framework for Action to Reduce the Harms Associated with Alcohol and Other Drugs and Substances in Canada*.



3.55 Trends in Methamphetamine Seizures in Canada

K. Richard, MA¹, B. Brands, PhD¹, and R. Hanson, MA¹

¹ Office of Research and Surveillance, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To explore trends in the methamphetamine market in Canada, the Office of Research and Surveillance undertook a study that examined samples analyzed by the Drug Analysis Service (DAS). This programme is responsible for testing all suspected drug samples sent to their labs by police and customs officials. By exploring data associated with samples seized, it allowed us to add to the knowledge on emerging methamphetamine trends in Canada.

DESIGN: DAS operates four laboratories across Canada. All methamphetamine seizures that were analyzed by DAS from 1988 to 2005 were included in this study. Exploration of DAS samples allows us to determine if cyclical patterns are evident, if methamphetamine is becoming more prevalent, and if the purity content of the substance is consistent over time.

OUTPUT/RESULTS: While, the number of samples containing methamphetamine was relatively low (1.58%) when compared with other substances; Canada did see a significant increase in seizures during this time period. In the past five years, the percentage in the number of samples analyzed that contained methamphetamine has increased from 1.4% in 2000 to 5.8% in 2005. Moreover, there has been a significant increase in the number of samples that contain multiple substances. In 2000, 91% of the samples contained just methamphetamine, while in 2005, this number decreased to 74%. Further, significantly more samples contained methamphetamine (24 163) than was originally suspected by police or customs (13 465).

IMPACTS/OUTCOMES/CONCLUSIONS: These analyses allow us to have a regular and systematic monitoring approach to trends in the illicit drug market and it assists in allowing for early detection of an emerging drug trend. This has serious implications for public health and law enforcement. It should be noted that: only samples that are going to trial are analyzed (cases in which a guilty plea has been entered are not analyzed) and therefore the data under-estimate the total number of illicit drug seizures. Further, it is not known whether the distribution of substances analyzed is similar to the quantities and distribution of illicit drug seizures by police and border services. Finally, the distribution of substances seized is a function of the resource allocation, priorities and effectiveness of police and border service activities. Additional research is needed to determine the extent to which the prevalence of substances seized differs from the prevalence of substances in the illicit drug market.

3.56 Evaluating the Impact of Ontario's Universal Influenza Immunization Program

I. Zverev, MA¹

¹ Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVES: To evaluate the impact of Ontario's Universal Influenza Immunization program.

DESIGN: We use data on the prevalence of influenza, number of influenza tests performed, the number of hospitalizations for influenza and cardiovascular diseases (CVD), as well as drug sales in Ontario and rest of Canada to evaluate the impact of Ontario's Universal Influenza Immunization Program (UIIP).

OUTPUTS/RESULTS: Relative to the Rest of Canada (ROC), Ontario experienced a sharp drop in the number of influenza cases in 2000/01 following the introduction of UIIP. The number of flu cases dropped by 70% following the introduction of UIIP, compared to a 21% decrease in ROC in the same period. The number of hospitalizations for influenza (77% vs. 49%) and CVD (61% vs. 5%) also significantly decreased. Relative contribution of UIIP to the overall reduction in influenza prevalence is difficult to determine due to a corresponding decline in the number of cases in the rest of Canada.

CONCLUSIONS: Introduced in 2000/01, UIIP provides free influenza vaccination to people above the age of 6 month. Ontario is the only jurisdiction to provide a free vaccine to all residents. Programs in other jurisdictions focus on medical staff and specific population groups at high risk of developing influenza-related complications.

Evaluating the effectiveness of UIIP is important for the development of pandemic preparedness for the potential avian influenza outbreak. Limited impact of UIIP on influenza prevalence in Ontario would mean that pandemic preparedness plan would have to focus on means of protecting Canadian population other than vaccinations. On the other hand, if it is clear that UIIP was instrumental in containing influenza outbreaks in Ontario, efforts should be focused on developing vaccine for the H5N1 strain of influenza.

3.57 Importance of Carcinogenic Alkyl Substituted and High Molecular Weight Polycyclic Aromatic Hydrocarbons at Contaminated Sites and Update of Toxic Equivalency Factors for Hydrocarbon Mixtures

A. Knafla, MSc, DABT¹, C. Ott, MSc², S. Petrovic, MSc³, S. Ramji, MSc³, C. Rowat, MSc³, and D. Schoen, MSc³

¹ Equilibrium Environmental Inc., Calgary, AB

² URS Canada Inc., Vancouver, BC

³ Contaminated Sites Division, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Cancer risks are assessed for polycyclic aromatic hydrocarbon (PAH) mixtures using a slope factor for benzo[a]pyrene (B[a]P), and relative potency equivalency factors (PEFs) for other PAHs. In Canada, the Priority Substance List Assessment Report contains PEFs for only 5 PAHs. Analysis of environmental samples have identified significant concentrations of many additional PAHs. The objective of this project was to conduct a literature review of available data for the carcinogenicity of PAHs, and recommend PEFs for them.

DESIGN:

Existing PEFs: Review existing PEFs of other regulatory agencies. If there is consensus on a PEF, recommend this value. If PEFs are within an order of magnitude, recommend the most conservative. If PEFs varied greatly, review the carcinogenicity data and recommend a PEF.

No existing PEFs: If a PAH is reported in environmental mixtures and/or indicates the potential for significant carcinogenic potency, conduct a data review and recommend a PEF.

RESULTS:

Existing PEFs: 20 PAHs were found with pre-existing PEFs and good evidence of genotoxicity/carcinogenicity. Only two were for alkylated PAHs. Nine PEFs (based on consensus), and 11 PEFs (based on analysis of the PEFs and carcinogenicity data) are recommended.

No available PEFs: PEFs are recommended for 33 PAHs with no published PEFs. Of these PAHs, 31 are alkylated, and 14 have potencies equivalent to or greater than B[a]P.

CONCLUSIONS: To promote consistency in the evaluation of carcinogenic PAH mixtures at contaminated sites, Health Canada should, where possible, recommend specific PEFs for individual PAHs. Based on this literature review, 53 PEFs are proposed. No regulatory agency has derived PEFs for several alkylated PAHs often present at contaminated sites. Currently, many of these compounds are simply ignored in risk assessments. Not considering alkylated PAHs in health risk assessments may significantly underestimate the carcinogenic potential of PAH mixtures.

3.58 Physician's Production of Primary Care in Ontario: Evidence from the 2004 National Physician Survey, Canada

S. Sarma, PhD¹, R.A. Devlin, PhD², and W. Hogg, MD³

¹ Microsimulation and Modelling and Data Analysis, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

² Department of Economics, University of Ottawa, Ottawa, ON

³ Department of Family Medicine, University of Ottawa, Ottawa, ON

OBJECTIVES: Recent years have witnessed a shortage of the family physicians in Canada. The dearth of family physicians is a major concern because they are the first point of contact for most Canadians, and are responsible for the lion's share of the management of chronic diseases and the delivery of preventive care. The amount of time family physicians spend in providing direct patient care and the number of patients they treat might be influenced by the method of remuneration. The objective of this study is to analyze the extent that different remuneration schemes and practice settings affect physician output.

DESIGN: We use the Ontario data from the 2004 National Physician Survey and analyze family physicians' patient visits as a function of hours worked providing direct patient care, remuneration schemes, demographic characteristics and practice settings. The theoretical framework underlying this study is a behavioural production function approach. The instrumental variable method of estimation technique is used to account for the endogeneity bias.

OUTPUTS/RESULTS: After controlling for physician demographics and a number of practice characteristics, we find that physicians paid on a fee-for-service are more productive in terms of number of patient visits per week than those who are paid under alternative payment schemes. However, this productivity gain is significantly reduced once we take into account the practice characteristics, especially the illness severity of patient population served in a practice. The group practices are substantially more productive than solo practices.

IMPACTS/OUTCOMES/CONCLUSIONS: Provides evidence supporting the view that remuneration schemes influence physician production of health care services. The results suggest that the productivity associated with fee-for-service be considered against the benefits offered by other practice styles for health policy formulation. The shortage of family physicians can be addressed by producing more of them and by ensuring remuneration and practice settings are optimized.



3.59 Reassessment of the Toxicological Risks of Polychlorinated Biphenyls (PCBs) for the Canadian Population

G. Carrier^{1,2}, M. Bouchard^{1,2}, N. Gosselin¹, N. El Majidi¹, et D. Schoen³

¹ Department of Environmental and Occupational Health, Université de Montréal, Quebec

² Institut national de santé publique du Québec, Montreal, Quebec

³ Safe Environments Programme, Health Canada, Longueuil, Quebec

This research has three components:

- Estimating, using a kinetic model, the average body burden of Canadians.
- Doing a critical analysis of all the published epidemiological studies to verify whether a body burden-response relationship exists.
- Compare the body burdens with the minimum body burdens for which effects have been observed and which largely meet the Hill criteria.

For the first component, the temporal profile kinetics of the body burden are studied using a model that allows for taking into consideration the gender of the study subjects, their age, variation in their weight and body fat, and various exposure scenarios throughout their lifetime. PCBs are grouped into four categories on the basis of the number of chlorine atoms. The exposure scenarios were established on the basis of the published data, which make it possible to estimate over time people's daily intake by age and gender, on the basis of the measured concentrations in food and ambient air in different periods. The model was validated using data from the literature on biomarker measurements in Canadians of both genders at all ages.

The results of the modelling show that a Canadian born in 2000 will, throughout his or her life, be exposed about 5 times less than a Canadian born in 1970, given that the current contamination will decrease much more slowly than did past contamination. It can be deduced that future PCB exposure of Canadians born in the 2000s will never be as high as the exposure of Canadians born before that period. Their risk of being affected by an exposure will therefore be equally lower.

3.60 Mutagenic Activation of the Food Contaminant Furan Through Reaction with Sodium Nitrite

T. Schrader, PhD¹, and I. Langlois, BSc¹

¹ Toxicology Research Division, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: Furan has been isolated from cooked or heated foods, apparently arising through reactions of amino acids, fatty acids, and ascorbic acid. Furan is carcinogenic in lab animals and has been classified as group 2B, possibly carcinogenic to humans. However, although some evidence for furan mutagenicity has been found in mammalian cells, no prokaryotic system has provided a positive response. To examine possible mechanisms for mutagenic activation, furan was incubated with acidified sodium nitrite, a common food preservative, and assayed using the Ames Salmonella test.

DESIGN: Furan, +/- nitrosylation with sodium nitrite in acetic acid buffer, pH 4, was tested for electrophilic activity using the colorimetric 4-(4'-nitrobenzyl)pyridine (NBP) assay. Native and nitrosylated furans were then tested for mutagenicity with the Ames Salmonella test, using strains sensitive to frameshift (TA97, TA98) and base pair (TA100, TA102, TA104) mutations, +/- rat liver S9 for metabolic activation.

OUTPUTS/RESULTS: When tested in the NBP assay up to 100 mg/ml, native furan produced little electrophilicity; however, nitrosylated furan displayed electrophilic activity at 20 µg/ml, the lowest concentration tested. Furan was negative as both a frameshift and base pair mutagen when tested up to 10 mg/plate, but 10 mg/ml of nitrosylated product produced a directly mutagenic species positive in Salmonella strains TA97, TA100, TA102 and TA104. Similar results, although with somewhat lower revertant numbers in TA97 and TA100, were found + S9.

IMPACTS/OUTCOMES/CONCLUSIONS: While furan was negative for both electrophilicity and mutagenicity, nitrosylation produced an electrophilic species with a rather weak direct-acting frameshift mutagenic activity in a run of C's (TA97) and base pair mutagenic activity at GC sites (TA100) as well as AT sites (TA102, TA104). These results demonstrate that dietary interactions can influence the mutagenic activation of food-associated chemical and that such approaches can expand the usefulness of a genetic testing regimen.



3.61 Environmental Monitoring of Bioproducts Using *Bacillus Thurgigiensis* Models and Nucleic Acid as Analyte

V.L. Seligy¹, G. Coleman¹, J. Crosthwait¹, K. Nguyen¹, P. Shwed¹, A.F. Tayabali¹, J. Rancourt², M. Mulvey³, and G. Rousseau⁴

¹ Environmental Health Science Bureau, HECSB, Health Canada, Ottawa, ON

² Consumer Products Safety Bureau, HECSB, Health Canada, Ottawa, ON

³ Public Health Agency of Canada, Winnipeg, MB

⁴ Environmental Monitoring, SOPFIM, Quebec

OBJECTIVES: To examine utility of the nucleic acid (NA) component of microbe-based bioproducts as analyte in tests to assess identification and environmental exposure.

DESIGN: 'Free' (fNA) and intracellular-NA were measured in supernate and pellet fractions of commercial Bt-bioproducts derived from *B. thuringiensis* (Bt) subspecies *israelensis* (Bti) and *kurstaki* (Btk), and cultures of them, and Bt13367 and *B. cereus*14579(Bc) of the *Canadian Environmental Protection Act* (CEPA 1999) DSL. Samples from Bt-bioproduct aerial sprays were also analyzed. Detection/quantification methods included colony count, scanning electron microscopy, NA hybridization and PCR methods, using gene probes in single or microarray format.

RESULTS: Bt-bioproducts produced similar-sized pellets (~30-35% w/w) containing comparable masses of spores (~ 1-4x10¹⁰ mL) and proteinaceous-NA aggregates, including parasporal-inclusion bodies (PIBs). Using non-spore disrupting extraction methods, both fractions contained fNA (~40% of total NA; range 0.02-20kb). As PCR templates, fNA was poor compared to spores (~ 10x) and vegetative cells (~50-60x). PCR, Southern blot and microarray assays (> 5000 Bc14579 or Ba A2015 genome features) indicated the fNA was genome related. Analysis of field samples along with calibrated spray droplets and Bt-product dilutions indicated that NA detection was limited (~ 0.1% of live cell values).

CONCLUSIONS/IMPACTS: As an analyte for quantifying environmental release of Bt-Bc-type bioproducts, the NA component has limited use with current NA detection tools. Gene-level detection is reduced by inefficient access to spore DNA, and high content of interfering fermentation residues like fNA. The fNA is clearly genomic in origin. fNA has potential to act on innate immunity via Toll-like receptors during bioproduct exposures, but its degraded state may not mediate significant genetic exchange with feral pathogen counterpart. Some fNA may come from lysed cells, however, given its abundance in Bti/Btk spore-phase cultures, we hypothesize that fNA is genomic residue of non-spore forming daughter cells dedicated to form the insecticide-containing aggregates or PIBs.

3.62 Expression and Characterization of Allergen Pen B 26 from Household Mold *Penicillium Brevicompactum*

M.S. Sevinc, PhD¹, V. Kumar, MSc¹, M. Abebe, PhD¹, S. Mohottalage, PhD¹, P. Goegan, MSc¹, R. Vincent, PhD¹, P. Kumarathasan, PhD¹, H.M. Vijay, PhD¹, and T. Cyr, PhD²

¹ Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

² Biologics and Genetic Therapies Directorate, HPFB, Health Canada, Ottawa, ON

OBJECTIVE: To develop a test kit for mass screening against the allergen *Pen b 26* of *Penicillium Brevicompactum*, a very prevalent indoor allergen

DESIGN: The allergen *Pen b 26* of *P. brevicompactum* was cloned and over-expressed as a 6x His-tagged, N-terminal fusion protein in *Escherichia coli*. The allergen was purified by his-tag affinity chromatography and characterized by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), immuno-blot and mass spectroscopy.

OUTPUTS/RESULTS: Immuno-blot analysis with atopic sera showed that *Pen b 26* was an allergen. BLAST search indicated that it had strong homology to 60 S ribosomal P1 proteins, which was also confirmed by immuno-blot analysis using human IgG antibody against ribosomal P proteins. Time-course expression of *Pen b 26* fusion protein showed that the concentration of the fusion protein in solution increased with the time after induction with IPTG, being greatest at 3 hours. However, the fusion protein migrated at about 7 kDa higher than the estimated molecular weight of 14.9 kDa of the cloned *Pen b 26* on regular SDS-PAGE. The discrepancy between the observed and estimated molecular weights was clarified by mass spectroscopy, which confirmed the size of the estimated molecular weight of *Pen b 26* as 14.9 kDa. Prevalence of antibodies against *Pen b 26* among atopic patients was also studied by immuno-blot analysis. It was found that about 25% of the atopic patients had antibodies against *Pen b 26*.

IMPACTS/OUTCOMES/CONCLUSIONS: *Pen b 26* was identified as 60 S ribosomal P1 protein and a minor allergen of *Penicillium brevicompactum* was successfully expressed in *Escherichia coli*. It is now possible to incorporate this cloned allergen into a kit for screening of individuals allergic to *Penicillium*. In addition, about 50% of the individuals allergic to 60 S ribosomal P proteins have also autoantibodies in their sera and susceptible to autoimmune diseases. Therefore, the kit for screening of *Pen b 26* allergen may also be used as a biomarker for screening of individuals susceptible to autoimmune diseases.

3.63 Identification of Differentially Expressed Genes in Time Course Microarray Experiments During Phagocytosis and Infection by *Bacillus Cereus* Group Organisms

P.S. Shwed, PhD¹, J. Crosthwait, BSc¹, A.F. Tayabali, PhD¹, and V.L. Seligy, PhD¹

¹ Safe Environments Program, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: We are developing genomic and proteomic-based methods and data to establish a baseline for toxicity/pathogenicity testing of *Bacillus* biotech-organisms regulated under the *Canadian Environmental Protection Act* (CEPA 1999) and the *Pest Control Products Act*. Here we report on data derived by gene-based micro array hybridizations and a statistical significance algorithm (SSA) to analyse temporal expression and validate function of select genes using real-time PCR (RT-PCR).

DESIGN: Mouse macrophage cells (J774A.1) were exposed to *Bacillus cereus* (Bc) group spores, vegetative cells and controls (unexposed cells, *Bacillus subtilis* or micron-sized latex spheres) for up to 3 hours. Expression of select autoimmune/inflammatory response genes was monitored using cDNA microarrays and a subset of samples was hybridized to oligonucleotide arrays in order to observe genome wide transcription. Differentially expressed genes were identified using SSA of time course data. Select inflammatory response genes, including the tumour necrosis factor gene were verified by RT-PCR and RNA:probe:capture bead hybridization and detection.

OUTPUTS/RESULTS: Cluster analysis allowed identification of gene groups (homeostasis, chemokines and receptors) that featured similar expression responses to bacterial spores and not latex spheres. Preliminary SSA carried out on data from a live vegetative cell exposure has yielded a significant gene list that includes genes identified by cluster analysis as well as transcription factor receptors and chemokines. Comparison of RT-PCR and RNA: probe: bead hybridization results for select inflammatory response genes show general agreement.

IMPACTS: This analysis significantly augments knowledge on macrophage-like cell exposures and Bc group organisms particularly common early gene responses during uptake. Exposure to Bc, Bti and Btk live vegetative cells induce rapid cytotoxic effects. The development and application of significance analysis coupled with hybridization assays will lead to the identification of significantly expressed genes and rapid validation.

3.64 Potential Health Implications Associated with Consumption of Donairs

B. Slater¹, D. Oudit², A. Hughes², M. Taylor³, and L. Hill¹

¹ Food Liaison, HPFB, Health Canada, Edmonton, AB

² Bureau of Microbial Hazards, HPFB, Health Canada, Ottawa, ON

³ Foodborne, Waterborne and Zoonotic Infections Division, Public Health Agency of Canada, Guelph, ON

OBJECTIVES: In September 2004, the Calgary Health Region investigated 84 cases of *Escherichia coli* O157:H7 attributed to the consumption of beef donairs. In order to mitigate the potential health risk in the future, there was a need to characterize the risk factors associated with the consumption of donairs and similar products in Canada.

DESIGN: A Federal/Provincial Working Group was established to collect information and evaluate current Canadian processing, preparation and handling procedures for donairs. The diverse nature of the industry necessitated studying the practices in both restaurants and manufacturing facilities of different sizes and with different food safety controls.

The Working Group also collected current research, reports of food-borne illness, and existing guidance to industry. Data sources included national and international food safety regulators, product manufacturers, and manufacturers of donair broiler machines.

OUTPUTS/RESULTS: The primary risk factors were identified as:

- a) an insufficient cooking process applied to raw donair cones
- b) the potential for cross-contamination and,
- c) end of day practices for partially used cones

The Working Group determined there is a fundamental absence of control measures in Canada to ensure that *E. coli* O157:H7, *Salmonella spp.* and *Campylobacter jejuni* are not present in donair meat served to consumers by food service operators that cook raw donair cones. Concurrent with this lack of control is an absence of guidance from Canadian regulators on appropriate food safety practices relating to donairs, and concern that existing food safety messages from the industry are neither consistent nor complete.

IMPACTS/OUTCOMES/CONCLUSIONS: This study provides the evidence required to support recommendations from food safety regulators and the Canadian food industry to improve preparation, cooking, cooling, storage and handling of donairs. Information sharing between stakeholders is an effective way to identify and address the risks associated with a food-borne illness outbreak.

3.65 Canadians' Exposure to Second-Hand Smoke

J. Stevenson, MA¹, and J. Snider, MSc¹

¹ Office of Research, Surveillance and Evaluation, Tobacco Control Program, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To monitor self-reported exposure to second-hand smoke (SHS) at home and in places other than the home in Canada.

DESIGN: The Canadian Tobacco Use Monitoring Survey (CTUMS) is an ongoing random digit dialing telephone survey of over 20 000 Canadians 15 years and older.

RESULTS: Based on the CTUMS annual 2005 results, 15% of Canadian households reported at least one person who smoked inside the home everyday or almost everyday (compared to 29% in 1999). Of those households without someone regularly smoking inside the home, 85% did not allow any smoking inside their home (compared to 74% in 2000).

Nine percent of Canadian children aged 0-11 years (382 000 children) were regularly exposed to second hand smoke in Canadian homes in 2005, a reduction from 26% (1.1 million children) in 1999.

Beginning in 2005, exposure to SHS in places other than the home was added to CTUMS. For the first half of 2005, almost 1 in 6 (14%) of Canadians reported being exposed to SHS everyday in places other than their home (e.g., inside a vehicle, in the workplace, at a restaurant/bar/tavern, etc.). The most commonly reported place of SHS exposure was at an entrance to a building (49%).

CONCLUSIONS: It is estimated that exposure to SHS is responsible for 1000 adult non-smoker deaths each year. Monitoring exposure to SHS will provide an indicator of progress made with the advent of provincial smoke free public place bylaws.

3.66 Personal, Indoor and Outdoor Exposure of Windsor Residents to VOCs in the Winter and Summer of 2005

C. Stocco, MSc¹, D. Wang, PhD², J. Brook, PhD³, and A. Wheeler, PhD¹

- ¹ Air Health Effects Division, Environmental Contaminants Bureau, HECSB, Health Canada, Ottawa, ON
- ² Analysis and Air Quality, Environmental Technology Centre, Science and Technology Branch, Environment Canada, Ottawa, ON
- ³ Meteorological Service of Canada, Air Quality Research, Science and Technology Branch, Environment Canada, Ottawa, ON

OBJECTIVE: As part of a multi-year personal exposure monitoring campaign, 24-hour personal, indoor, and outdoor levels of 188 polar and non-polar volatile organic compounds (VOCs) were obtained for 48 Windsor residents in order to assess their exposure to traffic-related VOCs as a result of their daily routine.

DESIGN: During the winter and summer of 2005 personal, indoor and outdoor locations for 48 participants were monitored. Every 24 hours, for a period of five days in each season, a 1.0 L Summa canister was deployed for personal VOC sampling and 6.0 L Summa canisters were used for indoor and outdoor VOC monitoring. The indoor VOC canister was placed in either the family or living room, while the outdoor VOC canister was located in the backyard, several meters away from the home and from combustion sources. The smaller Summa canister was placed in a backpack that the participants carried everywhere they went. In total, 1350 samples were collected. In order to investigate associations between participant activity and exposure to VOCs, a daily questionnaire and time activity diary were also administered. Samples were analyzed by capillary GC-MS, operated in selected ion monitoring mode.

OUTPUTS/RESULTS: Benzene results indicate that during the winter, mean concentrations for all 48 participants were 1.93 ± 1.30 , 2.10 ± 1.88 and 1.03 ± 0.47 $\mu\text{g}/\text{m}^3$ for personal, indoor and outdoor locations respectively. During the summer the personal and indoor mean concentrations increased to 2.67 ± 2.76 and 2.92 ± 3.48 $\mu\text{g}/\text{m}^3$ and outdoor concentrations were lower at 0.86 ± 0.49 $\mu\text{g}/\text{m}^3$.

Time activity diary information revealed that, on average in the winter, participants spent 93% of their time indoors (for example: at home, away from home, and at work), compared to 88% in the summer. Between the two seasons, there did not seem to be any difference in the amount of time spent in transit (vehicle use, walking and taking bus), which accounted for 5.5% of participant time. Further analysis may help us understand the seasonal differences in benzene exposure.

For the 48 participants there is greater inter and intra person variability for indoor and personal exposure to VOCs than is found outdoors. In addition, there seems to be more variability in the summer than in the winter. Preliminary analysis of the data also indicates that in homes where there are attached garages, traffic-related VOCs are higher indoors, and as a result, personal exposure levels are also higher than in homes without attached garages.

IMPACTS/OUTCOMES/CONCLUSIONS: Personal exposure to VOCs appears to be driven by indoor concentrations of VOCs rather than outdoor, which may be of concern as Canadians spend up to 90% of their time in indoor environments.



3.67 Murine Biomarkers During the Shock Response from Intratracheal Exposure to Domestic Substance List *Bacillus* Outgrowths

A.F. Tayabali, PhD¹, K.C. Nguyen, BSc¹, G. Arvanatakis², D. Johnston², M. Navarro, DVM³, S. Popovic³, K. Kittle³, D. Parks³, and V.L. Seligy, PhD¹

¹ Safe Environments Program, HECSB, Health Canada, Ottawa, ON

² Product Safety Program, HECSB, Health Canada, Ottawa, ON

³ Animal Resources Division, HPFB, Health Canada, Ottawa, ON

OBJECTIVES: According to the *Canadian Environmental Protection Act* (CEPA 1999), animate products of biotechnology must be assessed for harmful effects prior to use, import, or manufacture in Canada. In previous work, Domestic Substances List (DSL) bacteria from the *Bacillus* genus were used as models to screen for potentially harmful effects. Towards this goal, a multi-indicator immunologic strategy was established to test *Bacillus* inhalation effects in Balb/c mice. These findings showed that spores were cleared efficiently, but 2 hour exposures to washed outgrowths caused shock-like symptoms, neutrophil infiltration, and elevations in proinflammatory cytokines. The objective of the current study is to elaborate on biomarkers indicative of systemic responses and tissue damage during exposure to washed outgrowths.

DESIGN: Outgrowth cultures contain >90% live and dead vegetative bacteria, but also spores and extracellular culture constituents. These were washed of soluble material and used for intratracheal 4 hour exposures to Balb/c mice. Animals were evaluated for physical signs of recovery or distress, pulmonary and serum granulocyte and cytokine levels, as well as liver-expressed acute phase response proteins (serum amyloid A and fibrinogen). Several assays indicative of pulmonary oxidative stress (e.g., lipid peroxidation, DNA adducts) were also used.

OUTPUTS/RESULTS: Four-h shock-like symptoms included hypoactivity, hunched appearance, ruffled fur, respiratory distress, increased lethargy and ocular discharge. Pulmonary granulocytes were elevated by > 3-fold and hepatic and circulatory acute-phase markers were elevated by 1.5 to 4 -fold. Generally, pulmonary cytokine levels were indicative of severity of physical symptoms. For oxidative stress indicators, pulmonary myeloperoxidase was elevated by ~1.5-fold. Of the *Bacillus* strains tested, *B.cereus* 14579 and *B.thuringiensis* 13367 caused most severe effects, whereas effects of *B.thuringiensis* commercial strains were weak, and those of *B.subtilis*-inoculated mice were asymptomatic.

IMPACTS/OUTCOMES/CONCLUSIONS: The biomarkers described here are indicative of systemic (hepatic, blood) effects and generally correspond to appearance of physical symptoms. The results show that washed outgrowths of Bc and Bt, but not Bs, could result in health-related issues and should be evaluated further for potential adverse health effects.

3.68

3.69 Determinants of Prolonged Waiting Times for Non-Emergency Specialized Health Care Services in Canada

P. Tissaaratchy, MA¹

¹ Health Demand and Supply Analysis Division, Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON

OBJECTIVE: To explore, using recent Canadian survey data, determinants of prolonged waiting times for non-emergency specialized health care services.

DESIGN: A weighted logistic regression model is developed for surgical, diagnostic, and specialist physician services. The relationship between waiting time and socioeconomic status, health status, demography, cancellation, overnight stay, having a family physician, diagnostic condition, and access difficulties is examined.

A prolonged wait is defined as waits exceeding the i) median and ii) third quartile. A relative measure is used to compare characteristics of *all* patients who faced longer waiting times versus those who did not. (Medically acceptable waiting times apply to select procedures and would not capture all respondent information.)

RESULTS: For surgery, the probability of a prolonged wait is 5.0 times for those with hip/knee problems. Patient cancellation increases by 11.7 times the likelihood of a prolonged wait. For specialist services, patient cancellation increases the likelihood of a prolonged wait by 5.2 times. For diagnostic services, the probability of experiencing a prolonged wait is 5.7 times greater for those reporting difficulty obtaining a hospital bed. The likelihood of experiencing a prolonged wait is 7.0 times greater for those reporting difficulties obtaining an appointment/referral.

CONCLUSIONS: For all services, diagnostic conditions associated with higher mortality rates are associated with the lowest probabilities of a prolonged wait indicating prioritization. For diagnostic services (where private sector options exist), those with the highest income have the lowest probability. Those obtaining diagnostic scans in a public institution have a higher probability than those obtaining scans in private institutions. For surgery, patient cancellation is associated with the highest probability. Procedures requiring an overnight stay are associated with a higher probability. For diagnostic and specialist services, experiencing barriers to access is associated with the highest probability. For surgery and diagnostic services, absence of a family physician is associated with prolonged waiting.

3.70 Adjuvant Activity of Environmental Pollutants on Allergic Immune Response to *Alternaria Alternata* and *Dermatophagoides Farinae*

H.M. Vijay, PhD¹, V. Kumar, MSc¹, M. Abebe, PhD¹, M.S. Sevinc, PhD¹, and R. Vincent, PhD¹

¹ Safe Environment Programme, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: 1. To investigate the adjuvant effect of air pollutants on the sensitization of mice to molds and mites. 2. To investigate if air pollution exposure can be related to the prevalence of asthma.

DESIGN: Five groups, each consisting of 6 female BALB/C mice, were immunized as follows: group A was given IP injection of 100 ug of *A. alternata* mixed with 6 mg of EHC-93; and, group B with the same dose of *A. alternata* with 6 mg alum. The three control groups C, D, and E were given an IP injection of *A. alternata* extract, EHC-93 and alum alone, respectively. After four weeks, all the groups were boosted in a similar way except A, B and C, which received 10 ug of the extract. The animals were bled at 7, 14 and 21 days. The strength of the specific antibodies was determined individually by passive cutaneous anaphylaxis (PCA) reaction. Similarly, a second experiment was carried out using *D. farinae* as an immunizing agent. Total IgE in the sera of the animals was determined by ELISA.

OUTPUTS/RESULTS: Groups A and B gave strong PCA reaction (10x14 mm) indicating EHC-93 is equally as potent adjuvant as alum. The mice immunized with *A. alternata* alone gave very weak reaction and groups D and E were found to be negative. Similar results were found when the animals were immunized with *D. farinae*. Significant increase in the total IgE was observed in groups A and B.

IMPACTS/OUTCOMES/CONCLUSIONS: EHC-93 appears to exert strong adjuvant activity for the production of specific IgE antibody in BALB/C mice immunized with *A. alternata* or *D. farinae*. It could be hypothesized that influence of air pollution in both allergic sensitization and inflammatory response could be gene-environment interaction.

3.71 Maternal Contaminant Levels of Persistent Organic Pollutants and Heavy Metals in Canada

J. Van Oostdam, DVM, MPH¹, and M. Walker, PhD²

¹ Management of Toxic Substances Division, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

² Biostatistics and Epidemiology Division, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

INTRODUCTION: Canada is participating in the tri-lateral maternal blood contaminant monitoring study of persistent organic pollutants (POPs) and various metals under the North American Commission for Environmental Cooperation (NACEC). Levels of metals such as mercury and lead are likely to be quite low in this population but recent research has indicated that there may be significant health risks to the fetus at lower levels of exposure.

METHODS: This study will examine levels of POPs and heavy metals in the blood of twenty five first birth mothers from five centres across southern Canada. Hospitals and clinics in Halifax, Ottawa, Hamilton, Calgary and Vancouver are recruiting mothers. Samples are being analyzed at one central laboratory for a range of POPs (e.g., PCBs, DDT/DDE, chlordane derivatives, aldrin, dieldrin, hexachlorobenzene, mirex, hexachlorocyclohexane isomers) and various metals (i.e., mercury, lead, cadmium, arsenic). Each mother will complete a demographic and dietary questionnaire.

RESULTS: Comparative results from arctic Canada have found that Inuit mothers from the Baffin Region have significantly higher levels of PCB 153 compared to Caucasian mothers living in arctic Canada (131 vs 16 microgram/kilogram lipid). This regional data from southern Canada will be compared for a number of contaminants including PCBs, mercury, DDE, oxychlordane and other contaminants to the ethnic differences we have seen from arctic Canadian populations. The relationship between demographic characteristics, dietary intakes and contaminant levels will be assessed.

DISCUSSION AND CONCLUSIONS: This study will be the first national assessment of these contaminants in this important segment of the population and will allow initial regional comparisons plus provide information for larger national or regional studies. This information will have direct application for Canada in meeting its monitoring requirements for the Stockholm convention on POPs developed under the United Nations Environment Program, various obligations under NACEC agreements and will be valuable to risk managers and public health officials in Canada.

3.72 PFCAs, PPAR Ligands and Immunotoxicity

C. Woodland, MSc¹

¹ News Substances Assessment and Control Bureau, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: Global awareness of the need to incorporate routine immunotoxicity assessment in the safety evaluation of drugs and chemicals is reflected in the ongoing ICH process of harmonization of testing guidelines for immunotoxicity. In support of this approach, a review of international and domestic research was conducted to assess the potential immunotoxicity of PFCAs (Perfluorinated Carboxylic Acids) on human health, using PFOA (Perfluorooctanoic Acid) as a case study.

DESIGN: A literature review of the effects of PFOA and of the class of compounds to which PFOA belongs (peroxisome proliferators/PPAR [peroxisome proliferator activated receptor] ligands) on the mammalian immune system, with a focus on elucidation of the potential mode of action (MOA) of PFOA immunotoxicity in humans, was performed. Comparisons of *in vitro* human and animal data and reviews of *in vivo* animal data and of data generated by the pharmaceutical industry on the PPAR ligand MOA were made. The relative roles of the three PPAR isomeric forms in PFCA immunotoxicity and of peroxisome proliferation in PPAR ligand activation of human PPAR were investigated.

OUTPUTS/RESULTS: The alpha isoform of human PPAR, and possibly the PPAR gamma human isoform, have the potential to mediate PFCA immunotoxicity, as represented by potential PFOA and PPAR ligand immunotoxicity. *In vivo* assessment of a variety of rodent immunotoxicity endpoints (i.e., lymphocyte subsets, primary humoral response using ELISA and PFC assay, cell cycle effects, organ weight assessment) indicated severe immunosuppression with PFOA treatment. Human PPAR activation was unaccompanied by peroxisome proliferation.

IMPACTS/OUTCOMES/CONCLUSIONS: Concern for the potential of PFCAs, as PPAR ligands, to cause immunosuppression is warranted, particularly in the context of the totality of PPAR ligand pharmaceuticals in the environment. Pharmaceutical PPAR ligands have wide and frequent human use and given the potential for subsequent interactive effects, the potential for PFCA immunotoxicity to human health cannot be dismissed.

3.73 Cost-Benefit Analysis of Examining Pre-Diabetes Screening Interventions: An Application of Markov Modelling

B. Adhikari¹, C. Robinson¹, C. Yung², and I. Zverev²

¹ Health Demand and Supply Analysis Division, Applied Research and Analysis Division, HPB, Health Canada, Ottawa, ON

² Economic Analysis Unit, Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, Ottawa, ON

OBJECTIVES: Is Do It Yourself (DIY) urine dipstick testing a cost-effective method of detecting pre-diabetes and undiagnosed type-2 diabetes in Canadians with risk factors for the disease? Applying markov modelling techniques, we examine the potential economic costs versus benefits of urine dipstick screening for detecting type-2 diabetes.

DESIGN: To examine the effectiveness of DIY urine dipstick testing as a tool for detecting undiagnosed type-2 diabetics, we develop a markov model that allows us to track the diagnoses, treatment and complication paths of a representative cohort of Canadians ages 40-75 screened using urine dipstick testing. Based on individual characteristics of blood pressure, hemoglobin level (Hba1c), age, gender, body mass index (BMI), etc., and treatments, at each time period, we predict the number of individuals who develop type-2 diabetes, and the number of individuals within each complication state. Follow-up diagnosis after DIY screening is based on traditional diabetes clinical screening methods (fasting plasma glucose (FPG) and/or 2-hr oral glucose tolerance tests (OGTT)). Use of the urine dipstick testing is compared against the current status-quo testing and the Canadian Diabetes Association's current recommendations.

DATA: Baseline Characteristics of the Canadian population and cost data are collected from various Canadian and International administrative and survey data sources. Epidemiological and medical literature such as the United Kingdom Prospective Diabetes Study (UKPDS) and the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) were used to provide parameter estimates for transition probabilities between complication states.

OUTPUTS/RESULTS: Differences in detection rates across screening methods, affect the stage at which diabetes is diagnosed as well as subsequent complication rates. Comparing the urine dipstick testing with the current status-quo testing and the recommendation by the Canadian Diabetes Association, the optimal type-2 diabetes screening strategy is determined on the basis of cost-benefit analysis.

IMPACTS/OUTCOMES/CONCLUSIONS: In 1999/2000, an estimated 1.2 M Canadians were diagnosed as diabetic. Another 30% of all diabetes cases were estimated to be undiagnosed. The study will help us determine a cost-effective strategy for detecting type-2 diabetes in Canada.

3.74 Exploring the Utilization of Online Health Information: A Canadian Study

S. Zhang¹, and L. Curtis, PhD²

¹ Applied Research and Analysis Directorate, HPB, Health Canada, Ottawa, ON
² University of Waterloo

OBJECTIVES: As a greater proportion of the population become computer and Internet savvy, many people are using the Internet to look for health information. This study aims to examine factors associated with the likelihood of using the Internet for health purposes, paying special attention to individuals' unmet health care needs. This study also addresses the relationship between the use of online health resources and health care utilization, measured by physician visits.

DESIGN: We examined two national representative cross-sectional datasets. To determine factors associated with Internet use, logistic regressions are used, with Internet use as the response variable (yes/no). To determine how use of online health information is related health-care utilization, an ordered logit model is used, with family physician visits as the dependent variable, which is categorized into no visit, 1-4 visits, and 5+visits. Additional analysis is also performed to examine specialist visits and psychologist visits using logistic regressions.

RESULTS: As of 2003/04, over 70% of Canadians (15+) used the Internet, and over 40% of them used it to look for health information. Besides individuals' socioeconomic characteristics, individuals' experience with unmet health-care needs is identified as a significant factor associated with use of online health information (OR: 1.50, 95% CI: 1.27-1.77). However, use of online health information does not appear to be associated with a reduction in physician visits. On the contrary, it is found to be associated with an increased likelihood for visits to psychologists (OR: 1.63, P<0.02), specialists (OR: 1.22, P<0.08) and family physicians.

CONCLUSIONS: When consumers' health-care needs cannot be readily met, they are more likely to turn to the Internet for health resources, which implies that the current wait times issue in our health-care system may help create increased demand for Internet health resources. However, consumers' acquisition of online health information does not show an association with a reduced likelihood for physician visits, nor does it appear to be associated with consumers self-rated health knowledge.



3.75 Phenobarbital-Mediated Gene Expression Profiles in Mouse Liver

J. Zheng¹, A. Williams², A. Yagminas¹, C. Parfett¹, G. Zhou¹, G.R. Douglas¹, and C.L. Yauk¹

¹ Environmental and Occupation Toxicology Division, HECSB, Health Canada, Ottawa, ON
² Biostatistics and Epidemiology Division, HECSB, Health Canada, Ottawa, ON

OBJECTIVES: To characterize gene expression changes in the livers of phenobarbital-treated mice using oligonucleotide DNA microarrays. To investigate the correlation between blood chemistry, hepatic metabolism and gene expression profiles.

DESIGN: Male B6C3F1 mice (five mice/group) were dosed by oral gavage daily for three days with vehicle or 0.1, 1, 10 and 100 mg/kg/day phenobarbital and sacrificed 4 hours after the last dose. Serum samples were collected to measure standard biochemical markers for hepatotoxicity. Hepatic benzyloxyresorufin O-dealkylase (BROD) and ethoxyresorufin-O-deethylase (EROD) were measured. Total liver RNA was isolated and hybridized to the in-house custom oligonucleotide microarray (ToxArray™), containing 1600 genes predicted to be responsive to toxic exposures. Microarray data were normalized using a composite LOWESS and analyzed in MAANOVA. Selected differentially expressed genes using microarrays were confirmed by real time RT-PCR.

RESULTS: Phenobarbital treatment resulted in a significant ($p < 0.05$) increase in liver-body weight ratios at the highest dose. BROD activity was significantly elevated approximately 2-fold and 20-fold at 10 and 100 mg/kg/day doses. Consistent with these results, microarray analysis showed that Cyp2b9 and Cyp2b10 genes were significantly induced about 7 and 5-fold at 100 mg/kg/day; 3 and 2.5-fold at 10 mg/kg/day, which were further confirmed using real time RT-PCR. In addition, up to 36 differentially expressed genes were identified in microarray analysis. The predominant pathways represented among the genes that were differentially expressed include xenobiotic metabolism, cell development and differentiation, lipid metabolism, stress response and apoptosis, consistent with the known pathology of phenobarbital exposure.

CONCLUSIONS/IMPACTS: Our results demonstrate a correlation between biochemical endpoints and gene expression changes induced by phenobarbital, suggesting that microarray technology may be used as a tool for elucidating the mechanism of chemical-induced toxicity, predicting the adverse effects of environmental toxins and improving the process of risk assessment and safety evaluation. Further validation using other chemicals with known pathology is currently underway.

4.01 Critical Review of Soil Ingestion Rates for Use in Contaminated Site Risk Assessments

R.M. Wilson¹, I.A. Mitchell², D.R. Williams², S.A. Petrovic³, G.M. Richardson³, and H. Jones-Otazo⁴

¹ Wilson Scientific Consulting Inc., Vancouver, BC

² Meridian Environmental Inc., Calgary, AB

³ Contaminated Sites Division, Safe Environments Programme, HECSB, Health Canada, Ottawa, ON

⁴ Safe Environments Programme, HECSB, Health Canada, Toronto, ON

OBJECTIVES: For certain chemicals and land uses, the value selected for the rate of soil ingestion is one of the more sensitive values used in both human health risk assessment (HHRA) and soil quality standard development. Assumptions concerning soil ingestion rates for use in contaminated site risk assessments in Canada were first established by a working group of Health Canada in or around 1993 and have not been updated since that time, despite ongoing research. A critical review of the data and literature was completed with an aim to advise Health Canada of appropriate soil ingestion rates for use in contaminated site risk assessments.

DESIGN: In view of the need to update existing regulatory knowledge on soil ingestion rates, it was important to critically review research from 1993 until present and provide recommendations. The peer-reviewed scientific literature and guidance from Canadian and international agencies were reviewed to identify relevant sources of information, and were analyzed to derive updated soil ingestion rates that are appropriate for use in contaminated site risk assessment.

OUTPUTS/RESULTS: All regulatory agencies reviewed indicated that young children (less than six years) have the highest soil ingestion rate. Literature-based average soil ingestion rates for young children ranged from 6.8 - 200 mg/day. Regulatory agencies recommended soil ingestion rates for toddlers ranging from 40 - 1,000 mg/day. Provisional deterministic and probabilistic soil ingestion rates were recommended for each of the age groups typically considered by Health Canada, as well as for occupational exposures and individuals exhibiting soil pica behaviour. There was deemed to be insufficient data to derive provisional soil ingestion rates under traditional land use and camping scenarios.

IMPACTS/OUTCOMES/CONCLUSIONS: Additional studies are required on soil ingestion rates. Recommended future research includes soil ingestion studies on “typical Canadian” populations and on traditional land use, as well as a more thorough investigation of soil pica behaviour.

4.02 A Measure of Progress in Air Quality Management: Chilean Air Health Indicator

S. Cakmak, PhD¹, and C. Blanco, PhD²

¹ Environmental Health Science Bureau, HECSB, Health Canada, Ottawa, ON
² Conama, Santiago, Chile

OBJECTIVES: Although progress has been made in the last few decades at reducing ambient concentrations of air pollutants, scientific evidence suggests that there remains a risk to human health from exposure to these pollutants. In this paper, our objective is to determine to what extent air pollution, PM₁₀ in this study, is associated with non-accidental deaths in Chile. The extent will be introduced as an Air Health Indicator (AHI) for PM₁₀.

METHODOLOGY: Our base model includes time, temperature, day of the week, and air pollution level as risk factors. Air pollution related mortality is believed to depend on time and weather in non-linear fashion. A generalized additive Poisson regression model with smoothing techniques is used to relate these two time series, and the AHI is calculated as the percentage of the number of daily deaths attributable to exposure to the pollutant of interest.

RESULTS: Fairly steady progress in the management of particulate matter PM₁₀ can be observed for all the seven urban centers in Chile. The value of the AHI at the beginning of the study period, January 1, 1997, was 8.2% based on a weighted average of the community-specific values, while the value at the end of the study period, December 31, 2003, was 6.5%. Thus we predict that changes in ambient concentrations of PM₁₀ in 7 of Chilean communities contributed to a 1.7% reduction in the percentage of deaths attributed to pollution exposure.

CONCLUSIONS/IMPLICATIONS: The progress measure can be interpreted as a measure of accountability with respect to air pollution mitigation. PM₁₀ attributable-risk of death declined over time in conjunction with declining ambient concentrations suggesting that these improvements in air quality have in fact translated into improvements in population health. We have presented an approach to assessing the performance of air pollution management policies with respect to their effectiveness in improving population health. Our progress measure is a time dependent function of changes in ambient air quality, the number of health events, and the association between air quality and health. The measure can be determined at a national level or calculated for specific regions or communities. It can incorporate multiple pollutants and health outcomes.



Session B: International: Research Advances in Support of International Environmental Monitoring, York Salon, October 30, 2006, at 10:15 a.m.

4.03 Monte Carlo Simulations of Semi-Infinite Radioactive Clouds of Ar-41 & Xe-133

T.J. Stocki¹, L. Beaton^{1,2}, A. Tran^{1,2}, K. Bock^{1,2}, and R.K. Ungar¹

¹ Radiation Surveillance & Health Assessment Division, Radiation Protection Bureau, HECSB, Health Canada, Ottawa, ON

² Engineering Physics Co-op program, Carleton University, Ottawa, ON

OBJECTIVES: Health Canada maintains a number of detector networks. One of these networks consists of NaI(Tl) detectors that measure gamma dose rate in air. Located beside the NaI(Tl) detector in Ottawa is a radionuclide analyzer (which is part of Canada's contribution to preparation for the International Comprehensive Nuclear-Test-Ban Treaty), that measures the activity concentration of ^{131m,133m,133,135}Xe directly. The published conversion factor between these two quantities does not agree with our measurement. We focused on the NaI(Tl) detector to understand this discrepancy.

DESIGN: Two Monte Carlo methods are used. Firstly, a brute force method where a detector immersed in a semi-infinite radioactive source is modeled. The geometry of the series of simulations is like a "Russian Doll" where smaller dolls are encased in larger dolls. All the simulation results are added together yielding the total KERMA (Kinetic Energy Released in the Media); similar to putting all the dolls into each other without any gaps. This method has also been used to determine the detector's pulse height spectrum.

The brute force method proved to be very time consuming. The second method, the reciprocal transformation between source and detector, was employed to reduce the computation time.

OUTPUTS/RESULTS: The reciprocal transform method proved to be an acceptable estimate of the total KERMA. It decreases the computation time from months to hours. It was used at much greater distances than the brute force method can achieve. The results have helped explain the above discrepancy.

IMPACTS/CONCLUSIONS: Greater accuracy in the conversion value between the air KERMA and activity concentration will assist meteorological modelers verify their models. Environment Canada will more accurately model radioactive cloud movement in the event of an emergency from the measurements by Health Canada's NaI(Tl) network. From this meteorological model, a more accurate radiological dose assessment towards the public may be developed.



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Lower Level - Sous-sol

Salons Cartier Salons - I, II and III

Salon Albion Salon

Salon York Salon

Salon Elgin Salon

Salon Albert Salon

Salon Laurier Salon

2nd Floor - 2^e étage

Salle de bal Victoria Ballroom (North and South / nord et sud)

Salon Alta Vista Salon

Salon Capital/Carleton Salon

Salon O'Connor Salon

3rd Floor - 3^e étage

Victoria Ballroom Gallery/Mézzanine de la salle de bal Victoria

Salon Rideau Salon

Salon Dalhousie Salon

Salon Wellington Salon