Book of Abstracts

Message from the Acting Chief Scientist

I am pleased to greet all of you and to offer my appreciation for your participation in the Health Canada Science Forum, the most important science event on the department's annual calendar. Your contributions to cutting-edge science and to its applications in Health Canada, the Health Portfolio and across the national science and innovation system, are very valuable and greatly appreciated.

This year's overall theme *"Integration of Science, Regulation and Policy for Healthier Canadians"* recognizes that Health Canada, as a federal science-based department, relies on sound science to make its regulatory and policy decisions. For these decisions to be optimal, the interface between the science work of the department and its regulatory and policy functions must be as open and communicative as possible. Presentations and discussions to will be structured around three sub-themes: 1) Emerging Science and Technologies; 2) Interaction Between Health and the Environment; and, 3) Knowledge Transfer and Translation. As you can see, the Organizing Committee has again done a great job in identifying topics that will, I am sure, generate fascinating presentations and animated discussions.

I would like to thank the Organizing Committee and the Scientific Review Committee, as well as personnel in the Office of the Chief Scientist, for their dedication and outstanding work in planning this event. I hope you will find this year's Forum interesting and a valuable opportunity to develop or strengthen collaborations in support of departmental and other national priorities.

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Acting Chief Scientist and
Chair of the Health Canada Science Forum Organizing Committee

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

FNIHB: First Nations and Inuit Health Branch
HECSB: Healthy Environments and Consumer Safety Branch
HPFB: Health Products and Food Branch
HPB: Healthy Policy Branch
PMRA: Pest Management Regulatory Agency
PACRB: Public Affairs, Consultation and Regions Branch

Other Acronyms:

PHAC: Public Health Agency of Canada

1.01 Toxicology or Urban Particulate Matter: *In Vitro* and *In Vivo* Bioassays

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SUMMARY: We have developed a set of tools to better assess the toxicity of air pollution particles. These tests performed in cells and in animals (mice) are used to evaluate the toxicity of particles with different chemical compositions. The cellular tests are also useful in predicting particle toxicity in animals.

OBJECTIVES: Exposure to urban air particulate matter (PM) is epidemiologically associated with increased incidences of respiratory and cardiovascular diseases in humans. We are interested in the development of sensitive *in vitro* and *in vivo* endpoint assays that can be utilized for a high-throughput screening of PM toxicity with respect to their source and chemical composition.

DESIGN: We have examined the cytotoxicity of PM in human lung epithelial (A549) and murine macrophage (J774A.1) cell lines. Cell viability, proliferation, cell membrane integrity, cytotoxicity, metabolic activity and pro-inflammatory cytokine/ chemokine profiles were assessed in cell cultures exposed to various urban particles (EHC-93, EHC-98, EHC-2000, SRM-1648, SRM-1649, PM2.5) and mineral particles (cristobalite, titanium dioxide).

OUTPUTS/RESULTS: The bioassays revealed differential responses that were cell type-specific, particle-specific and concentration-dependent. We have also performed an intratracheal instillation of particles in Balb/c mice, and examined a number of cytotoxicity, oxidative stress and cardiovascular endpoints, in order to validate the *in vivo* potency predictive potential of the *in vitro* panel of assays.

IMPACTS/OUTCOMES/CONCLUSIONS: With this work, we hope to provide a better tool for the assessment of health impacts of urban air pollution, to enable more informed policy decisions in the regulation of air pollutants.

1.02 Toxicokinetic and Biodistribution of Nano Materials (Quantum Dots)

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SUMMARY: Nanotechnology is a growing technology utilized in drug and device development. Biocompatibility of nano material is a major focus of supportive nano toxicological research. New types of nano materials such as quantum dots may demonstrate compatibility issues. In this study, we examined the result of various biocompatible coatings such as lung targeting peptides as well as a polymer composition. The results demonstrate that more systematic toxicological studies are needed in order to develop new nano products such as quantum dots.

OBJECTIVE: To examine effect of coating on organ absorption of quantum dots and thereby its potential toxicity.

DESIGN: One preparation of QDs was used, representing colors of bare CdSe QDs and of CdSe/ZnS core shell QDs. Size distributions were determined from fluorescence emission spectra and high-resolution transmission electron microscopy (TEM) as well as atomic force microscopy. CGFECVRQCPERC peptide (denoted as GFE), which binds to membrane dipeptidase on the endothelial cells in lung blood vessels was used to coat the quantum dots.

This peptide was synthesized by *N*-(9-fluorenylmethoxycarbonyl)-L-amino acids chemistry with a solid-phase synthesizer and purified by HPLC. The composition of the peptide was confirmed by MS. Biodegradable polymeric micelles for drug targeting were obtained from University of Montreal (1). Stability tests were performed according to procedures suggested by Konkar et.al. Both formulations were injected injected into the tail vein of rats for *in vivo* distribution experiments using histology, light and electrone microscopy.

OUTPUTS/RESULTS: Protein assays revealed about 100 peptide molecules per QDs when peptide only was coupled. Distribution and absorption of QDs was significantly different among two groups of coatings (peptide versus polymer coating). Stability patterns were significantly different for the two formulations. Peptide coating GFE did not accumulate in organs but adhered to the blood vessels. The polymer coated dots did not accumulate either but adhered to blood vessels in various organs. Cellular accumulation patterns such as accumulation in mitochondria were also observed with the use of polymer formulation.

IMPACT/OUTCOMES/CONCLUSION: Surface chemistry and coating composition of nano particles such as quantum dots may change the pattern of accumulation and distribution of these particles. More toxicological studies are required to investigate potentials hazards associated with these materials.

1.03 An Improved Method for Determination of Benzene in Soft Drinks at sub-ppb Levels

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SUMMARY: The method used in previous survey to determine benzene in soft drinks was further improved to allow detection of benzene in soft drinks at lower levels. This improved method was used in a follow-up survey to determine benzene in samples of 139 soft drink products.

OBJECTIVES: To improve the method used in previous survey and apply it in the follow-up survey to investigate levels of benzene in beverages containing benzoate salts and generate data for risk assessment of human exposure to benzene.

DESIGN: The automated, simple, and reproducible method based on isotope dilution headspace gas chromatography/mass spectrometry developed previously for determination of benzene in soft drinks was further improved by using sodium sulfate, increasing sample injection volume, and lowering the GC oven starting temperature to narrow peak width, and was used in this survey to assess benzene levels in samples of soft drinks and beverages.

A total of 139 products were collected, 110 of them were the same products as those collected in the 2006 survey, and the other 29 products collected in this survey were either new products or not available in previous survey. These products contained benzoate salts according to their product labels (or known to contain benzioc acid as a natural constituent for cranberry drinks). The reformulated Kool Aid drinks, which do not contain benzoate salts, were also collected. The 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 by volume) drinks, and energy drinks packaged in aluminum, plastic, or glass containers.

OUTPUTS/RESULTS: Benzene was detected in 93 products, or 67% of the 139 products, due to the lower method detection limit (0.016 ug/L) of the improved method. Compared to previous survey, the average benzene concentrations in most products from this survey decreased, and only a few products had benzene at elevated levels.

IMPACTS/OUTCOMES/CONCLUSIONS: The results from this study are provided to the Chemical Health Hazard Assessment Division for risk assessment of human exposure to benzene, and will be communicated to manufacturers to assist in reformulations of products to avoid excessive formation of benzene and to confirm the effectiveness of their mitigation strategies.

1.04 Gene Expression Analyses of *Campylobacter jejuni* 11168 Biofilm, Pellicle and Plate Cultures: Multiple Profiles of Immobilized Growth

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SUMMARY: Each year, an estimated 1% of the population is afflicted with Campylobacter-induced gastroenteritis, mainly from poultry consumption, but other foods (i.e., meats, raw milk, water) have been associated with infection. This high rate of infection is a conundrum, as this organism does not appear to survive well outside of its animal host. Using genomic technologies, we are investigating biofilms as a potential environmental survival strategy for *Campylobacter*.

OBJECTIVES: Recent studies have shown that *C. jejuni* possesses the ability to form biofilms, structures, which may reduce its normally high susceptibility to atmospheric oxygen levels and many other environmental stresses (i.e., temperature, pH, drying). To improve our understanding of biofilm formation in this organism, we have performed comparative gene expression analyses of *C. jejuni* under various immobilized growth conditions.

DESIGN: Cells were grown in biofilms on glass fibre filters, in pellicles formed at the air-liquid interphase of broth cultures, on agar plates, or as planktonic cells in broth cultures in MH media under reduced oxygen at 37°C. RNA was isolated from cells grown under these conditions and was labelled with fluorescent dyes prior to hybridization to a whole genome DNA microarray of *C. jejuni* 11168. Labelled genomic DNA was concurrently hybridized to the same array for normalization.

RESULTS: Results of the comparative analysis of biofilm and planktonic cells correlated well with a previous proteomic analysis, with higher transcript levels in biofilm-grown cells for genes encoding proteins involved in the motility complex and in the general stress response. There were marked differences in expression profiles among the three forms of immobilized growth examined. Notably, higher levels of transcripts for genes encoding proteins involved in iron uptake were observed in pellicles and on plates, and higher levels of transcripts for genes encoding proteins involved in the respiratory chain and in flagellar biosynthesis were observed in biofilms.

IMPACTS/OUTCOMES/CONCLUSIONS: The differences in expression profiles observed may represent different stages in the progression of biofilm formation, or may point to different strategies for the formation of biofilms in *C. jejuni*. These results highlight potential mechanisms used by *C. jejuni* to form biofilms for increased survival under unfavourable environment conditions.

1.05 Characterization of Regions of Genomic Plasticity Among *Bacillus cereus* Group Microorganisms

J. Crosthwait[1], BSc, P.S. Shwed[1], PhD, and V.L. Seligy[1], PhD

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SUMMARY: We are studying bacteria that are used in the Canadian environment by examining their gene content at specific locations within their genomes. One segment of the genome was identified as a region of gene exchange and we have compared it in related bacteria, which are of interest for biotechnology applications.

OBJECTIVE: This study involves the genomic characterization of *Bacillus* biotech-organisms covered under the CEPA 1999 and Pest Control Products acts. *Bacillus thuringiensis* (Bt) is a genetic member of the Bc group containing *B. cereus* (Bc) and *B. anthracis* (Ba). There is a lack of Bt insecticidal strain genome information but the syntenic nature of Bc group genomes allows for direct comparisons. The Bc genome has been reported to contain three distinct genomic islands (BCGI1-3) resulting from horizontal gene transfers. Similar regions were examined in Bt biotech strains to compare their gene content.

DESIGN: The BCGI-1 site spans Bc14579 ORFs1261-1272. The corresponding regions in Bt *israelensis* (Bti) and *kurstaki* (Btk) derived commercial strains were mapped using clones from genomic libraries and analyzed using an ABI 3100xl capillary sequencer. Sequence identification and comparative analyses were carried out using Basic local alignment search tool (BLAST, NCBI). Genomic microarray data was used to confirm the absence/presence of genes in Bti and Btk.

RESULTS: Compared to Bc (23kb) the BCGI-1 location in Bti and Btk genomes was smaller (8kb). Sequences confirmed the BCGI-1 island is absent in Bti and Btk however, additional gene sequences related to cation transport were identified with no homologues for Bc or Ba genes in the corresponding region. A 1.3kb insertion, unique to Bti, was identified and showed similarities to the insertional elements flanking the pathogenicity island of Ba Ames Ancestor virulence plasmid (pX01).

OUTCOMES: The region corresponding to the BCGI-1 island in Bc is highly variable among Bc group members. The observation of an insertion element indicates a possible gene transfer between Bti and Ba. The characterization of genomic islands in Bt strains will provide insight into gene flow and help to identify species-specific markers as well as potential for adverse effects on the environment or human health.

1.06 Toxicological Assessment of Transgenic Salmon in a Rodent Developmental Study

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SUMMARY: The study described here is a modified one-generation toxicology study using a rodent model to evaluate transgenic versus wild-type salmon as a food source.

OBJECTIVES: The current study was conducted to identify any adverse or beneficial effects due to growth-enhanced genetically modified salmon (constitutively expressed salmon growth hormone gene) in the diet of rodents.

DESIGN: Three modified AIN93G diets were prepared containing 20%casein protein (Diet1), 20% wild-type salmon protein (Diet2) or 20% transgenic salmon protein (Diet3). All diets were balanced for lipids (7.8%)and mineral and vitamin content. Pregnant Sprague Dawley dams (day 7 gestation; 10 per group) were brought in and immediately put on diet. The dams and subsequent pups were monitored for weight and food consumption on a weekly basis. Pups were weaned at postnatal day (PND) 21 and maintained on the same diet as their dams until PND 28 or 80. Dams were euthanized upon weaning of the pups.

OUTPUTS/RESULTS: The study found few significant changes between dams on the three diets evaluated. In pups, males were more frequently affected than females by Diet3 (TG salmon) for parameters such as body weight, clinical chemistry and hematology. Interestingly, male pups fed Diet3 were larger on average than those fed Diets1 or 2 for duration of the study. Female pups were initially significantly heavier on Diet3, but by PND40 pups fed Diet2 were larger on average. Since there was little effect on organ weights, body weight differences may have been due to differences in body fat levels or other parameters. Typically the greatest number of changes were observed between rats fed the casein diet and the fish diets.

OUTCOMES/CONCLUSIONS: Overall the study design was sufficient to determine growth and general health status in rats fed the three diets. Differences observed in F1 rats in the short term (PND28) tended to be transient and less discernable in the long term (PND80). Timing is critical in assessing the health of young animals and exposure periods longer than PND28 would be useful to effectively evaluate the persistence of subtle postnatal health changes.

1.07 The Effects of Water, Phosphate Buffered Saline, or HL-60 cells on the Degradation of the PLGA 85/15 Scaffolds for Tissue Engineering

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SUMMARY: A co-polymer of polylactic acid and glycolic acid was used to manufacture a model scaffold for studying, evaluating and identifying, under *in vitro* conditions, important aspects of degradation of scaffolds designed for tissue engineering applications.

OBJECTIVE: To study the degradation of PLGA 85/15 porous scaffolds in the presence of water, PBS or HL-60 cells, to understand the performance properties needed in tissue engineering scaffolds.

DESIGN: In this study, HL-60 cells were used because just like white blood cells, they can attack foreign materials. The PLGA 85/15 is a documented biomaterial. It is used as a model for in-vivo temporary structures, that when implanted in the body, would allow the body's own cells to grow and form new tissues. In most tissue engineering designs, the presence of a scaffold is of critical importance, as it provides a framework for growing cells, to replace damaged or defective tissues (e.g., bone). In this project however, the interaction of HL-60 cells and the 85/15 PLGA were studied for the first time to understand any new physical properties of the polymer and its biocompatibility or degradation to non-toxic by-products.

OUTPUTS/RESULTS: Results showed that 84 days of incubation of the scaffolds in distilled water or PBS, as well as 28 days in HL-60 medium, all at 37°C and pH 7.4, produced negligible mass losses (0 - 4%), suggesting that this new scaffold would remain stable and viable in a hydrophilic environment for at least 3 months. The measured water-uptake for this scaffold, after 7 days of incubation, varied; 0 - 100% for PBS, and 0 - 150% for distilled water, meaning that the initial phase of degradation involving hydrolytic chain cleavage would be slower in PBS, but faster in distilled water.

IMPACT/CONCLUSIONS: In addition to published requirements of high porosity and high interconnectivity of the pores, characterization of mass loss and water-uptake of implantable scaffolds is necessary in understanding more about scaffolds. This knowledge will be shared with manufacturers and regulators of tissue engineered medical devices.

1.08 Identification of Novel Biomarkers of Exposure to Environmental Thyroid Hormone Disruptors during Mouse Brain Development Using Advanced Genome Wide Approach

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SUMMARY: Numerous chemicals in our environments can affect thyroid hormone balance and potentially impact neurodevelopment. We used chromatin immunoprecipitation and DNA microarrays (ChIP on chip) to identify regions of DNA that were bound to thyroid receptors during mouse cerebellar development. The data provide information on the mode of action of thyroid receptor; this insight is necessary for risk evaluation of thyroid disrupting chemicals. In addition, potentially novel biomarkers of thyroid hormone disruptors that affect brain development were identified.

OBJECTIVES: Several studies have demonstrated that maternal thyroid hormone (TH) insufficiency retards brain development in childhood. Environmental contaminants such as PCBs and dioxins have measurable adverse effects on neuro-development that may be mediated by disruption of TH homeostasis. This project aims to provide insight into the mode of action of TH disruptors and to identify novel biomarkers of exposure. TH interaction with the TR results in gene regulation mediated through thyroid responsive elements (TREs) in the DNA. We studied TH-mediated brain-development using ChIP-on-chip, which is a powerful global approach used to determine what regions of DNA bind to TR and regulate gene expression.

DESIGN: Cerebellum from mice at post-natal day (PND) 4 and 15 (5 each) were homogenized. DNA fragments bound to TH receptor were isolated using TH receptor antibody. TR-bound DNA was hybridized with custom promoter DNA microarrays against total genomic DNA. Enriched regions were identified. Significantly enriched probes were confirmed by PCR or reporter assays. Candidate biomarkers were examined in animals exposed to PCB or Benzo(a)pyrene.

RESULTS: We found more than 150 and 300 genes whose promoters contain one or more TREs in cerebellum at PND4 and PND15, respectively, with some overlap between the time points. We selected 13 genes, which have the highest enrichment ratios in both time points, for further examination using ChIP-PCR. ChIP-on-chip results were confirmed for 9 genes. Transcription activity of the promoters of two genes (Mag and Sms) that were highly enriched was validated using a luciferase reporter assay. The expression of Mag and Sms was also regulated by TH in cultured TH receptor over-expressing cells. Interestingly, the expression of these two genes in cerebellum of mice treated with PCBs or BAP was significantly up-regulated.

IMPACT: We identified two potential biomarkers for exposure to environmental TH disruptors, providing a potential tool for risk assessment and insight into the mechanisms of TH insufficiency-induced neural system disorder.

1.09 A Sensitive Method for Measuring Monophthalic Metabolites in Urine by PAEKI-capillary Electrophoresis-tandem Mass Spectrometry

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SUMMARY: A reliable and sensitive method was developed to measure the metabolites of environmental exposure phthalates in urine samples with capillary electrophoresis hyphenated to tandem mass spectrometry (CE/MS/MS). A new preconcentration injection technique was introduced in this study to enhance the method sensitivity. A good reproducibility and recovery was achieved.

OBJECTIVES: To Develop a quick, reliable and sensitive method with capillary electrophoresis-tandem mass spectrometry (CE/MS/MS) for identifying and measuring nine monophthalic metabolites of environmental exposure phthalates in urine.

DESIGN: The pressure assisted electrokinetic injection (PAEKI) is based on the concept that the movement of running buffer caused by electroosmotic flow (EOF) in column can be stopped by balancing the EOF with an opposite external pressure in the electrokinetic injection process and this balancing way can provide on-line pre-concentration of ionized analytes up to several thousand folds in the application of capillary electrophoresis hyphenated to mass spectrometry. Therefore, this enhancement technique can provide high sensitivity way to measure ionisable monopthalic metabolites of phthalates in urine.

OUTPUTS/RESULTS: To measure both free and conjugated monophthalates, samples were treated without and with enzyme digestion for free and conjugated monophthalates, respectively. After digesting process, samples were cleaned up by using Oasis HLB cartridges. Final eluates were dried by nitrogen flow and re-dissolved in water for analysis. The detection limits of monophthalates in urine defined as three times of signal to noise ratio (S/N) were in the range of 0.5 – 1.3 ng/mL even with a single quadrupole mass spectrometry, which is comparable to the LC/MS/MS system reported. The relative standard deviation with seven replicates of measurement for 10 ppb of standards was from 6 – 17%. The overall recoveries for all nine monophthalates were within in a range of 88% to 106% with this method.

IMPACTS/OUTCOMES/CONCLUSIONS: The study results provide an alternative sensitive method to measure monophthalic metabolites in urine. Urine is an important bio-matrix to monitor those monophthalates using for assessment of the human exposure to phthalates. The online PAEKI CE/MS/MS system will be a powerful tool in the biomonitoring of human exposure to phthalates.

1.10 Challenges in Protecting Terrestrial Habitats and Controlling Invasive Weeds: The Impact of Non-Spray Buffer Zones

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SUMMARY: The PMRA will develop an approach to address invasive weed control while ensuring that herbicide products will have a minimal impact on sensitive terrestrial habitats. An ongoing project, therefore, will be initiated to examine the issue of non-spray buffer zones in the context of invasive plant control.

OBJECTIVE: For many herbicide products, non-spray buffer zones are required for protection of sensitive terrestrial habitats that consist of native plants and other non-target vegetation. Buffer zones, however, appear to sometimes contravene the need for controlling invasive weeds. Herbicide applicators have indicated that if invasive weeds are not controlled in the buffer zone areas, a refugia for these weeds remain which enables them to re-establish in the treated site. Applicators have also reported no evidence of any long-term impact on plant diversity following herbicide treatment. Contrary to this, researchers have indicated that off-site movement of herbicides, have altered plant diversity without signs of recovery in subsequent years. In these cases, herbicides impacted the sensitive plants more readily than the more resistant ones resulting in a selection for resistant plants adjacent to the areas where the herbicides were applied. The objective, therefore, is to develop an approach to address invasive weed control, while ensuring that the use of herbicide products will have a minimal effect on the diversity of sensitive terrestrial habitats.

METHODS: Review of current scientific data and consultation with expertise in related fields.

OUTPUTS: Determine: 1) the relative ecological significance of “terrestrial habitats” (that appears on herbicide labels) in agroecosystems; 2) which terrestrial habitats are more susceptible to invasive weeds; 3) the ‘invasive’ potential and ecology of some key weed species in Canada; 4) the comparative risk to terrestrial habitats resulting from observance and non-observance of buffer zones; and, 5) the impact of invasive weed control on plant diversity.

IMPACTS: Provides an integrated approach that facilitates a refinement of the requirement for non-spray buffer zones.

1.11 Ethics, Emerging Technologies and Public Consultation

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SUMMARY: Sometimes the emergent quality of a technology (such as nanotechnology) suggests a need for greater diligence and horizontal coordination than may be currently apparent in the government's early approaches to risk management and stewardship. For other technologies posing distinctively ethical risks, it appears more in-depth and innovative public engagement approaches will increasingly be needed.

OBJECTIVES: To provide an opportunity for Science Forum participants to discuss and enhance the understanding of issues raised at a February 13, 2007 session of HC and PHAC policy staff and invited academic researchers. These relate to public consultation on ethical issues in emerging technologies, including: (1) those with very little understood potential elements of risk to public health; and, (2) those with distinctive risks of impacting on psychological and cultural norms of what is a good or right way of life (ethical risks).

DESIGN: A presentation of the issues raised by three distinguished Canadian academic researchers, including the following topics: (1) Public engagement on ethically sensitive technologies as seen through the example of assisted human reproduction (AHR) policy and legislation; (2) The ethical, environmental, economic, legal and social issues around nanotechnology as a test case for Canadian governmental stewardship of a broad category of emergent technology; and, (3) Links between public engagement considerations and current risk management theory.

OUTPUTS: An appreciation/understanding of the extent to which Science Forum participants agree with the two broad consensus claims reached by participants at the February 13 session. (1) The emergent quality of a technology, at least in the case of nanotechnology, suggests a need for greater diligence and horizontal coordination than may be currently apparent in the government's *de facto* early approaches to risk management and stewardship. This apparent gap probably reflects resource constraints which sometimes make it more attractive short-term to delay implementing a plan until higher authorities mandate the step. (2) For some new technologies (e.g., AHR), one can speak of a distinctive class of ethical risks which, by their very nature, may call for in-depth public engagement approaches, regardless of how well the strictly technical aspects of the new application are understood.

CONCLUSIONS: These views also raise a number of related questions, any of which invite further exploration in the science and policy communities. Among them: (1) How do we assess the degree of ethical risk, or the speculativeness of emergent risks, as one requiring a comprehensive public engagement process, thus ensuring consistency of rigour for all relevant policy issues? Because ethics calls for an open-ended, iterative dialogue emphasizing narrative context and inter-subjective,

affective elements, more traditional approaches to public consultation do not readily suffice; (2) Are our assumptions about what is acceptable in practical interpretation of RM frameworks worthy of critical public engagement in their own right? and, (3) How proactive can the Public Service be in exploring emerging policy areas without further complicating relations with the government in power.

1.12 How Should we Evaluate Potential Health Risks from Nano-Materials Involving Metals? A Stable Isotope Tracer Approach for Possible Application to Metal-Containing Nano-Materials in an Animal Model

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SUMMARY: Among the emerging nano-materials in use or projected for use, are those comprising of nanometallic particles. Just how differently (or similarly) such materials might interact in the human body is poorly understood. A possible tracer method for metals (stable isotopes) that might be useful for examining where such materials end up in mammalian tissues is described.

OBJECTIVES: The project describes the further application of an award winning Health Canada approach, in elucidating biological mechanisms by which toxic metals accumulate in - and are released from - the body. In this case, the problem to be addressed is the application of the method to the emerging issue of health risks posed by nano-materials, and in particular, whether the characteristics of emerging metal containing materials affect exposure and uptake and tissue distribution in the mammalian body.

DESIGN: The approach (in an animal model) utilizes the natural properties of some metal elements (those having more than one stable isotope). A dosing solution/suspension or other composition is prepared for the metal (e.g., Pb, Hg, Cd or Ag) where the abundances of the different isotopes have been altered from that normally found in nature, by including the presence of a known amount of an enriched isotope. This altered - and now unique - 'dose mixture' is then distinguishable, using analytical techniques such as I.C.P.M.S., T.I.M.S. or GC/High Resolution M.S, so that disposition in selected tissues and organs in the body can be determined.

OUTPUTS/RESULTS: Results are presented for two reproductive studies (in a primate and a mouse model) showing how the approach has been successfully used in the case of two 'non-nano' metals, lead and methylmercury. The authors demonstrate transplacental transfer for lead (Pb) and for methylmercury (MeHg) and the accumulation of the enriched isotope tracers in fetal tissues, including the brain.

IMPACTS/OUTCOMES/CONCLUSIONS: 'Proof of concept' for the (non-nano) method has been accomplished and the stable isotope method - developed at Health Canada and the University of Texas in two animal models - could offer a promising method for testing whether exposure to nano-material formulations of particular metals might be different from metals administered in a "non-nano" form.

Depending on the route of administration to be tested (e.g., oral, dermal or inhalation) the enriched isotope could be incorporated in the structure of the nano-material (with its unique isotopic fingerprint) that would then allow subsequent measurement in selected target tissues.

1.13 Towards a Nanotechnology Risk Management Framework

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SUMMARY: In collaboration with the Departmental Biotechnology Office and the Office of the Chief Scientist, the Health Portfolio Nanotechnology Working Group drafted an issue paper to address risk issues related to nanotechnology. It is intended to provide a basis for a risk management strategy for the regulatory community in Canada.

OBJECTIVES: Serving as a collective reference document, the "Health Portfolio Nanotechnology Issues Identification Paper" has been produced in collaboration with the Health Portfolio Nanotechnology Working Group to address risk issues related to nanotechnology.

DESIGN: This paper has been prepared through consultations with Healthy Environments and Consumer Safety (HECS) Health Products Branch. It was designed to combine science and policy components and to address evaluation issues for products and substances as well as environmental impacts of nanotechnology. Consultations involved several academic institutes as well as NGOs. It also includes broader science and strategy components, such as consultations with other federal departments, such as Environment Canada and Industry Canada as well as several international agencies.

RESULTS: The paper has been used as a basis of a recent workshop and has provided a platform for establishment of risk management strategies in Health Canada.

IMPACTS: This paper is an example of a successful collaborative effort, which brings together various departments and provides both scientific, as well as policy insight, and helps us address upcoming challenges in the area of nanotechnologies. It is an example of cross-departmental and international collaboration, which helps all sectors in Health Canada.

1.14 Regulation of Tissue Engineered Medical Devices

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SUMMARY: In the coming years, more medical devices, with tissue-engineered components, will enter the market and MDB (Medical Devices Bureau) will be required to review and regulate these new devices. A literature review of tissue engineered medical devices was prepared. The focus of the review is the identification of pre market information that should be included in licence applications for tissue-engineered devices. Post market regulatory issues of tissue-engineered medical devices are also identified.

OBJECTIVES: The objective of this review is to identify pre market and post market regulatory issues specific to tissue-engineered medical devices.

DESIGN: A comprehensive literature review of tissue engineered medical devices has been conducted and written to meet the needs of HC regulators.

OUTPUTS/RESULTS: The review will be presented to pre and post market evaluators and scientists. In order to help in advancing the field of regulatory sciences, a review paper will be prepared and submitted for journal publication. For example some of the important safety and efficacy parameters of scaffold structures include biodegradation rate, pore characterization, size distribution, interconnectivity, controlled release of bioactive molecules and vascularization. Standardised methods to measure these parameters need to be established and used by the industry and the pre-market review process.

IMPACT/OUTCOMES: This comprehensive review will assist HC regulators in providing science based pre market evaluation and post market surveillance of tissue engineered medical devices.

1.15 Intratracheal Aerosol Delivery and Fate of Nanoparticles in Mouse Lungs

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SUMMARY: Health effects of inhaled nanoparticles have not been well characterized. Following nanoparticle delivery into mouse lungs, we observed particles in the deep lungs with relatively even distribution between the right and left lobes. Using this methodology and the data produced, the risk associated with inhaled particles can be analyzed.

OBJECTIVES: To characterize the efficiency and level of penetration of nanoparticles in murine lungs following intratracheal aerosol delivery.

DESIGN: Red fluorescent nanobeads (40nm diameter) were intratracheally delivered to murine lungs using the PennCentury MicroSprayer system. Mice were sacrificed at 0 or 24 h following aerosol delivery. Trachea, left and right lobes of the lungs, oesophagus, stomach lining and contents were collected separately. Tissues were dried, weighed and placed in Cellusolve solution to dissolve the nanobeads, releasing fluorescence into the solution. Fluorescence signal was measured using a fluorospectrometer (NanoDrop).

OUTPUTS/RESULTS: Delivery of nanobeads to the lungs was successful in 15 of 18 mice. Of the 15 mice, 12 showed an even distribution of beads between the left and right lobes, in the remaining 3 mice the majority of beads reached only the left lobe.

In the 15 mice, 80% of intratracheally delivered beads were recovered in the trachea, bronchi and lung lobes. The remaining 20% of beads were lost to the pharyngeal compartment or retained in the cannula. Of the total particles delivered from the cannula, 50% were distributed to the pulmonary compartment and 30% were distributed to the tracheobronchial compartment. Understanding lung distribution of experimental doses is essential for interpretation of local effects.

IMPACTS/OUTCOMES/CONCLUSIONS: Nanoparticles present a potential risk to human health. Very little is known about the fate of nanomaterials penetrating the respiratory system resulting in uncertainties of estimated internal doses. This study addresses some of these knowledge gaps, enabling better estimates for internal doses of nanoparticles in risk assessment and regulatory toxicology.

1.16 Approaches to Assess the Applicability Domain of (Quantitative) Structure Activity Relationships ((Q)SAR) Models

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SUMMARY: Two approaches to assess applicability domains of (Quantitative) Structure Activity Relationships ((Q)SAR)-based predictive toxicity models are proposed. These would not only serve as useful tools for risk assessors to determine if a query chemical is relevant to (Q)SAR models used but also help make more robust the process of hazard-based regulatory assessments of chemicals.

OBJECTIVES: Develop a deduction method for determination of domain of applicability (DA) of toxicity prediction models using structural analysis to be used in hazard-based regulatory assessments of chemicals.

DESIGN: Chemoinformatic tools that facilitate structural comparisons were employed to analyze training sets of some of the cancer and mutagenicity models in the Casetox and Topkat programs with reference to a set of query chemicals taken from the Canadian Domestic Substances List. These chemicals do not belong to any of the model training sets. First approach identifies key structural features of query chemical followed by determination of their coverage in model training sets. Second approach applies cluster analysis based on a predefined similarity criterion to generate information on extent of structural similarity that existed between the query structure and training set.

OUTPUTS/RESULTS: Both approaches provided information on whether a query chemical lies within or outside the domain of applicability of a given (Q)SAR model. According to fragment-based computations, 93 out of the total 110 situations, the chemical under consideration lies within the model's DA. However, the cluster-based analysis indicates that, in only 46 cases, the chemical lies within the model's DA. In all, there are 36 situations where both fragment-based as well as cluster based DA agree that a chemical lies within the model's DA whereas in 6 cases they agree that the chemical lies outside the model's DA.

IMPACTS/OUTCOMES/CONCLUSIONS: From a regulatory perspective, the model generated information on chemical safety needs to be as reliable as possible. For this, it is important to know if a given query chemical falls within the predictive boundary i.e., DA, of the concerned (Q)SAR model. The methodologies presented could serve as useful tools for regulators to make preliminary assessment of (Q)SAR based systems and in turn help the process of hazard-based regulatory assessments of chemicals.

1.17 *In Vitro* Toxicity of Carbon Nanotubes in A549 Human Lung Epithelial Cells

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SUMMARY: Carbon nanotubes, a new class of engineered nanomaterials are investigated for toxicity by exposing lung epithelial cells to these materials and measuring various endpoints of toxicity. Cellular cytotoxicity tests and proteome profiles implied marked differences that can be attributed to physicochemical characteristics and reflected potential toxicity of these materials.

OBJECTIVES: There are limited toxicological studies on engineered nanomaterials such as carbon nanotubes. Our objective was to investigate whether carbon nanotubes elicited toxic responses by conducting in vitro toxicity assays, as well as to see if physicochemical characteristics influenced their potency values. A proteomic analysis method was developed for screening of cell lysates to assess peptide/protein profile changes that can be used as a tool to map carbon nanotubes toxicity.

DESIGN: A459 human lung epithelial cells were exposed to single-walled and multi-walled carbon nanotubes. We compared pristine carbon nanotubes and their oxidized counterparts. Pristine single-walled carbon nanotubes and multi-walled carbon nanotubes were oxidized by reacting with H_2SO_4/HNO_3 and sonication for 2h. Clarified, oxidized carbon nanotubes were characterized by Fourier Transform Infra-Red spectroscopy for functional analysis. A549 cells were exposed (24h) to these nanomaterials (0.1 µg/well-30 µg/well, 96-well plates) in serum-free medium, and cytotoxicity was determined (Alamar blue, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, Lactate dehydrogenase, Neutral Red assays). Shot-gun proteomic analyses of cell lysates were done by direct Matrix Assisted Laser Desorption/Ionization-Time Of Flight-Mass Spectrometry, with saturated alpha-cyano-4-hydroxycinnamic acid as matrix. The mass spectral profiles were analyzed using ClinProTools by k-nearest neighbors clustering algorithm in order to identify candidate biomarkers of cell response, and establish discriminatory models.

OUTPUTS/RESULTS: Our preliminary findings revealed dose-dependent and carbon nanotubes -dependent cytotoxicity: single-walled carbon nanotubes -oxidized > single-walled carbon nanotubes-pristine > multi-walled carbon nanotubes -oxidized > multi-walled carbon nanotubes -pristine. An optimized proteomic screening method was developed for cell lysates. Peptide/protein patterns generated using this method clearly indicated carbon nanotubes-dependent changes and these nanomaterials could be discriminated based on alteration in levels of about 25 candidate peptide/protein markers. Best –fit model comprising a set of candidate markers that was generated by the k-nearest neighbors clustering algorithm using a training dataset, was able to classify blind samples into the proper exposure groups.

IMPACTS/OUTCOMES/CONCLUSIONS: Identification of these peptides/proteins and their inter-relationships should provide new insights into the biological effects of

nanomaterials, and the potential differences in potencies associated with changes in the structure and functionalities of such materials. The knowledge on association between toxicity mechanisms and physicochemical properties can impact on formulations that would result in safer nanomaterials, therefore permitting their use without any health concern especially, in the field of medicine.

1.18 Development and Validation of a Method for Speciation of Mercury in Hair by Cold Vapor Atomic Fluorescence Spectroscopy (CVAFS)

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SUMMARY: This presentation will demonstrate the development and validation of an automated method to measure total and inorganic mercury in hair samples by Cold Vapor Atomic Fluorescence Spectroscopy (CVAFS). The presentation will explain how the performance of the CVAFS method was evaluated.

OBJECTIVES: Develop and evaluate an automated method for the speciation of mercury in hair by measuring total and inorganic mercury by CVAFS to replace an existing automated method using cold vapour atomic absorption spectrometry (CVAAS), for which the instrument has been decommissioned. The new method should have comparable performance for throughput, precision and accuracy and have lower limit of detection for both total and inorganic mercury.

DESIGN: Manufacturers of CVAFS instrument were evaluated by the results of their analysis of blind samples using the basis of our existing CVAAS method. After selection of the CVAFS system the method was developed to obtain the desired performance. Method validation was achieved by using certified reference material, interlaboratory studies, correlation with existing techniques and the use of control charting.

RESULTS: Presentation will show results for the evaluation of CVAFS systems and for the correlation with existing CVAAS system.

Preliminary results for the evaluation of the CVAFS method.

	CVAAS		CVAFS	
	Total	Inorganic	Total	Inorganic
precision (%)	10.0	13.9	17	20*
accuracy (%)	2.5	NA	2.0	NA
# samples per day	100	100	50	50
limit of detection (ppm)	0.4	0.3	0.02	0.02

NA: not available, no certified value
*: limited data

IMPACTS/OUTCOMES/CONCLUSIONS: The method for the speciation of mercury in hair by CVAFS has comparable performance than the existing CVAAS method with lower limit of detection.

A method for the speciation of mercury in hair by CVAFS allows the FNIHB Laboratory to continue monitoring the exposure to mercury of First Nations and Inuit and the capability to monitor non-exposed population to generate knowledge of mercury exposure for Health Canada.

1.19 Exploring Cells Used in the Production of Biologics and Their Susceptibility to Prion Infection

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SUIMMARY: Prion proteins have been linked to various neurodegenerative diseases. Our goal is to test various cells and cell lines for their susceptibility to prion infection. This will help in establishing regulatory requirements regarding cells used for the production of biologics and therapeutics throughout Canada.

OBJECTIVES: Two objectives exist: 1) Develop a method to identify susceptibility to prion infection in any cells used in the production of biologics or involved in human therapeutics; and, 2) Establish a more sensitive method to identify prion proteins using the Western blot methodology.

DESIGN: Various cell lines including mouse neuroblastoma (N2a), Chinese hamster ovary (CHO-K) and peripheral blood dendritic cells (PBDCs) were grown in the presence of either scrapie or murine-adapted bovine spongiform encephalopathy (BSE) prion proteins.

Using a technique known as cell blotting, cell lines were tested for their susceptibility to infection by being grown on cover-slips, transferred to a PVDF membrane, treated with proteinase K (to remove all non-infections prions) and probed with anti-prion antibodies.

In cell lines that demonstrated signal via cell blotting, Western blotting was performed to confirm and visualize the typical forms of infectious prion proteins (three bands ranging from 20-30KDa).

Samples were treated with TCA precipitation to determine if this would increase sensitivity when performing the Western blot.

OUTPUTS/RESULTS: Preliminary data demonstrate that cell lines N2a, PBDC's and CHO-K cells showed the potential for infection to murine-adapted BSE infections via cell blotting. N2a cells were confirmed to be susceptible to scrapie infection when tested with both the cell blot and the TCA/Western blot methods. Optimization of the newly developed TCA precipitation protocol demonstrated a 10-fold increase in sensitivity when used for Western blotting, compared to the more commonly used methanol precipitation technique.

IMPACTS/OUTCOMES/CONCLUSIONS: The data collected from this *in vitro* study demonstrate two things: 1) that some cell lines and biologics may in fact be susceptible to prion infections; and, 2) that TCA precipitation used in conjunction with Western blotting is an effective, simple and inexpensive method to increase the sensitivity of a Western blot when testing for prion proteins.

1.20 Activity of Traditional Chinese Medicines on Cytochrome P450 Family-mediated Metabolism

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SUMMARY: Traditional Chinese Medicines (TCMs) may affect drug metabolism, potentially affecting the safety and efficacy of the drug or other TCMs.

OBJECTIVE: This study was undertaken to characterize the effect of TCMs on cytochrome P450 family 3A4, 2D6 *1/*10, 19-mediated metabolism.

METHODS: TCMs were obtained from commercial outlets: Extracts - Chrysanthemum Flower (CF); Kudzuvine Root (*Radix Puerariae*); Isatis Root (*Radix Isatidis*); Du Huo (*Radix Angelicae pubescentis*); Chai Hu (*Radix Bupleuri*); Indian Bread with Hostwood (IHB, *Sclerotium poriae* Circum Radicem Pini); Dang Shen (*Radix Codonopsis*); and tablets - Thunder God Vine (TGV, *Triptergium wilfordii*). TGV extracts were also prepared from source material. Go Ji (Wolfberry, *Lycium barbarum*) was wild crafted locally. Aqueous and methanol extracts (5, 25 mg/ml in DW and 5 mg/ml in methanol) were prepared fresh and examined for their effect on CYP 3A4, 2D6*1/*10-mediated metabolism was determined using *in vitro* bioassays. TGV was further examined against CYP 19. Aliquots of traditionally prepared Go Ji tea were also incubated alone with CYP 3A4 and analyzed by HPLC.

RESULTS: Our data indicates that methanolic extracts of both TGV samples had greater than 90% inhibition of CYP 3A4 and CYP 19, whereas low (0-30%) to high (60-90%) inhibition was generally detected with the other TCMs. Of note was 25 mg aqueous extracts of CF (~58% inhibitory effect on 2D6 *1 and *10). HPLC analysis detected several new peaks from Go Ji after CYP 3A4 incubation.

CONCLUSIONS: The majority of the traditional medicines examined would not be expected under normal conditions to affect drug safety and efficacy; however, some products such as Go Ji, CF, IHB and TGV have pharmacological properties that may affect clinical safety and efficacy of many drugs. Further studies are warranted against a wider range of cytochrome P450 isozymes and to determine if these effects are clinically significant.

1.21 The Development of Regulatory Policy on the Use of Human Embryos for Research under the *Assisted Human Reproduction Act* (AHRA)

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SUMMARY: This poster will review health and safety risks and ethical issues, and the policy options to address such concerns, for the use of in vitro embryos for research under the *Assisted Human Reproduction Act* (AHRA).

The use of human embryos to derive embryonic stem cells may be of tremendous potential value for the treatment of many diseases. In Canada, human embryo research is governed by various authorities and more recently by the AHRA. Health Canada has a mandate to develop the components of the regulatory framework under the AHRA and to establish an Agency that will license and enforce the regulations.

OBJECTIVES: To provide analysis of the health, safety, and ethical risks and to present issues and explore policy options for the use of *in vitro* embryos for research under the AHRA.

DESIGN: Research and analysis of the scientific and ethics literature, and existing international policy documents on the use of human embryos for research purposes will be performed.

OUTPUT/RESULTS: The creation of human embryos is permitted under the AHRA to create a human being, to improve or provide instruction in assisted reproduction procedures. Although *in vitro* embryos cannot be created specifically to derive human embryonic stem cells under the AHRA, excess human embryos that were created for the purpose of creating a human being can be donated for research after having written informed consent from the gamete and embryo donors. Several issues will be addressed: the qualifications that an individual must have in order to undertake research involving an *in vitro* embryo; defining the broad categories of research objectives for which licenses can be granted; and the development of a licensing scheme for embryo research to ensure that the use of *in vitro* embryos is carried out in a manner consistent with the guiding principles of the AHRA.

IMPACTS: The development of regulatory policy for the use of *in vitro* embryos for research under the AHRA will address health, safety, and ethical risks.

1.22 Defining the Tropism of *Listeria monocytogenes* using a Comparative Genomics Approach

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SUMMARY: A serious disease known as listeriosis is often manifested by ingestion of foods contaminated with the pathogen *Listeria monocytogenes*. DNA chips developed specifically for *L. monocytogenes* have been constructed to identify bacterial factors potentially involved in the organism's ability to survive in certain foods, environments and animal/human hosts.

OBJECTIVES: The purpose of this project is to investigate genomic differences in clinical, environmental and food isolates of *L. monocytogenes*, including those attributed to the misrepresentation of the 3 (of possible 12) serovars most often detected in human cases of listeriosis. The mixed-genome array approach is also targeting genomic markers that contribute to the tropism of the organism for a specific niche.

DESIGN: Three different hybridization techniques were used to elucidate genomic differences in *L. monocytogenes* isolates: mixed-genome DNA microarrays, dot-blot hybridizations and suppressive subtractive hybridization (SSH). PCR and bioinformatic sequence analysis were used to further investigate specific genomic sequences identified by the genomic DNA microarray and dot-blot hybridizations.

OUTPUTS/RESULTS: Several genomic features have been identified as present, absent or significantly different in food, environmental and clinical isolates using in-house constructed mixed genome DNA microarrays and dot blot hybridization. Sequences that appear as present or absent among genomes tested include homologies to glucarate dehydratases, reverse transcriptase from retron ec67 and conserved, hypothetical proteins. A sequence with homology to a glycosyl transferase appears to be absent or significantly different in *L. monocytogenes* serotypes 1/2a, 1/2c and 3a. These serotypes are predominant in *L. monocytogenes* strains isolated from food sources, suggesting a potential role for this genome feature in the adaptation of the organism to the food environment. While SSH was able to identify genomic differences between *L. innocua* and *L. monocytogenes*, it currently has not been able to identify the differences in *L. monocytogenes* isolates seen in the array results.

IMPACTS/OUTCOMES/CONCLUSIONS: These techniques will provide insights into the mechanism(s) by which clinical, environmental, and food strains are able to adapt and survive in different niches, allowing for identification of host and/or bacteria-specific markers required for infection to occur. Results will aid in refining the Health Canada *Listeria* policy for ready-to-eat foods.

1.23 Dietary Soy Protein and Isoflavones have Differential Effects on Hepatic ATPase Activity in Rats

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SUMMARY: ATPase/ATP synthase is an important enzymatic complex responsible for energy homeostasis and normal physiological performance. We showed that dietary soy protein modifies ATPase/ATP synthase protein phosphorylation status and affects its enzymatic activity in rats, suggesting an important effect of consumption of soy foods like soy-based infant formulas on energy homeostasis.

OBJECTIVES: Health safety and nutritional quality of consuming soy foods such as soy-based infant formulas and soymilk are not fully assessed. A proper functioning of ATPase/ATP synthase is essential for energy homeostasis and normal physiological functions. This study has used ATPase/ATP synthase as a biomarker to examine the potential effects of different soy components (protein and isoflavones) on hepatic energy metabolisms.

DESIGN: In Expt. 1, Sprague-Dawley rats were fed diets containing either 20% casein or 20% alcohol-washed soy protein isolate (SPI) with or without supplemental isoflavones (ISF, 250 mg/kg diet) for 70 d. In Expt. 2, weanling Sprague-Dawley rats were fed diets containing 20% casein with or without added ISF (50 mg/kg diet) or 20% SPI for 90 d. ATPase/ATP synthase protein content and isoelectric points (pI) as well as mitochondrial ATPase activity were measured.

OUTPUTS/RESULTS: Hepatic mitochondrial ATPase activity was significantly higher in the rats fed SPI than in those fed casein (103.74 ± 15.25 vs. 54.49 ± 8.97, $p < 0.05$). Addition of ISF to SPI eliminated the action of SPI. ATPase/ATP synthase β protein contents in the liver were unchanged; however, the two dimensional patterns (or pI) were different among dietary groups. The rats fed SPI or SPI plus ISF demonstrated three new protein spots that are believed to be dephosphorylated isoforms of ATPase/ATP synthase β protein. Dephosphorylation of hepatic mitochondrial proteins from the rats fed casein with alkaline phosphatase produced the same ATPase/ATP synthase β patterns as observed in the SPI-fed rats, and significantly elevated the ATPase activity.

IMPACTS/OUTCOMES/CONCLUSIONS: These results suggest that consumption of soy-based products may have different impacts on energy homeostasis compared to milk protein. This information is important for Health Canada in the evaluation of related health claims for soy products, and may be critical in the safety management of soy foods such as soymilk and soy infant formulas.

1.24 Identification of Optimal Sample Processing Method(s) for fingerprinting of Rat Plasma Proteom

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SUMMARY: Rat plasma proteome changes were analyzed by matrix-assisted laser desorption ionization-time of flight-mass spectrometry. Plasma samples were purified using different methods either by magnetic bead separation or molecular weight cut-off filtration. These methods yielded complementary mass spectral information, suggesting the necessity for multiple methods for increased coverage of plasma proteome.

OBJECTIVES: The objective here was to identify a reliable sample processing method that will allow fast screening of peptide/protein profiles in rat plasma samples with increased coverage that can be applied towards pattern recognition approach and to identify markers of effects for environmental toxicology studies.

DESIGN: Plasma from Sprague Dawley rats were processed using either magnetic beads, based on hydrophobic interaction chromatography or weak cation exchange solid-phase extraction techniques or via molecular weight cut-off filtration (10 kiloDalton (kDa), 30 kDa). All samples were spotted directly on Anchorchip® targets (Bruker Daltonics) with saturated alpha cyano-4-hydroxy-cinnamic acid as matrix. Mass spectrometry detection was in linear mode (range, 0.8-10 kDa). All instrument conditions were held constant for all analyses.

OUTPUTS/RESULTS: Analytical reproducibility was comparable for all methods. Ten kDa molecular weight cut-off filtration gave a wide range of mass/charge (m/z) coverage (1 to 5 kDa) with more analytes seen < 3 kDa. Sample processing using magnetic beads based on hydrophobic interaction chromatography (MB-HIC18) exhibited comparably fewer m/z values < 2 kDa and four dominant m/z values (1949.6, 2791.6, 3511.1 and 7019.6 Da) that are not seen in the 10 kDa molecular weight cut-off filtration method. The magnetic beads based on weak cation exchange solid-phase extraction technique gave dominant peaks at m/z 2792.4 and 4966.8 Da.

IMPACTS/OUTCOMES/CONCLUSIONS: In conclusion, sample preparation plays a critical role in proteomic analyses. Although, molecular weight cut-off filtrations give enhanced protein coverage and are optimal for protein profile fingerprinting approach, the complementary nature of information obtained through magnetic beads methods will provide additional information on proteome analysis. This information is vital for screening for patterns or identification of peptide/protein markers of toxicity-related biological effects. Additional results will be presented at the forum.

1.25 On the Wrong Track: Deficiencies in Clinical Trial Design for Biologics

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SUMMARY: The Clinical Evaluation Divisions in CERB/BGTD are responsible for assessing safety and efficacy data to support Canadian market authorization for biologics. Although manufacturers are aware robust clinical trial data are essential for granting authorization, critical issues are frequently not addressed in submitted trials, resulting in negative decisions by reviewers.

OBJECTIVES: Due to the nature of patient populations and diseases to be treated, many clinical trials submitted to CED/CERB are employing clinical trial designs other than 'gold standard' robust Phase-III double-blind placebo-controlled clinical trials.

Objectives of this project were to describe the:

1. Deficiencies in clinical trial design,
2. Qualities of poorly- and well-designed studies, and
3. Evidence-based decisions for biologic submissions.

Common issues for reviewers have been identified and are discussed, and examples of unacceptable trial designs and common qualities of well-designed studies are explored.

RESULTS: The challenges presented by biologic clinical trials are recognized and discussed. CED bases its decisions on evidence collected from clinical trials; deficiencies in trial design result in negative decisions.

Examples of non-'gold standard' clinical trials assessed included:

a) open-label,
b) control patients crossing over early to treatment with the test biologic,
c) historical controls,
d) short duration, and
e) small trials.

In addition to being intrinsically less robust, some of these trial designs were flawed or were applied improperly, and lacked critical data. Such deficiencies resulted in negative decisions by the reviewers, a Notice of Non-Compliance (NON) or a Notice of Deficiency (NOD) being issued, and market authorization being withheld.

CONCLUSIONS: We in the CED understand the balance we must strike between ensuring biologics are available to the Canadian public in a timely fashion, and ensuring through a thorough, knowledgeable, and timely review process that their clinical benefits outweigh their risks. Sponsors have been encouraged to have pre-submission meetings with CED to discuss clinical trial design and other related

issues, which should decrease the number of negative decisions and ensure robust clinical trial data.

1.26 *In Vitro* Assays to Predict Pathogenicity of Selected Pseudomonas Strains Used in Biotechnology

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SUMMARY: Several human and murine cell lines were tested for their ability to distinguish between harmful and safe bacteria intended for use in biotechnology. For this, a combination of immune indicators, cytotoxicity assays and bacterial killing tests were used to reveal potentially unsafe strains.

OBJECTIVES: Under the *Canadian Environmental Protection Act* (1999), screening level risk assessments are required for Domestic Substance List (DSL) microorganisms. Because certain types of mammalian cells might be very effective in such tests, the aim of this study was to determine if any of the six selected mucosal and immune cell lines could predict the toxicity and pathogenicity potential of DSL-listed *Pseudomonas* strains.

DESIGN: All cells were from the American Type Cell Collection (ATCC). Human (HT29, HL60, MOLT4, CL) or murine (J774A, and RAW264.7) cells were exposed for 2 to 24h to strains of *P.aeruginosa* (Pa) (31480, 700370, 700371), *P.fluorescens* (Pf) (13525, 31483), and *P.stutzeri* (Ps) (17587). Levels of cytokines, cytotoxicity, nitric oxide (NO) production and bacterial killing capacity of these cells were measured using multiplex bead /cytokine arrays, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, Griess method and phagocytosis/clearance assay, respectively.

OUTPUTS/RESULTS: Depending on the test cell, all three Pa strains caused expression of specific cytokines, while Pf and Ps strains did not. The Pa strains also induced high (31480) or moderate (700370 and 700371) levels of NO by J774A cells. In 24-h exposures Pa strains caused 20-50% cytotoxicity of all test cell lines, while cytotoxicity from Pf and the Ps strains was 0-10%. Only J774A cells showed high killing capacity towards all bacteria strains, 70-80% in 4-h exposures. However, for Pa strains this capacity was reduced substantially in 6-h assays, possibly due to bacterial growth.

IMPACTS/OUTCOMES/CONCLUSIONS: The *in vitro* results showed that DSL Pa strains, and especially 31480, were more toxic and immunogenic than Pf or Ps strains. This screening method enables a prioritization of bacterial strain for *in vivo* exposure tests. Further efforts focus on *in vivo* validation of the tests and augmentation of parameters to enhance this initial screening system and to further reduce the need of animal use.

1.27 Consumer Exposure Scenarios in the Health Canada Existing Substances Program

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SUMMARY: The Ministers of Health and the Environment recently completed the "categorization" (priority setting) of approximately 23 000 substances on the Domestic Substances List, which will require subsequent screening assessment. Health Canada has developed an approach to estimate human exposures to consumer products in order to further prioritize the substances that were categorized.

OBJECTIVES: To develop an initial first tier approach to quantitatively estimate the maximum plausible exposure to individuals of the general population to a chemical substance through the use of consumer products (e.g., cosmetics, household cleaners, etc.). These quantitative estimates can be used to set priorities for screening assessment of existing substances and, in future, if further refined, could be used to estimate human exposures in screening assessments. This exercise was performed in order to make conservative estimates of human exposure to chemicals contained in consumer products.

DESIGN: The poster will outline the approach used which involved compiling and comparing existing consumer product exposure models, such as ConsExpo (RIVM) and CEM (EPA), with the proposed Complex Exposure Tool (ComET) approach, developed by LifeLine and Health Canada. The various exposure factors (e.g., room size, amount of product used, number of events per year, etc.) found in these models and from other sources were also compiled and compared. The most conservative, but realistic factors were selected to be used in the first tier approach.

OUTPUTS/RESULTS: This exercise revealed that most of the models provided the same results when using the same exposure factors. The Existing Substances Division decided that a standard set of algorithms for each route of exposure could be used for all of the various consumer product scenarios. Use of the most conservative exposure factors available ensures that a worst-case exposure estimate is obtained for all age-groups. This iterative approach addresses the most common use/product categories and the most conservative default values first, and is both transparent and defensible.

IMPACTS/OUTCOMES/CONCLUSIONS: The approach can be used to further prioritize substances that may require screening assessment (i.e., identify non-priorities or move substances forward for further work). It has also produced opportunities for collaborative developments both within the department and internationally.

1.28 Substance Profiling for Categorization and Screening Health Risk Assessments of Existing Substances Under the *Canadian Environmental Protection Act* (CEPA)

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SUMMARY: The Ministers of Health and the Environment recently completed categorization of approximately 23 000 substances on the Domestic Substances List. Categorization identified approximately 4300 substances requiring a screening assessment. Health Canada developed Use Profiles and a robust search strategy to efficiently identify relevant data to further prioritize and assess chemical substances.

OBJECTIVES: Use Profiling is an early stage in a tiered approach to prioritization and assessment of substances. It increases efficiency by investing only as many resources as are required to set a substance aside as a non-priority, and it delineates the focus of the screening level risk assessment stage. It is a method of gathering and tabulating preliminary information on a substance using electronic and printed information sources including common reference works.

DESIGN: The poster will outline what a Use Profile is, the type of information contained in the profile, how the profiles are used, and some of the advantages and disadvantages of this product.

OUTPUTS/RESULTS: A document that outlines some of the basic information about a substance (e.g., physical and chemical properties, uses, releases) that will aid in exposure assessment. Completing Use Profiles has led to the development of a robust search strategy, which aids in the identification of relevant data for various types of substances. It is also an important first step in identifying the key consumer products that will be used to model human exposure which will aid in the decision of whether a substance is set aside or will require further assessment.

IMPACTS/OUTCOMES/CONCLUSIONS: Provides an efficient first step in the assessment process and may be used for prioritization in the future. It has become an important resource for the Chemical Management Plan and is being used by risk assessors and risk managers at Environment and Health Canada.

1.29 Comparative Gene Expression Analysis in Developing Rat Brain Exposed to Mixtures of Methyl Mercury, Polychlorinated Biphenyls and Organochlorine Pesticides

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SUMMARY: Microarray analyses were conducted in developing rat brain to compare the impacts of environmentally relevant contaminant mixtures. This study revealed gender-modulated response to neurotoxicological insults and interaction between mixture's components. This illustrates the potential of genomic methods to characterize the physiological response following exposure to chemical mixtures.

OBJECTIVES: Human populations are continuously exposed to complex mixtures of contaminants. The effects of such exposure on the developing brain transcriptome are poorly characterized. The main objective of this study was to compare the transcriptional perturbations induced by the Northern Contaminant Mixture (NCM; derived from the blood contaminant profile of Canadian Arctic populations) to the effects of its main components (Methylmercury, Polychlorinated Biphenyls and Organochlorine pesticides) administered separately, in the post-natal rat brain.

METHODS: Sprague-Dawley rat dams were dosed daily from gestational day (GD)1 to post-natal day(PND) 14 with NCM (5mg/kg body weight (bw)), Methylmercury (2 mg/kg bw), Polychlorinated Biphenyls (1.1 mg/bw) or Organochlorine pesticides (1.9 mg/kg bw). cDNA microarrays were used to study gene expression in the cerebellum of male and female offspring at PND 14. Expression profiles were compared among treated and control groups. Select genes were validated with qPCR in cerebellum and in hippocampus.

RESULTS: Microarray analysis identified 50 genes perturbed by toxicant exposure, which included genes involved in neuronal migration (*Sparcl*), differentiation (*Tspan 5*) and myelination (*Mbp*). Comparison of gene expression revealed that 10% (5/50) of these genes were common to both sexes and the effects of NCM were lesser than its sub-components administered separately. qPCR gene expression analysis in cerebellum and hippocampus confirmed these observations.

CONCLUSIONS: Our results indicate that: i) gender is a crucial biological variable influencing genomic response to environmental contaminants; and, ii) contaminant co-exposure significantly masks the effects of individual components. These observations suggest that exposure to environmental contaminants may pose gender-specific health risks, and that extrapolation of genomic response to a specific mixture based on data obtained from single compound exposure may not always be appropriate.

1.30 A Novel System for Simultaneous Identification and Genotyping of Norovirus in Food Samples

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SUMMARY: Noroviruses (NoVs) account for up to 90% of all human epidemics of non-bacterial gastroenteritis in Europe and in North America. The development of a universal, rapid and easy-to-use method for the simultaneous identification and characterization of NoVs was achieved with the NoroChip version 3.0.

OBJECTIVES: Viral infections passing through the gastrointestinal tract cause millions of illnesses in North America each year, with the source and epidemiology of viral outbreaks not always pinpointed. The proposed research aims at developing a rapid and universal viral microarray-based system for the simultaneous detection and molecular characterization of NoVs by coupling amplification of nucleic acid to subsequent microarray analyses.

DESIGN: Target viral RNA, extracted and detected using reverse-transcriptase polymerase chain reaction (RT-PCR), generated a fragment of 2.4 kb that was labelled with a Cy3 fluorescent dye and hybridized against the NoroChip V3.0. NoroChip V3.0 is an oligonucleotide-based array platform designed to contain representatives of all known NoV genotypes. The hybridization results confirmed the isolation of norovirus (i.e., RT-PCR), via the use of broadly reactive features. NoV sub-genogroups were then delineated using strain specific features. Identification and molecular characterization of NoVs was achieved in as few as 28 hours.

RESULTS/OUTPUTS: The NoroChip V3.0 has been printed and standard protocols developed for each step of the analysis, including the generation of a 2.4 kb RT-PCR amplicon from a variety of NoV strains with high genetic variability. Products from 15 NoV samples have been labelled, hybridized and analyzed in triplicate. Analyses of hybridization patterns indicate that unrelated strains have unique hybridization profiles, and that different isolates of the same strain have similar profiles. Algorithims and bioinformatic analyses are being optimized into Standard Operating Procedures (SOPs) so that field laboratories using this technology may be able to quickly and objectively analyze data.

IMPACTS/OUTCOMES/CONCLUSIONS: As reporting systems for viral infections lag significantly behind their bacterial counterparts, the molecular epidemiological data obtained from this work will be useful in future risk assessment studies. This microarray system provides a valuable tool for both routine surveillance and outbreak investigation of food and environmental samples.

1.31 A Multi-Endpoint Study of the Effect of Peroxisome Proliferators on Human Hepatocytes - Preliminary Report

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SUMMARY: There are uncertainties regarding the risk assessment of substances in the PPARa agonist category because of: 1) the relative refractoriness of human liver to peroxisome proliferation; and, 2) the lack of information on other more recently reported PPARa-dependent effects (energy metabolism, oxidative stress). We have designed multi-endpoint, human hepatocyte based studies to address these issues.

OBJECTIVES: To provide relevant data for risk assessment, the following toxicological issues need to be resolved:

1) Current opinion is that rodent peroxisome proliferation data maybe of little relevance in human risk assessment. However, only a limited number of chemicals have been tested. It is uncertain if and to what extent new PPARa agonists affect humans.

2) Emerging data indicate that PPARa agonists interfere with energy metabolism in rodents through suppression of the tryptophan-NAD pathway. It is not known if this effect also occurs in human.

3) It was not clear if PPARa agonists cause oxidative stress and related cellular toxicity in human.

DESIGN: Cell-based toxicity studies with the following activities have been initiated:

- Conduct literature reviews, select chemicals of interest with PPARa agonist property;
- Select and validate key endpoints; and
- Conduct toxicity studies on human and rodent hepatocyte primary cultures.

OUTPUTS/RESULTS:

- Test chemical selected: Di(2-ethylhexyl) phthalate (DEHP), perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS). Clofibrate (CLO) used as positive control.
- Key endpoints selected and validated:

1. Palmitoyl Co-A oxidase activity (endpoint for peroxisome proliferation)
2. N-methylnicotinamide (NMN) (endpoint for tryptophan-NAD pathway)
3. Thiobarbituric acid-reactive substances (TBARS) (biomarker of oxidative stress).

- Preliminary results indicated that human hepatocytes were very weakly responsive to CLO (1mM) with approximately 25% increase in palmitoyl CoA oxidase activity, and non-responsive to DEHP (5 mM), PFOS (0.1 mM) and PFOA (0.1 mM). In contrast, CLO, DEHP and PFOA produced approximately

70%, 67% and 260% increase in palmitoyl CoA oxidase activity in rat hepatocytes, and PFOS was without effect.

IMPACTS/OUTCOMES/CONCLUSIONS: Human hepatocytes were successfully used in cellular toxicity studies of PPARa agonists. DEHP and PFOA induced peroxisome proliferation in rat but not in human hepatocytes. PFOS was without effect on both species. The concentrations tested were at least 300 times higher than those found in blood of exposed individuals. Ongoing studies on biomarkers of energy metabolism (NMN) and oxidative stress (TBARS) will provide a more complete picture of the effects of these chemicals on humans.

1.32 The Canadian Alcohol and Drug Use Monitoring Survey (CADUMS): The Future of Alcohol and Other Drugs Surveillance in Canada

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SUMMARY: The presentation will cover the history of surveying alcohol and other drugs in Canada; the challenges of implementing an ongoing survey; the consultation process with stakeholders; the set of indicators; and, what the future holds for a strategy of surveillance across Canada.

OBJECTIVE: This presentation covers the history of surveying alcohol and other drugs in Canada; the challenges of implementing an ongoing survey; the underlying consultation process; the set of indicators measured; and, the survey's position and role as part of a surveillance strategy of alcohol and other drugs.

To date, the monitoring of alcohol and other drugs in Canada has been conducted through occasional repeated cross-sectional surveys (1989, 1994 and 2004). Relying on disconnected surveys has caused methodological problems (database compatibility), and conceptual difficulties (examination of trends or incidence), has posed management challenges (high variations in budget and human resources) and has contributed to gaps in the monitoring of alcohol and other drug use in Canada.

DESIGN: To support the collection of ongoing, reliable data, Health Canada recognized the necessity to develop a dedicated, ongoing survey. Work has been initiated mid-2006 for the development of the Canadian Alcohol and Drug Use Monitoring Survey (CADUMS) with the objective of implementation in FY 2007/08. The CADUMS objective is to obtain data about the prevalence, patterns of use, and harms associated to alcohol and other illicit drugs in a timely, reliable and continuous basis.

It has been recommended that the CADUMS be an ongoing general population telephone survey employing Random Digit Dialling (RDD) and Computer Assisted Telephone Interviewing (CATI) to interview 10 080 Canadians annually. The sample frame will cover Canadians 15 years and older distributed equally across the 10 provinces. The CADUMS is developed under the leadership of Health Canada with advice from an expert advisory committee comprised of representatives of stakeholders from across the country.

OUTCOME: From past to future, the current presentation will showcase the CADUMS from its roots to its present state. This poster is a summary of an oral presentation given at the 2007 International Council on Alcohol and Addictions (ICAA) conference.

1.33 Examination of Nitrosylation on Furan Food Contaminant Mutagenic Activation Using a Modified Ames Salmonella Test

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SUMMARY: Several furan compounds are formed in food during cooking or heating. The mutagenicities of the major contaminants were characterized with and without reaction with acidified sodium nitrite, a common food preservative, using a potentially more sensitive version of the Ames assay. Mutagenic species were detected in several reaction mixtures.

OBJECTIVES: Several furan-related contaminants have been isolated from cooked or heated foods, apparently arising through reactions of amino acids, fatty acids, and ascorbic acid. When examined in the Ames *Salmonella* test, furan was previously shown to become weakly mutagenic when incubated in the presence of acidified sodium nitrite, a common food preservative. Native and nitrosylated furans were therefore further examined using an Ames assay made more sensitive for some classes of mutagenic nitro-containing chemicals by incorporating *Salmonella* strains expressing nitroreductase and acetyl CoA:N-hydroxyarylamine O-acetyltransferase activities.

DESIGN: Furan, as well as 2- and 3-methyl, 2-ethyl, and 2-pentyl derivatives were nitrosylated by reaction with sodium nitrite in acetic acid buffer, pH4 and tested for mutagenicity in an Ames *Salmonella* test incorporating the frameshift sensitive strains YG1020 (parental control), TY1021 (nitroreductase+), YG1024 (acetyltransferase+) as well as the corresponding base-pair sensitive strains YG1025, YG1026 and YG1029. All chemicals were tested +/- rat liver S9 for metabolic activation.

OUTPUTS/RESULTS: While all native compounds were negative as frameshift mutagens when tested up to 20 mg/plate, nitrosylated furan, 3-methylfuran and 2-pentylfuran resulted in severalfold increased mutagenic activity at 1-10 mg/plate. The presence of acetyltransferase enhanced nitrosylated 2-pentylfuran mutagenicity 2-4-fold, but otherwise nitroreductase or acetyltransferase produced minimal effect. Furan, 3-methylfuran, 2-ethylfuran and 2-pentylfuran were weak base-pair mutagens; however, nitrosylation again increased mutagenic potency severalfold, with 200 µg/plate nitrosylated furan and 3-methylfuran increasing revertant colony formation significantly. Nitroreductase activity increased base-pair assay sensitivity for most nitrosylated compounds but the presence of acetyltransferase had minimal effect.

IMPACTS/OUTCOMES/CONCLUSIONS: Furans are not only found in food as unwanted byproducts but several related compounds are also added to various foodstuffs as flavour enhancers. These results demonstrate that dietary interactions can influence the mutagenic activation of food-associated chemicals and that such approaches would expand the usefulness of a genetic testing regimen.

1.34 Impact of Systems Biology on Drug Development and Regulation in Omics Era

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SUMMARY: This study examined the regulatory impact in Canada due to the development of drugs based on the high-throughput technologies, such as mapping protein-protein interactions in human cells and gene expression profiles.

OBJECTIVES: To assess the regulatory impact on drug development of high-throughput technologies, such as mapping protein-protein interactions in human cells and gene expression profiles, given that there is, currently, a lack of relevant policies, guidelines and regulation pertaining to this issue for the industry, drug reviewers and regulatory staff in Health Canada.

DESIGN: The scientific literatures on human protein-protein interaction mapping generated by high-throughput technologies and on gene expression profile for a predictive drug response that were performed were assessed. The impact on drug development and regulation in the “omics era” is reviewed.

OUTPUTS/RESULTS: The first large-scale study of protein-protein interaction mapping in human cells carried out by using IP-HTMS (Immunoprecipitation and high-throughput mass spectrometry) generated a dataset from 6463 interactions between 2235 distinct proteins. This was cross-validated using previously published and predicted human protein interactions. Identification of predictive gene expression profiles using high-throughput methodologies, were performed on various cancers and other diseases to help predict a therapeutic response and allow selection of patients who would benefit most from treatment.

IMPACTS/OUTCOMES/CONCLUSIONS: High-throughput dataset analysis forms a basis to understand the operation of complex biological systems, to develop predictive models of human disease and predict drug response. Health benefits for Canadians via gene expression could include a predictable treatment response and reduction of risk related to adverse drug reactions. Predictability would have a significant impact on the review of products by defining how such information should be included in the benefit/risk evaluation of a drug and on how this research should be included in the Product Monograph. Therefore there is a need to highlight these deficiencies and provide guidance for industry and reviewers to evaluate the data generated using these techniques in both animals and humans. The omics era will continue to pose such challenges for the regulatory system.”

1.35 Comparison of Transcriptional Responses of Macrophage-like Cells During Phagocytosis and Infection by *Bacillus cereus* (Bc) Group Organisms

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SUMMARY: For safety assessment of microbes for environmental applications, we are developing a mouse cell test, which measures genetic responses during microbe exposures. Exposures of two immune system-related cell types to a particular bacterium showed one type is more responsive and useful in tests than the other.

OBJECTIVES: We are developing genomic-based methods for in vitro exposure tests of *Bacillus cereus* (Bc) group biotech-organisms covered by the *Canadian Environmental Protection Act* and *Pest Control Products Act*. We have observed that the mouse macrophage-like cells (J774A.1) and monocyte/macrophage-like cells (RAW264.7) differ in the amount of phagocytosis of Bc group spores in 3h exposures. With longer exposures, both cell lines are unable to prevent spore outgrowth and are killed. Our goal is to characterize the transcriptional responses of the two cell lines to clarify their use in toxicity tests.

DESIGN: Triplicate 90 minute cell exposures to Bc spores (spore:cell ratio of 1), or fresh culture medium, were carried out to allow for maximal spore uptake. Total RNA was extracted, converted into cDNA and PCR profiled by a panel of 89 toll-like receptors, inflammatory response and housekeeping genes. The fold difference in transcript levels between spore and control exposures were calculated by the comparative Ct method and the T-test statistic was used to identify genes whose transcript levels were significantly different.

OUTPUT/RESULTS: Compared to controls, RAW264.7 cells exposed to Bc spores for 90 min produced a greater than 2 fold difference in levels of transcripts for pro-inflammatory receptor (Tnf, Il1a, Il1b) and immune response genes. In contrast, J774A.1 produced very few genes with greater than 2 fold difference in transcript levels (Btk, Pglyrp, Tlr2).

IMPACTS/OUTCOMES/ CONCLUSIONS: This analysis shows that the two immune-cell lines differ in response to Bc spores at the transcript level. In order to evaluate the potential gene expression trends, the exposure study will be expanded to include additional time points. The comparison of molecular changes in the two cells lines will highlight differences in how the cell lines recognize and phagocytize Bc group spores and will provide more comprehensive data for screening-level risk assessment of microbes.

1.36 The Development of a Quantitative Approach for the Risk Assessment of Compounds Causing Allergic Contact Dermatitis Provides an Evidence-Based Framework Supporting Risk Assessment and Management of New Substances

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SUMMARY: Risk assessments of new substances causing allergic contact dermatitis have not previously been able to consider dose-response or relative potency because of some limitations of the available animal models. The acceptance of a new mouse model has allowed the consideration of these factors using an approach that we describe.

OBJECTIVES: Allergic contact dermatitis (ACD) is an immune-mediated inflammatory skin reaction induced by dermal exposure to some chemical substances. In the past, methods to determine if a substance causes ACD have been limited to guinea pig tests that do not provide indications of dose-response, thresholds or potency. Many risk assessments have not previously been able to consider the existence of thresholds for ACD, which may have lead to regulatory action where none was warranted. The development of a new model for ACD, the mouse local lymph node assay (LLNA), has provided a much more quantitative measure of potency and has demonstrated that thresholds for ACD clearly exist. The purpose of the current work is to develop a means to integrate dose-response and potency data from the LLNA into new substance risk assessments for ACD as well as to describe risk management approaches for new substances found in products available to the public that are likely to cause ACD.

DESIGN: We have integrated the most salient aspects of multiple approaches to design a model framework for the quantitative risk characterization of ACD for new substances.

RESULTS: Based on potency measures from the LLNA, a sensitization reference dose (SRfD) can be calculated that accounts for various uncertainties and represents an exposure threshold that is unlikely to cause ACD in an exposed human population. Estimates of the potential for exposure are considered with the SRfD in a standard margin of exposure approach to determine if the substance should be considered for risk management action.

OUTCOMES: This quantitative risk assessment approach for ACD provides a more evidence-based, mechanistic means to assess the risk of ACD induction in a human population exposed to a new substance in a consumer product, which considers both thresholds for induction and relative potency.

1.37 Microelectrode Array Characterization of Pharmacological Responses of Cryopreserved Neonatal Rat Cardiomycytes in Culture: Cardiac Cell Chip

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SUMMARY: Using a multi-electrode array (MEA) system and cryopreserved neonatal cardiomyocytes, the eletrophysiology was monitored in the presence of therapeutic products. The results were consistent with clinical findings supporting the use of this system to determine the potential of health products alone and in combination, to effect safety.

OBJECTIVE/DESIGN: Primary cells in culture are an important tool for investigating physiological mechnisms and responses to pharmaceuticals or toxicants. Cryopreservation of large batches of dissociated embryonic cells has proven to be a valid and convenient substitute for fresh dissections as a source of cells for primary neuronal cultures of cortex, hippocampus, striatum and dorsal root ganglia. We sought to expand on previous reports that benefits of convenience, animals care concerns and economies of scale could be derived from the cryopreservation of neonatal rat cardiomyocytes.

RESULTS: Using our method for isolation and cryopreservation of cardiomyocytes we obtained rat cardiomyocytes that could be subsequently thawed and plated in a variety of multi-well formats and in MultiElectrode Array (MEA) chambers. At intervals from 1 to 5 weeks cultures were fixed and immunostained for alpha-actinin and connexin 43 (Cx43). MEA recordings were made at comparable time points. In some experiments cultures were treated with drugs directed toward gap junction coupling. The cardiomyocytes were observed to beat and to show electrical activity 24 to 48 hours after plating. Correlation of activity across individual electrode points of the MEA and Cx43 immunofluorescence indicated formation of an electrical syncytium. Treatment with isoproterenol and carbachol caused predictable alterations in excitation-contraction.

CONCLUSIONS: These data show that cryopreserved neonatal cardiomyocytes, when thawed and cultured, maintain the important characteristics of freshly cultured cardiomyocytes.

1.38 Compliance Monitoring of Market Authorizations: Products Indicated for Erectile Dysfunction - A Collaborative Approach

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SUMMARY: Compliance monitoring of market authorizations (CMMA) activities are mainly the responsibility of the HPFB Inspectorate but also require the contribution of other directorates across the department and of international partners. A CMMA project on products with an indication for erectile dysfunction and not labelled with prescription drugs will be presented.

OBJECTIVE: To conduct a CMMA project on products with an indication for erectile dysfunction and not labelled with substance(s) found on Schedule F of the *Food and Drugs Act* (i.e., not labelled with prescription drugs as ingredients).

DESIGN: Eight products were purchased by compliance officers in each of the five regions of the country. The samples were submitted to Inspectorate Laboratories and screened for active ingredients and drug related substances using various techniques: e.g., TLC, LC-PDA, LC-MS, LC-MS-MS and GC-MS. Data on lab results and related compliance actions were collected and summarized.

OUTPUTS/RESULTS: Of the 40 samples, 13 were found to contain active pharmaceutical ingredients, medicinal ingredients that may be allowed below certain levels or new compounds. These were given the status “Investigative” or “Unsatisfactory” by the lab, depending on the ingredient and its concentration, and the results were sent to the Natural Health Product Directorate or Therapeutic Products Directorate for health hazard evaluations (HHEs). In one sample a substance was found which appeared to be an analog of tadalafil. The identity of this compound was confirmed by scientists from the Biologics and Genetic Therapies Directorate using LC-MS-MS and NMR techniques. Assistance in the identification was also provided by the US FDA. The compound was quantified by NMR.

IMPACTS/OUTCOMES/CONCLUSIONS: Lab findings of tadalafil in two samples resulted in Type I recalls and the posting of warnings to the Health Canada website. A summary of all the ensuing compliance actions will be presented. CMMA projects require extensive coordination of people with many skill sets but are an important tool to help ensure that health product providers are compliant with the *Food and Drugs Act and Regulations* and that the health of Canadians is protected.

1.39 Dietary Exposure of Canadians to Perfluorinated Carboxylates and Perfluorooctane Sulfonate Via Consumption of Selected Foods

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SUMMARY: Selected foods were analyzed for a number of perfluorinated compounds used in water and grease-repellent coatings. The average dietary intake of these compounds was estimated to be 250 ng/day for Canadians = 12 years old. This estimated dietary intake is of low concern from a public health point of view.

OBJECTIVES: 1) To estimate Canadians' dietary intake of perfluorinated carboxylates and sulfonates; and, 2) To estimate the relative importance of diet as a source of Canadians' exposure to perfluorinated carboxylates and sulfonates.

DESIGN: Fifty-four solid food composite samples collected as part of the Canadian Total Diet Study (TDS) were analyzed for perfluorocarboxylates and perfluorooctanesulfonate (PFOS) using a methanol extraction liquid chromatography tandem mass spectrometry method. Foods analyzed included fish and seafood, meat, poultry, frozen entrees, fast food, and microwave popcorn collected from 1992 to 2004 and prepared as for consumption.

OUTPUTS/RESULTS: Nine composites contained detectable levels of perfluorinated compounds: four meat-containing, three fish and shellfish, one fast food, and one microwave popcorn. PFOS and perfluorooctanoate (PFOA) were detected the most frequently; concentrations ranged from 0.5 to 4.5 ng/g.

IMPACTS/OUTCOMES/CONCLUSIONS: The average dietary intake of total perfluorocarboxylates and PFOS for Canadians was estimated to be 250 ng/day, using results from the 2004 TDS composites and available food intake data. A comparison with published data regarding the intake of perfluorocarboxylates and PFOS via other routes (air, water, dust, treated carpeting, and apparel) suggested that diet is an important source of these compounds. Diet accounted for approximately 60% of the estimated exposure to perfluorocarboxylates and PFOS. There was a substantial margin of exposure between the toxicological points of reference and the magnitude of dietary intake of perfluorinated compounds for Canadians = 12 years old. Separate exposure evaluations and analysis of a wider variety of composites are required for younger Canadians.

1.40 Development of a High-Throughput Assay for Radiation Biological Dosimetry

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SUMMARY: In a mass casualty radiological event, it is imperative to quickly identify exposed individuals for the purpose of medical intervention and first responders who must be restricted from further exposure. The accepted method for biological dosimetry is labour intensive and time consuming, therefore we are developing a high throughput assay.

OBJECTIVES: The dicentric chromosome assay, the internationally recognized standard for radiation biological dosimetry, is sensitive and radiation specific but is extremely time consuming and labour intensive. Therefore, it is imperative to develop alternative techniques to increase the throughput of biological dosimetry in mass casualty events. To address this gap, we are adapting a flow cytometry-based assay that enumerates micronuclei in cultures of immortalized cells for use with primary human lymphocytes.

DESIGN: In this assay, lymphocytes are isolated from whole blood and stimulated with PHA for 48 h. Cells are then incubated with the nucleic acid dye ethidium monoazide (EMA). Whereas healthy cells exclude EMA, the compromised membranes of necrotic and apoptotic cells permit labelling. Subsequent to a photoactivation step that covalently binds EMA to chromatin of dead and dying cells, cytoplasmic membranes are lysed to release intact nuclei and sub-2n particles. Differential staining with SYTOX (a pan-DNA marker) and DiA (membrane marker) is applied to differentiate between nuclei/micronuclei, free metaphase chromosomes and other cellular debris. The isolated nuclei are then analysed by flow cytometry and identified as either whole or micronuclei.

OUTPUTS/RESULTS: Preliminary data have demonstrated that this high-throughput technique displays a highly reproducible dose-response relationship in the 0 - 4 Gy range, with a sensitivity limit of at least 1 Gy. This work is now being validated using microscope scoring of the micronuclei.

IMPACTS/OUTCOMES/CONCLUSIONS: Once fully validated, this assay has the potential to greatly increase throughput for analysis of individual radiation exposures, which would be particularly beneficial for emergency triage purposes.

1.41 Issues with Comparative Genomic Analyses Using a Common Reference Design

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SUMMARY: This study explores the statistical issues for comparative genomics through the application of a common reference design. Commercial reference RNA samples are commonly used in microarray experiments. Establishing the references reproducibility across experiments, laboratories and investigators over time is crucial for their use in normalizing and pooling data across experiments and for their application as microarray quality control standards.

OBJECTIVES: This study investigates the reproducibility of signal intensities from a commercially-available RNA reference standard (Stratagene Universal Reference RNA) when applied to the Agilent mouse oligonucleotide microarray platform across different experiments.

METHODS: Data from a variety of experiments using the Agilent mouse microarray (G4121A) with the Stratagene common reference were collected. The raw absolute signal intensities were normalized using three commonly used techniques for one colour studies. Kolmogorov-Smirnov tests were conducted for all pairwise comparisons on each of the 20 752 probes on the microarray. P-values within each comparison were adjusted using the false discovery rate.

RESULTS: After false discovery rate adjustment, there remained strong evidence that greater than 50% of the probes had signal intensity distributions that were statistically different between experiments. Experiments conducted by the same technician and/or conducted within one year showed minimal differences with no more than 12% of the probes having significantly different underlying distributions. The choice of normalization was also significant; quantile normalization performed the best (least number of significant probes) while dividing by the median had the worst performance when comparing experiments with higher levels of discrepancy.

CONCLUSIONS/ IMPLICATIONS: Data for the vast majority of microarray experiments are made publicly-available. Therefore, the ability to pool data from different experiments is desirable, especially because most microarray experiments have small sample sizes. Using publicly-available data to explore the condition space is a cost effective alternative to generating new data. However, the present study demonstrates that for comparative genomic analyses, the Stratagene Universal reference is not consistent enough to be used to pool experiments even when conducted within the same laboratory. To pool data across experiments to obtain meaningful information will require sophisticated statistical models to explain the potential nesting effects that are present in these studies.

1.42 Should Regulatory Agencies Facilitate Innovation by Facilitating Market Access to Pharmaceutical Companies?

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SUMMARY: Pharmaceutical innovation brings immense benefits, but also costs. Should it be promoted by reducing the length of the drug review process? Our research shows that the answer depends on the relative impact of the length of review process on the number of drug introductions and the incidence of adverse reactions.

OBJECTIVES: Pharmaceutical innovation has brought about significant improvements in the quality of life. Given these improvements the conclusion seems to be that such innovation should be fostered. Yet the new technology can have unintended consequences. These benefits and side effects of innovation have contributed to a growing debate around the role of the regulatory bodies in promoting innovation. In this project we attempt to determine whether regulatory agencies like Health Canada should promote innovation by speeding up drug reviews.

DESIGN: The project consists of a theoretical and an empirical part. The theoretical part of the project weighs benefits and risks associated with pharmaceutical innovation, and provides a criterion, which determines when to shorten drug reviews. The empirical part of the project uses data from the Adverse Drug Reactions and Drug Product databases to evaluate the predictions of the theoretical model.

OUTPUTS/RESULTS: The results indicate that the choice of the optimal length of the drug review process depends on the impact of the length of the review process on two key indicators: number of new drugs generated by the industry and the incidence of adverse drug reactions.

IMPACTS/OUTCOMES/CONCLUSIONS: The theoretical part of the project demonstrates that the regulatory agencies should be promoting innovation as long as the impact on the new drug introductions outweighs the impact on the incidence of adverse drug reactions. The empirical part of the project will provide a policy recommendation on the optimal length of the drug review process, given its historic relationship with new drug introductions and adverse drug reactions.

2.01 The Effect of Altering the Linoleic Acid/Alpha-Linolenic Acid (LA/ALA) Ratio at a Low LA Content in the Diet on Lipid Metabolism of Hamsters

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SUMMARY: Omega-3 fats found in fish oils protect against cardiovascular disease. However, fish consumption among Canadians is not sufficient to provide the recommended amounts. Therefore, this study examines dietary manipulation aiming at increasing the production of this type of fats in the body from a precursor commonly found in vegetable oils.

OBJECTIVES: To examine the effect of decreasing the LA/ALA ratio in the diet by increasing ALA and maintaining a low LA content on the levels of omega-3 fatty acids (FA), in particular eicosapentaenoic (EPA) and docosahexaenoic acids (DHA), in blood and tissues and plasma lipid profile.

DESIGN: Male Golden Syrian hamsters (n = 18/group) were fed for six weeks diets containing LA at 2% and ALA at either 0.5%, 1%, 2% or 4% of total energy, providing LA:ALA ratios of 4:1 (A), 2:1 (B and E), 1:1 (C) and 0.5:1 (D), respectively. The fat blend of diet E was supplemented with 3% menhaden oil. At the end of the feeding phase, the hamsters were euthanized and blood and tissues were collected for the analysis of FA composition and circulating plasma lipids.

OUTPUTS/RESULTS: Relative levels (%) of ALA and EPA increased in all tissues with decreasing LA/ALA ratio, whereas those of DHA increased only in liver phospholipids ($P<0.01$). Conversely, % of arachidonic acid decreased in all tissues with decreasing LA/ALA ratio ($P<0.01$). Plasma triglycerides, total and HDL cholesterol were similar across all groups. However, plasma non-HDL cholesterol was significantly lower with diet E compared to diets A, C and D ($P<0.05$), but not diet B containing the same LA/ALA ratio.

IMPACTS/OUTCOMES/CONCLUSIONS: These results suggest that ALA can be converted to EPA and DHA at decreasing LA/ALA ratio when the LA content of the diet is low. Because high levels of EPA and DHA in tissues are associated with improved cardiovascular health, such a dietary approach, if demonstrated in humans, could be recommended in the context of an overall healthy diet.

2.02 Molecular Diversity of *Vibrio Parahaemolyticus* Associated with Molluscs Harvested in Canada

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SUMMARY: Seafood is a popular choice for healthy living. Consumption of fishery products are on the rise and consequently, seafood-borne illnesses are rising. Canada's reputed aquaculture industry exports seafoods and generates revenue. Our project '*Vibrio* species in seafood' monitors and investigates the bacterial hazards associated with seafoods.

OBJECTIVES: To investigate the diversity among *Vibrio parahaemolyticus* isolated from molluscan shellfish harvested from sites on either coast of Canada, and assess the hazards associated with consuming such products, as a result of human activity and global warming.

DESIGN: Molluscan shellfish were harvested from sites in the coastal waters of British Columbia (B.C., oysters) and the Gaspé Peninsula and Îles de la Madeleine in Québec (clams, mussels) between May and October (2002 to 2005). Harvested molluscs were shipped to the collaborating laboratories on either coast of Canada, packaged and mailed to our laboratory, under refrigerating conditions (4°C to 10°C), for analysis. Microbiological isolation and characterization of *V. parahaemolyticus* were done by standard and published methods.

Ribotyping was used to evaluate the diversity among the *V. parahaemolyticus* isolates. Ribopatterns were generated using an automated RiboPrinter (DuPont Qualicon, Wilmington, Delaware) with accessories from the same manufacturer, which included membrane-processing packs and all the reagents from cell lysis, deproteinization, restriction digestion and hybridization to image processing.

RESULTS: Until the end of 2005, 45 out of 76 (59%) and 12 among 50 (24%) of the samples from western and eastern coastal waters, respectively, yielded 83 *V. parahaemolyticus*isolates. The occurrence of *V. parahaemolyticus* was highest in the mid-summer months. Two reference and 127 clinical strains were combined in the analysis with all the (83) seafood isolates of *V. parahaemolyticus* from Canada, and genetic diversity-based on ribotyping generated 65 ribotypes, reduceable to 23 types using 85% similarity. Cluster analysis placed several *V. parahaemolyticus* strains into groups containing both clinical and food isolates. Isolates from either coast also demonstrated diversity when they were analyzed separately.

IMPACT: Intraspecies diversity indicates the potential for harbouring strain-specific virulence factors. Occurrence of *V. parahaemolyticus* in molluscs from Canadian coastal waters and its molecular association with the clinical strains indicates the presence of potential human health risk if such molluscs are consumed raw. The present study on Canadian *V. parahaemolyticus* isolates showed a very diverse community of the biotype. Therefore, unknown factors including emerging virulence traits could be present and molecular fingerprinting will continue to assist in the process.

2.03 Copper Transporter 2 Promotes Copper Uptake in Mammalian Cells

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SUMMARY: In this study we investigated the role of human copper transporter 2 (hCtr2) in maintaining copper balance within the cell and examined the effects of other metals on hCtr2-dependent copper uptake.

OBJECTIVES: Copper is an essential nutrient that plays an important role as a catalytic co-factor for a variety of metalloenzymes. Zinc strongly interferes with copper absorption and consequently diets high in zinc can lead to decreased copper status. Fortification of foods with zinc has led to a large proportion of children consuming levels of zinc exceeding the Tolerable Upper Intake Levels. Presently, the role of hCtr2 in copper transport is poorly understood. The primary aims of this study were to determine the function of hCtr2 in copper trafficking and effects of zinc and other metals on hCtr2-dependent copper transport.

DESIGN: RNA interference experiments and transient over-expression of a hCtr2-green fluorescent protein fusion protein (hCtr2-GFP) in COS-7 (monkey kidney) cells were used to investigate the role of Ctr2 in copper transport. Fluorescence microscopy and biotin labeling experiments were used to assess the subcellular localization of Ctr2.

OUTPUTS/RESULTS: Ctr2 was localized on the outer membrane of cytoplasmic vesicles and the plasma membrane and promoted saturable copper uptake with a K_m of approximately 10 μM. Cells over-expressing hCtr2-GFP hyper-accumulated copper, while cells depleted in Ctr2 by siRNAs accumulated lower levels of copper. Copper uptake by Ctr2 was unaffected by zinc, iron or manganese, but was strongly inhibited by silver.

IMPACTS/OUTCOMES/CONCLUSIONS: Together, these data suggest that Ctr2 functions at the cell surface as a low affinity copper uptake protein in mammalian cells and the antagonism of zinc on copper involves a block in a copper transport mechanism distinct from Ctr2. Understanding the function of genes involved in copper metabolism and how they are affected by other metal nutrients is necessary to accurately assess health risks associated with consuming diets low in copper or high in zinc and to set precise Dietary Reference Intakes for copper and zinc.

2.04 Evaluation of Interactions Between Contaminants and Nutrients: Effects of Labrador Tea (Rhododendron Tomentosum Extract) on MeHg-Induced Toxicity

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SUMMARY: Methylmercury presents a significant environmental health risk for Inuit who rely on a traditional diet. Using rat perinatal exposure model, we investigated a potential nutritional mitigative approach and contaminant-nutrient interactions using a traditional Inuit tea whose antioxidant properties may antagonize methylmercury-induced stress and neurotoxicity.

OBJECTIVES: Human epidemiology studies and environmental assessments of contaminants in the Arctic indicate that methylmercury (MeHg) is a serious environmental health threat. A growing body of literature supports the role of oxidative stress as a mechanism of MeHg's neurotoxicity. Labrador tea (*Rhododendron tomentosum* subsp. *Subarcticum*) is the most commonly referenced medicinal plant for First Nation People of North America, which is traditionally used by the Inuit of Canada for the prevention of illness and the treatment of respiratory infections. It is well known for its high antioxidant properties. This study assessed the ability of *R. tomentosum* extract to mitigate the neurotoxicity resulting from rat perinatal exposure to MeHg.

DESIGN: Dams were dosed daily with 2 mg MeHg/kg b.w., 100 mg tea extract/kg b.w., or 2 mg MeHg + 100 mg tea extract/kg b.w., throughout pregnancy and lactation. Pup growth, mortality, neurodevelopment, neuromuscular development, tissue oxidative stress and residue analysis, liver enzymatic activity, brain neurochemistry and gene expression profiles were assessed.

OUTPUTS/RESULTS: Perinatal MeHg exposure was associated with decreased pup survival, alteration in developmental milestone timing, perturbations in neuromotor functions and behaviour, and oxidative stress. *R. tomentosum* supplementation was able to mitigate the effect of MeHg on some of these endpoints. A specific subset of genes were found to be differentially expressed following MeHg-nutrients co-exposure present potential biomonitoring targets.

IMPACTS/OUTCOMES/CONCLUSIONS: Our preliminary results suggest that *R. tomentosum* may mitigate some of the effects of MeHg exposure. If future tests at lower exposure levels confirm these findings, Labrador tea may represent a locally available and culturally relevant item that health care professionals in the north may encourage as apart of a healthy traditional diet.

2.05 Developmental Immunotoxicity of a Commercial Polybromodiphenylether (PBDE) Mixture

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SUMMARY: The effects of polybromodiphenylether flame retardants on the developing immune system were examined in rat pups exposed to a commercial PBDE mixture in utero, during lactation and during juvenile development. The data indicate that PBDE exposure during the perinatal period was mildly immunostimulatory, and that PBDEs have the potential to influence the development of appropriate immune responses in juvenile animals.

OBJECTIVES: PBDEs are used as flame retardants in textiles and plastics and are found at ppb levels in human blood, milk and tissues. Few studies have examined the immunological effects of PBDEs in adult animals and none have looked at juveniles. Therefore, rats were exposed to PBDEs throughout the perinatal period and changes in immune parameters were assessed.

DESIGN: Adult (F0) rats (8/sex/group) were administered PBDEs (DE-71 technical mixture) by gavage at doses of 0, 0.5, 5 or 25 mg/kg body weight/day for 10 weeks, after which the rats were bred. Oral exposure of F0 rats continued through breeding, gestation and lactation. Weanling (F1) rats (13-18 rats/sex/group) received corresponding doses of PBDE by gavage until postnatal day 42, when pups from each dose group were sacrificed to assess clinical, hematological and histopathological changes.

RESULTS: Dose-dependent increases in apoptotic lymphocytes and tingible macrophages in the thymus and mesenteric lymph nodes of F1 males and females were not accompanied by significant changes in numbers of circulating white blood cells. There were no histopathological changes in the F1 spleens as a result of PBDE exposure; however, splenocyte proliferation was increased in a dose-dependent manner in unstimulated and mitogen-stimulated cultures. To assess the functional effects of immune changes, a group of F1 rats was challenged with the T-dependent antigen keyhole limpet hemocyanin (KLH). Humoral (anti-KLH IgG) responses were not significantly altered by PBDE exposure. Delayed type hypersensitivity (DTH) responses to footpad injections of heat-inactivated KLH were significantly elevated in female rats exposed to 0.5 but not in rats exposed to 5 or 25 mg PBDE/kg bwt/day.

CONCLUSIONS: The results indicate a mild immunostimulatory effect of PBDE exposure during the perinatal period, which may influence the development of appropriate immune responses in young animals.

2.06 A Preliminary Radon Map for Canada in the Unit of Health Regions

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SUMMARY: The risk of developing lung cancer is proportional to the cumulative exposure to indoor radon. In order to assess population risk due to radon the knowledge of the spatial distribution of indoor radon levels is essential. Here we present a preliminary radon map for Canada based on historical radon measurements collected in 6,016 locations across Canada with the health region as the basic geographic units.

OBJECTIVE: This project aims to construct the first residential radon map of Canada based on historical radon measurements collected over last thirty years across Canada. Epidemiologic studies of uranium and other underground miners have consistently shown that miners exposed to high levels of radon are at an increased risk of lung cancer(1). The recent pooled analyses of residential radon studies in Europe(2) and North America(3) have concluded that the risk of developing lung cancer is proportional to the cumulative exposure to indoor radon. In order to assess population risk due to radon at local, provincial and national level we need to conduct comprehensive exposure assessment. The radon mapping of Canada is important tool for investigation of spatial patterns in residential radon and is essential element of the exposure assessment. The identification of radon prone areas is of particular interest both to the public and to the management needs for a regional or national radon program.

DESIGN: The historical radon measurements data available in various formats have been entered into one database designed at Radiation Protection Bureau. All relevant information about monitoring type and duration are included in database. Radon measurements were carried out using one of five types of monitoring methods: Alpha-Track, CAIRS_ALPHA-TRACK (Canadian Institute of Radiation Safety modified Alpha track method), and Charcoal Canister, E-PERMs and Kusnetz method. Duration of monitoring varied for different monitoring methods: with 33 – 2271 days for Alpha-Track, 2 – 15 days for CAIRS alpha-track, and 14 days for E-PERMs. Each measurement site (home, hospital, school) had x and y coordinates assigned according to its address. There are a total of 6016 address locations and 16 745 radon test results in the radon database.

Once the data was geo-coded, it was possible to investigate various aspects of spatial distribution of radon levels. In this paper we present characteristics of historical radon levels for 127 health regions of Canada (Figure 1).

RESULTS: Results of radon measurements are available for 52 of the 127 health regions. Each health region was assigned a colour according to radon characteristics in the region. We have focused on two radon characteristics: 1) the average level; 2) percentile of observations above the Canadian action level of 200 Bq/m^3. A preliminary radon map of the average radon levels in Canadian health region is shown in Figure 2. This map suggests that radon levels are the highest in

Central and Atlantic Canada. In the second radon map, Figure 3, we present the percentile of observations above the Canadian action level in Canadian health regions. Only five out of 52 health regions have more than 20% dwellings with radon concentrations over 200 Bq/m^3. In eight regions, 10% – 20% dwellings might require remedial measures. However, most regions (39 out of 52) have less than 10% dwellings for which an action to reduce radon exposure would be needed.

CONCLUSION: The available data is very heterogeneous in both quantity (number of measurements per 1 square kilometre, or 100 000 inhabitants) and quality (short or long term measurements). Nevertheless, the radon maps can be very useful in helping to identify information gaps, and to design future residential radon surveys. The map might also prove interesting for public communication, demonstrating to the public that radon concentrations can vary widely and how likely a dwelling in a given health region could have a radon concentration higher than the new Canadian action level.

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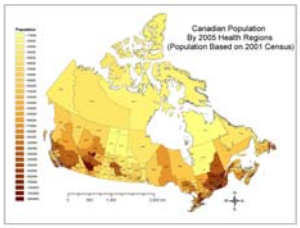
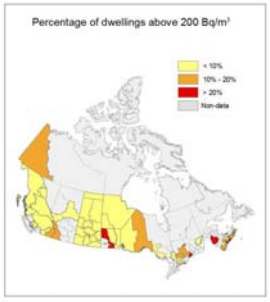
List of Figures

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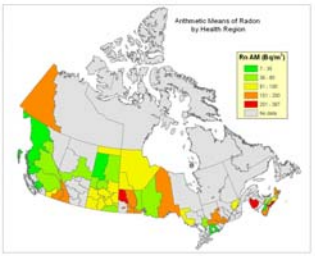
Arithmetic Means of Radon
by Health Region

2.07 A Pilot Indoor and Soil Radon Survey in Ottawa

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SUMMARY: Soil gas radon survey and indoor radon measurements were conducted in Ottawa area. The results indicated that 12% of Ottawa houses have radon concentrations above the new Canadian radon guideline of 200Bq/m3. It is recommended that every home needs to be tested for radon.

OBJECTIVE: This study is to provide basic information of radon distribution in Ottawa. It contains two parts: indoor radon measurements and outdoor soil gas radon survey. The study is aimed to establish the relationship between soil gas radon level and indoor radon potential. It serves as a pilot study of the national soil gas radon survey.

DESIGN: The City of Ottawa is the fourth largest city in Canada with an area of 2760 square kilometres. 40 public park sites are to be surveyed during the summer 2007. At each site, soil moisture, soil permeability, soil gas radon concentration as well as ground gamma radiation spectrum are measured with a suit of equipments identified and protocoled by the North-American Soil Geochemical Landscaping Project. In addition to the field survey, indoor radon measurements were performed in 169 homes with electron chambers.

RESULTS: The results of 169 tested homes indicated that 59% of Ottawa houses have radon concentrations below 100 Bq/m^3, 29% between 100 and 200 Bq/m^3, and 12% above the new Canadian radon guideline of 200 Bq/m^3. Relationship between soil radon concentrations and indoor radon levels can be established for nine communities in Ottawa.

CONCLUSION: This study indicates that radon concentration in Ottawa homes is much higher than the national average as estimated by the last cross-Canada radon survey. Although more measurements are needed for detailed radon mapping within the city of Ottawa, this study has found that houses with radon above 200 Bq/m^3 exist in various communities of Ottawa. Results of soil gas radon survey provide geological explanation of radon distribution in Ottawa. Because indoor radon concentration varies significantly due to various environmental factors and housing characteristics, the best way to protect families from radon exposure is to measure radon in every home and take appropriate actions if required.

2.08 Influence of Dietary Plant Sterols and Stanols on Diastolic Blood Pressure and the Expression of Genes Involved in Cholesterol Metabolism in SHRSP and WKY Inbred Rats

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SUMMARY: The health effects associated with increased consumption of plant sterols and stanols (PSS) were evaluated in stroke-prone and normotensive rats. The data indicate that consumption of PSS increases blood pressure in stroke-prone rats and alters the expression of genes involved in cholesterol metabolism of both rat strains.

OBJECTIVES: In many countries, the addition of plant sterols and stanols (PSS) to foods for the treatment of hypercholesterolemia is permitted. However, increased retention of PSS accelerates the onset of stroke and reduces the life span of SHRSP rats and sitosterolemia patients and increases the risk of premature CVD in hypercholesterolemic individuals. The objectives of this study were to investigate the health risk and the molecular pathogenic mechanisms associated with increased consumption of PSS in hypertensive SHRSP and normotensive WKY *inbred* rats, which have a mutation in *Abcg5* and increased PSS retention.

DESIGN: SHRSP and WKY *inbred* rats were fed a control diet or a diet supplemented with plant sterols or stanols (2 g/kg diet) for five weeks. Blood pressure, hepatic levels of plant sterols and stanols, and expression of sterol regulatory genes in liver and intestine were assessed.

OUTPUTS/RESULTS: Plant sterol or stanol supplementation increased hepatic total plant sterol or stanol accumulation in SHRSP and WKY *inbred* rats. Plant sterol addition significantly decreased hepatic cholesterol concentration of both rat strains. Interestingly, SHRSP rats fed the plant sterol or stanol diet demonstrated a significant increase in diastolic blood pressure compared to rats fed the control diet. As well, plant sterol or plant stanol supplementation up-regulated the intestinal mRNA expression of *NPC1L1*, the gene thought to be mainly responsible for cholesterol absorption. Plant sterol addition also up-regulated intestinal *Abcg8* as well as hepatic *Abcg5*, *Abca1*, and *HMGCR* mRNA levels. Whereas, plant stanol supplementation down-regulated intestinal *Abcg5* mRNA expression.

IMPACTS/OUTCOMES/CONCLUSIONS: PSS may contribute to premature heart disease by increasing diastolic blood pressure and/or altering sterol metabolism. Further studies are warranted to investigate the relationship between increased retention of PSS in the body and hypertension as well as abnormalities in sterol metabolism as these studies may impact safety assessments of PSS.

2.09 Sodium and Potassium in Food Composites from the Canadian Total Diet Study

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SUMMARY: Sodium and potassium are essential nutrients for which appropriate amounts must come from our diet. Canadians tend to consume too much sodium and not enough potassium, both of which can contribute to elevated blood pressure. The Total Diet Study provides an opportunity to monitor intakes of essential nutrients, and thereby to inform policy and regulatory activities pertaining to foods and nutrition.

OBJECTIVES: To determine the content of sodium and potassium in food composites collected in the Canadian Total Diet Study (TDS). To evaluate sodium and potassium intakes of Canadians, based on these laboratory analyses.

DESIGN: We have analyzed the sodium and potassium content of 141 food composites from the Canadian TDS collection conducted in 2000 in Ottawa. These composites were selected to be broadly representative of the foods most commonly consumed by Canadians.

Foods were purchased from commercial outlets, prepared as if for home consumption, composited and homogenized, and stored frozen until analyzed. Distilled water was used in cooking and no salt was added during food preparation.

Samples were prepared by pyrolysis and acid digestion and analyzed by atomic emission spectrophotometry.

TDS composites were matched to food intakes reported in the provincial nutrition surveys, and estimates of sodium and potassium intakes were derived for specific demographic groups of Canadians.

OUTPUTS/RESULTS: Processed foods and soups contain large amounts of sodium (with several TDS composites containing 25-50% of the sodium intake Reference Standard, per reference amount), and make the greatest contribution to sodium intakes of Canadians. Fruits and vegetables, nuts, seeds and meat contain large amounts of potassium (with several composites containing 10-20% of the potassium intake Reference Standard, per reference amount). Meat, fruits and vegetables make the greatest contributions to potassium intakes of Canadians.

IMPACTS/OUTCOMES/CONCLUSIONS: Canadians tend to consume too much sodium and not enough potassium. Both of these situations can contribute to high blood pressure and related health concerns. Ongoing monitoring of which foods contribute the most sodium and potassium to the diets of Canadians is a key input, to inform nutrition policy and guidance designed to assist Canadians in maintaining and improving their health.

2.10 The Canadian Total Diet Study - Research with a History

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SUMMARY: The Canadian Total Diet Study, started over 35 years ago as a collaborative research effort, provides average dietary intakes of toxic and nutritional chemicals by Canadians in different age/sex groups for the risk assessment and risk management of these chemicals in foods.

OBJECTIVES: The objectives are to continuously monitor priority toxicants in the diet, to estimate average dietary intakes of the chemicals by different age/sex groups, to obtain data on background concentrations of chemicals in foods as they are eaten, to identify foods which are unusually contaminated, and to monitor changes in dietary intakes of chemicals with time.

DESIGN: Foods are purchased at the retail level, prepared as for consumption by the Kemptville Campus, Guelph University, following defined recipes, and the prepared foods are combined into 141 different food composites. The composites are homogenized and kept frozen at -20°C until analysed. Foods were analysed for background concentrations of PCB's, dioxins, select pesticides, toxic and nutritionally important trace elements, radionuclides, polybrominated diphenyl ethers, and perfluorinated organics.

The concentration of many chemicals is below the limit of detection of most conventional analytical methods. Thus, the analysis of foods for background concentrations of chemicals requires research expertise and sophisticated (and expensive) analytical instrumentation to achieve low detection limits.

The concentrations of the chemicals in the food composites are multiplied by the amount of each food consumed by an age/sex group (Nutrition Canada Survey), and the sum of the products is an estimate of the average dietary intake of the chemical by the specific age sex group.

OUTPUT/RESULTS: Some examples showing that the total diet study has been a cornerstone of the research program are: 1) the first in the world discovery of lead contamination of raisins from Turkey; 2) dietary intakes of cadmium by young children approach the WHO provisional tolerable weekly intake (PTWI); and, 3) dioxin-like toxic equivalent intakes exceeded the PTWI for all children under 5 years age.

IMPACT/OUTCOMES/CONCLUSIONS: The Canadian total diet study has been instrumental in identifying major food contamination sources, creating the research/expertise foundation to deal with emergencies, making scientific risk

assessments for chemicals, generally, and for at-risk groups, for making risk management decisions, and for setting priorities both in research and surveillance. Data are used both within Health Canada and by external national and international organizations responsible for food safety.

2.11 The Relative Ability of Cannabis and Tobacco Smoke to Induce Chromosomal Damage in Murine Pulmonary Cells

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SUMMARY: This study examined the relative ability of cannabis and tobacco smoke condensates to induce chromosomal damage in a mouse lung cell line. Tobacco smoke condensates induce micronuclei in a dose dependent manner, while cannabis condensates are more acutely toxic to the cells, which may be masking potential genotoxic responses.

OBJECTIVES: The prevalence of cannabis smoking is increasing among Canadian youth, and often it is perceived that cannabis smoke is less harmful than that of tobacco. Currently, the risks of adverse effects from cannabis smoke, as compared to tobacco smoke, are not well understood. This study examined the relative ability of cannabis and tobacco smoke condensates to induce cytogenetic damage, measured as micronuclei (i.e., fragments or whole chromosomes packaged separately from the nucleus), in a murine lung epithelial cell line (FE1 cells).

DESIGN: Condensates of main- and side-stream smoke from hand-rolled cannabis and tobacco cigarettes were prepared using standard (i.e., ISO) smoking conditions, as well as “extreme” conditions designed to reflect cannabis smoking habits. Pulmonary cells were exposed to smoke condensates for a four hour period, followed by a 28 hour growth period in the presence of cytochalasin B. Two thousand binucleated cells were scored from each treatment for the presence of micronuclei.

OUTPUT/RESULTS: The results indicate that cannabis samples were more cytotoxic and cytostatic than tobacco samples, as demonstrated by the lower cell proliferation indices. However, at the concentrations tested, no significant increases in micronuclei were observed in cells exposed to any of the cannabis condensates. In contrast, significant increases in micronuclei were observed in cells exposed to mainstream tobacco condensates smoked under the standard conditions, and both with and without the addition of exogenous a metabolic activation mixture (i.e., rat liver S9).

OUTCOMES/CONCLUSIONS: Tobacco and cannabis smoke differ substantially in their cytotoxicity, cytostasis and in their ability to induce chromosomal damage. Cannabis condensates, and smoke condensates prepared under the extreme smoking regime, are more acutely toxic to the cells, and be masking any potential genotoxic responses before they can be observed with this assay. In contrast, mainstream tobacco smoke condensates smoked under the standard regime appear to induce micronuclei in a dose dependent manner. Until there is a better understanding of the mechanisms underlying the observed effects, the significance of the results in a human health context cannot be determined. Current research is

employing DNA microarray technology to determine the mechanism(s) of action of both tobacco and cannabis smoke condensates.

2.12 Characterization of Norovirus Capsid Stability

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SUMMARY: Noroviruses are the leading cause of infectious gastroenteritis worldwide. In order to control the spread of infection, we must understand viral stability in its environment. Since noroviruses do not grow in cell culture, we are generating a virus-like particle model to compare the stability of various norovirus strains.

OBJECTIVES: To generate virus-like particles containing the VP1 (major capsid protein) using a recombinant baculovirus system. The assembled particles will be purified and biochemical tests carried out in order to characterize their stability under different conditions.

DESIGN: Use Reverse-Transcription Polymerase Chain Reaction (RT-PCR) to amplify VP1 coding sequence from four representative strains: the current surrogate Murine norovirus (MNV), a well studied previous surrogate Feline Calicivirus (FCV), and the unculturable GI and GII human noroviruses. Transfect an insect cell line to generate recombinant baculoviruses expressing these four VP1 major capsid proteins. Purify capsid proteins and produce virus-like particles. These can be subjected to various environmental factors such as changes in pH and temperature. Degradation of the capsids will be monitored using electron microscopy (EM), circular dichroism spectroscopy, UV absorption spectroscopy, dynamic light scattering (DLS), and trypsin digests.

OUTPUTS/RESULTS: At present, coding sequences of the VP1 capsid from MNV, FCV and GI have been amplified using RT-PCR. This VP1 region from FCV has been successfully introduced into the recombinant baculovirus. This has established the potential of the baculovirus expression system for the study of norovirus virus-like particles.

IMPACTS/OUTCOMES/CONCLUSIONS: Results demonstrate that the baculovirus expression system is successful in generating virus-like particles. Minor modifications in the experimental procedure should enable us to successfully clone the MNV, GI, and GII noroviruses into the baculovirus vector. Once this task has been completed, the transfection of insect cells will be carried out and the expressed virus-like particles will be isolated for characterization.

2.13 Monitoring Residuals Along Treatment Processes at Drinking Water Plants Using Aluminium Coagulation

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SUMMARY: All treatment stages of water purification plants were monitored during warm and cold seasons. The residual turbidity remained low, and the residuals of aluminium and precursors of disinfection by-products (DBPs) consisted mainly of dissolved fractions. Only dissolved Al showed large variations, indicating scope for minimization of residual Al.

OBJECTIVE: To understand/improve levels of treatment residuals by studying their variations during the treatments.

DESIGN: Dissolved and total organic carbon as well as dissolved Al and total acid-leachable Al (dissolved + particulate) were monitored alongside turbidity and other key parameters at selected water purification plants using chlorination and conventional aluminium-based coagulation systems. Samples were collected throughout the sequential treatment stages, including rapid mixing, slow mixing (flocculation), sedimentation and filtration. Sampling series were done during cold and warm seasons. In parallel, controlled temperature jar-tests were conducted to take into account seasonal variations.

OUTPUTS/RESULTS: When considering raw and finished water levels measured at the treatment plants, measurements performed during cold and warm seasons did not show changes in turbidity removal and reduction of DBPs precursors. Changes in dissolved Al were mainly observed. These changes could keep Al at levels higher than the recommended 100 µg/L for many months and could be attributed to variations in coagulation temperatures. The effect of temperature was confirmed in the laboratory by jar-test experiments. However, interestingly, the monitoring of the treatment stages showed that the Al levels could stabilize quickly at the mixing stages or gradually change over all stages. As well, the seasonal changes could be a decrease or increase in residual Al. These observations cannot only be attributed to temperature, but other parameters such as the pH and the type of coagulant can also be of concern with regard to minimizing residual Al.

IMPACTS/OUTCOMES/CONCLUSIONS: The main goals of these treatments are turbidity removal, reduction of DBPs precursors and minimization of residual Al. A lack of control of these parameters can have impacts on population health. The Al results suggest that the residual Al can still be minimized further. The treatment modification however should not negatively impact other goals but, if possible, also improve these.

2.14 Development of a Method for the Isolation and Detection of Verotoxigenic *Escherichia coli* (*E. coli*)

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SUMMARY: The verotoxigenic Escherichia coli (VTEC) serogroup O157 is an established public health threat and the non-O157 VTEC serogroups are an emerging threat. The aim of this collaborative project is to develop a comprehensive detection and isolation scheme for the non-O157 VTEC.

OBJECTIVES: Verotoxigenic *Escherichia coli* (VTEC), including *E. coli* O157 are recognized as significant foodborne pathogens in Canada. Currently, there is no standard protocol for the detection of VTEC serogroups, other than O157, available to Canadian regulatory and public health agencies. The aim of this project is to develop a method for the detection of VTEC, as part of a major joint interdepartmental initiative between HC, AAFC, PHAC and CFIA.

DESIGN: Samples from food, clinical or environmental samples undergo enrichment in the presence of selective antimicrobials to inhibit background flora, followed by screening by PCR for the verotoxin genes (*stx*1 and *stx*2), and the additional virulence factors *eae* and *hlyA*. Samples positive for *stx* are plated onto selective media for isolation of individual VTEC strains, confirmatory PCR and biochemical, serological and molecular characterisation.

OUTPUTS/RESULTS: To develop an optimized enrichment process for VTEC the inhibitory concentrations for six antimicrobials were determined for a panel of VTEC strains. In addition, the possibilities of increasing selectivity by acid shock or incubation temperature were investigated. Commercially available selective media for *E. coli* were evaluated for use in post-enrichment recovery of VTEC. These methods will be coupled with PCR screening methods to develop the final protocol.

IMPACTS/OUTCOMES/CONCLUSIONS: Once the protocol development has been completed, the performance characteristics will be evaluated in a multiple laboratory study and the protocol will be circulated to the laboratories of the participating agencies. The protocol will be available for use in the VTEC research community for ecological, surveillance and epidemiological studies and as a basic reference method for the development of novel rapid methods.

2.15 A Look at Potential Health Impacts of Wind Farms in Consideration of Long-Term Landowner Agreements

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SUMMARY: The EA Division of HC works with other federal and provincial departments and project developers towards the successful assessment of health impacts of Wind Farms in Canada. This poster considers the issue of long-term landowner agreements and how Health Impact Assessment can reduce or eliminate associated health impacts.

OBJECTIVES: The Environmental Assessment Division of HC provides expert advice to federal and provincial departments required to undertake an environmental assessment under the *Canadian Environmental Assessment Act* or the *Canada-(province) Agreement on Environmental Assessment Cooperation*, respectively. This poster provides insight into the proper assessment of Wind Energy Generation Projects in Canada promoted by HC for use by stakeholders and regulators in the decision making process.

METHODOLOGY: The poster will review the potential bio-physical and socio-economic human health impacts typically associated with wind energy projects, describe the components of a comprehensive health impact assessment, and discuss the implications of long-term proponent-landowner agreements.

OUTPUTS/RESULTS: This overview of health impacts associated with long-term landowner agreements forms a basis for discussion of effects not fully recognized and assessed in Canada due to the newness of the technology. The incorporation of protective and proactive assessment procedures is critical as the level of installed wind energy is expected to increase 10-fold over the next decade (CWEA, 2006) to satisfy greenhouse gas and other pollutant reduction targets and promote renewable sources of energy. HC's provision of expert advice to the assessment processes results in an increased consideration of health and safety issues for landowners and workers in the project area.

CONCLUSIONS: Health impacts from wind energy projects have been recognized globally. HC participates in the environmental assessments of these facilities to promote more comprehensive evaluation of potential effects to landowners entering into long-term agreements with project developers. Proponents, responsible federal authorities, and provincial regulators required to undertake or evaluate an environmental assessment of a wind energy project should consider the potential health impacts presented in this poster and provide mitigation measures as appropriate.

2.16 Mainstream Tobacco Smoke Downregulates Plasminogen Activator Inhibitor-1 Transcription in Murine Heart (Male and Female): Lessons from Genomics Data

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SUMMARY: Gene expression profiling of heart tissue provides a novel approach to study the molecular mechanisms operating in cardiovascular response to mainstream tobacco smoke (MTS). High density DNA microarray analysis identified plasminogen activator inhibitor-1 (PAI-1), inhibitor of fibrinolysis, as a novel candidate biomarker of exposure and potential adverse effect.

OBJECTIVES: To evaluate biological implications of Genomics data. To test the hypothesis that MTS induced changes in PAI-1 gene expression in heart will be predictive of eventual cardiovascular pathology.

DESIGN: Male and female C57B1/CBA mice were exposed to MTS from two cigarettes daily, 5 days/week for 6 or 12 weeks. Sham-exposed mice were placed in restrainers only. Mice were sacrificed immediately after, or six weeks following, the last cigarette smoke exposure. Whole hearts were 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. Microarrays were normalized using a global LOWESS approach and analyzed by MAANOVA 2.0 and SAM.

OUTPUT/RESULTS: MTS significantly downregulates (microarray and real time RT-PCR) PAI-1, which, is known to play a role in atherosclerosis and other associated cardiovascular diseases. PAI-1 inhibits the activity of tissue plasminogen activator (tPA) thereby preventing fibrinolysis. Transcriptional downregulation of PAI-1 in response to MTS does not change the total amount of PAI-1 protein synthesized. However, the total tPA protein levels are significantly affected. Furthermore, ELISA shows that total activity of PAI-1 and tPA is altered in heart tissue. We will further measure PAI-1/tPA complex, total free tPA and its activity in plasma.

Our results also revealed up-regulation of Cyp1A1 (14-fold), downregulation of cysteine-rich angiogenic inducer 61 (Cyr61) and the chemokine CXCL-1. Changes in gene expression were transient and were mostly reversed when smoking was discontinued.

IMPACTS/OUTCOMES/CONCLUSIONS: This work identifies several candidate biomarkers of exposure and potential adverse effects of MTS. PAI-1 downregulation in response to MTS is a novel finding and may provide a new mechanism by which MTS influences the fibrinolytic system and increases the risk of cardiovascular disease.

2.17 The Heat Inactivation of the Hepatitis A Virus

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SUMMARY: One significant source of foodborne Hepatitis A outbreaks is mussels. Our goal is to determine accurate time/temperature recommendations for inactivation of HAV in mussels to protect the health and safety of Canadians. We have begun by inactivating HAV in disodium phosphate buffer and will expand these studies to include mussels.

OBJECTIVES: To determine the heat inactivation profile of the Hepatitis A virus (HAV) and use this information for risk assessment and to recommend safe cooking procedures for mussels.

DESIGN: Fetal Rhesus Monkey Kidney (FRhK) cells were grown and maintained. HAV was subjected to heating from 55°C to 90°C in five degree intervals, with samples taken at time intervals from 10 seconds to 10 minutes. For example, at 55°C, HAV was heated for 60 minutes, with samples taken every 10 minutes. The FRhK cells were infected with HAV, and plaque assays were performed in order to obtain virus titre in PFU (plaque forming units) per ml. Virus reduction at each temperature was determined and used to calculate the heat inactivation parameters for this virus. The D-value is the time required at a certain temperature to kill 90% of the organisms being studied, while the Z-value is the temperature required for the thermal destruction curve to move one log.

OUTPUTS/RESULTS: Standardized protocols have been developed for virus inoculation and for the titration of HAV before and after heat treatment. Results are preliminary, starting with lower temperatures and longer inactivation times. Initial results suggest that at 55°C in buffer, the time required for a 1-log decrease in HAV titre is 50 minutes.

IMPACTS/OUTCOMES/CONCLUSIONS: Experiments will be continued with other temperatures in order to determine time/temperature combinations required to inactivate the virus. Results reveal semi-logarithmic survival curves for HAV at specific temperatures used to derive D and Z values in buffer medium. Using the latter, experiments will be expanded to mussels, a common food vector for the HAV virus, which will enable us to recommend safe cooking procedures for mussels. Preliminary findings indicate that HAV is more heat stable than many bacteria; this highlights the importance of collecting HAV-specific data.

2.18 Significant Deficiencies in Health and Safety Information in Material Safety Data Sheets of Hazardous Workplace Chemicals

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SUMMARY: Significant deficiencies in safety information are found in Material Safety Data Sheets of hazardous chemicals used in Canadian workplaces. Since only a fraction of such data sheets is examined by the Hazardous Materials Information Review Commission annually, the scope of the problem in the workplace by extrapolation can be disconcerting.

OBJECTIVES: To explore the range of deficiencies in health and safety information in Material Safety Data Sheets (MSDSs) of hazardous chemicals used in Canadian workplaces and to focus in particular on those deficiencies in toxicology that have the potential to impact on reproductive health and cancer.

DESIGN: MSDSs of hazardous workplace chemicals for which manufacturers are seeking protection of confidential business information are reviewed by the Hazardous Materials Information Review Commission (HMIRC) for accuracy and completeness. The HMIRC is an independent agency within the Health Canada portfolio with a mandate linked to the Workplace Hazardous Materials Information System (WHMIS), which requires manufacturers to provide health and safety information to Canadian workplaces. Each segment of the MSDS is reviewed by the HMIRC and the deficiencies identified. Manufacturers are then required to correct the MSDSs and forward these to the workplace.

OUTPUTS/RESULTS: Based on its reviews, the HMIRC has identified significant errors and omissions in the MSDSs particularly in the areas of toxicology, first aid and ingredient identification. These three together represent 57% of the deficiencies with ingredient identification/concentration being 14%, first aid 15% and toxicology 28%. In those specific areas of toxicology pertaining to impact on reproductive health, about 6% of the toxicology deficiencies (representing 19% of the hazardous products reviewed annually by the HMIRC) relate to reproductive health and cancer.

IMPACTS/OUTCOMES/CONCLUSIONS: It is estimated that there are over 750 000 hazardous chemicals in use in the Canadian workplace and based on previously reported studies, about one-half are found to be deficient in health and safety information. Assuming that 19% of that half have errors and omissions in the area of reproductive health and cancer, it can be projected that over 71 000 chemicals are used in workplaces with erroneous MSDSs. This situation could be alarming.

2.19 Selenium and Vitamin E Modulate Methylmercury-Induced Systemic Inflammatory Response in Rats

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SUMMARY: Epidemiological study revealed a link between methylmercury body burden and risk of cardiovascular disease in which systemic inflammatory response plays an important role. Our results from an animal study suggest that dietary supplementation with selenium and vitamin E can affect serum inflammatory markers and also modulate methylmercury-induced systemic inflammatory response.

OBJECTIVES: Fish and marine mammals as important components of Northern traditional diet are rich source of selenium (Se) and vitamin E (V_E). Unfortunately, they are also route of exposure to Methylmercury (MeHg). A study was conducted to investigate the effects of dietary Se and V_E on MeHg mediated changes in systemic inflammatory response in male Sprague Dawley (SD) rats.

DESIGN: SD rats were fed starch-based casein diet (CD), or casein diet supplemented with 1 (S1) or 3 (S3) mg Se/kg diet, or 250 (V250) or 750 (V750) mg V_E/kg diet for 28 days. The rats were then gavaged with 0 or 3 mg MeHg/kg body weight/day for 14 days. Blood samples were measured for leukocyte counts (contract with Vita Tech, Toronto). Serum was analyzed for C-reactive protein (CRP), oxidized LDL (Ox-LDL), intercellular adhesion molecule-1 (ICAM-1), monocyte chemotactic molecule-1 (MCP-1) using commercial ELISA kits.

RESULTS: In the vehicle control rats, neutrophil counts were significantly higher for S1 than V750 group; serum ICAM-1 was significantly lower for CD than all other groups. MeHg significantly increased monocyte counts in the CD group; serum Ox-LDL in the CD, V250, and V750 groups; serum ICAM-1 in the S1 and V750 groups; serum MCP-1 in the CD, S2, and V750 groups.

CONCLUSIONS: Both MeHg and dietary supplementation with Se or V_E imposed significant effects on some of the systemic inflammatory markers examined. Supplementation with Se or V_E modulated the effects of MeHg on these markers. Supplementation with either 1 or 3 mg Se/kg diet or 250 mg V_E/kg diet to some extent minimized MeHg-induced systemic inflammatory response. Results of this study will contribute towards characterizing the beneficial effects of dietary constituents in managing health risks associated with mercury exposure.

2.20 Simple and Complex Tools for Prioritizing Substances on the Domestic Substances List on the Basis of Potential Hazard to Human Health

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SUMMARY: Simple and complex health hazard tools were developed by Health Canada to systematically prioritize existing substances for further assessment. The tools provide guidance for the next stages of assessment and their applicability can be extended to other programs where there is a desire to determine relative priorities of chemical substances.

OBJECTIVES: Under the *Canadian Environmental Protection Act 1999*, the Ministers of Health and the Environment were required to "categorize", by September 2006, the approximately 23 000 substances on the Domestic Substances List (DSL) in order to identify substances considered to be persistent, bioaccumulative and inherently toxic to humans or non-human organisms, or that present the greatest potential for human exposure in Canada. As part of an integrated framework incorporating both health and exposure components, simple and complex tools were developed by Health Canada to systematically prioritize substances for further assessment on the basis of health hazard.

DESIGN: The simple hazard tool capitalized on the work of other national and international assessment programs to identify high and low priorities for assessment, while the complex tool was developed to address substances that had not previously been adequately assessed. The complex hazard tool involved a hierarchical consideration of numerous effects of concern for human health. Endpoint specific criteria were developed, as well as a stepwise approach to consideration of various sources of relevant information, including reviews, original study reports, predictive models and others.

OUTPUTS/RESULTS: The results of application of these efficient yet credible, transparent and health protective tools, and the information compiled, not only contributed to the categorization of the DSL, but also provided guidance concerning directions for the next stages of assessment. Approximately 1150 substances are now being considered as either high or moderate health priorities for further action.

IMPACTS/OUTCOMES/CONCLUSIONS: The applicability of these hazard tools is not limited to categorization of DSL substances, but can be extended to other areas or programs within Health Canada or other organizations where there is a desire to determine relative priorities of chemical substances.

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2.21 The Mutagenic Hazard and Carcinogenic Risk of Complex PAH Mixtures in Contaminated Soils

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SUMMARY: We evaluated methods that are used to assess the cancer risk posed by mixtures of polycylic aromatic hydrocarbons (PAHs) and found that traditional methods, which assume that the known components of the mixture are additive, may be conservative, however they fail to account for the risks of all mixture components.

OBJECTIVES: To evaluate the validity of current risk assessment methods employed for soils contaminated with mutagenic carcinogens (e.g., polycyclic aromatic hydrocarbons or PAHs) using an in vitro, mammalian cell mutation assay.

DESIGN: Organic components of PAH-contaminated soils (70 – 9300 µg PAH/g soil) were extracted using pressurized fluid extraction, and separated on silica gel into non-polar (PAHs) and polar aromatic fractions (oxy-PAHs and N-heterocyclics). Synthetic mixtures containing 16 priority PAHs were prepared using results of chemical analyses. The mutagenic activities of the soil fractions, corresponding synthetic PAH mixtures and individual PAHs were assessed using the *lacZ* mutation assay in FE1 Muta™Mouse cells. The excess lifetime cancer risk of each of the soils was calculated using a standard method (i.e., an additive approach that focuses on priority analytes), and a novel mutagenic potency ratio (MPR) method that employs mutagenic potencies to derive estimates of carcinogenic risk.

OUTPUTS/RESULTS: A significant, concentration-related increase in *lacZ* mutations was observed for all non-polar fractions, polar aromatic fractions, synthetic PAH mixtures, and 5 priority PAHs. The mutagenic activities of the soil fractions ranged from 0.7 to 522 mutants x 10^{-5}/mg soil/ml. Predictions of soil mutagenic activity, based on additivity of individual PAHs or synthetic PAH mixtures, were greater than the mutagenic activities observed for the soil fractions. In most cases, the excess cancer risk estimates for the soils that were calculated using the novel MPR method were at least 2-fold lower than those calculated using the standard method.

IMPACTS/OUTCOMES/CONCLUSIONS: The total mutagenic/carcinogenic hazard of a complex PAH mixture may be less than that calculated using an assumption of additivity. Thus, targeted risk assessments that focus on priority PAHs will likely provide conservative predictions of mutagenic (or carcinogenic) activity. However, routine risk assessments cannot account for the hazard/risk contributed by unidentified compounds (e.g., oxy-PAHs and N-heterocyclics).

2.22 Less Hazardous Tobacco Products: Fact or Fiction? The Canadian Experience

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SUMMARY: In Canada, so-called “less hazardous” products are available for sale and may give a false impression of risk to the smoker. The results indicate that toxic emissions of cigarette-like or modified cigarette products that are perceived or presented as less hazardous are, in fact, similar to traditional Canadian cigarettes, and thus are susceptible to produce the same health hazards than smoking any other cigarettes such as cancer, respiratory diseases, etc. These data provide evidence required for the Tobacco Control Programme to address emerging risks posed by novel products.

In Canada, so-called “less hazardous” tobacco and non-tobacco products are available for sale. These include herbal cigarettes, Native brands, and tobacco cigarettes using bio-filters and ingredients that may give a false impression of risk to the smoker.

The purpose of this study was to characterize 27 compounds present in smoke emissions from some of these products available in Canada and to compare these results against the Canadian market. The tobacco emission analyses are performed using a sub-set of ten different analytical methods mandated by the Tobacco Reporting Regulations.

Results indicate that, except for nicotine, the smoke emitted by herbal cigarettes is similar to that emitted from tobacco cigarettes both in type of compound and in amount, except for low-molecular weight carbonyls, HCN and ammonia which is found in higher amounts.

Among the novel cigarettes, “*vitaminized”* cigarettes (Vita-Cig) and “*100% additive-free natural tobacco*” (Natural American Spirits), generally behave like other cigarettes under similar conditions. The toxic emission values printed on the package of “*Bio-Filtra technology*” cigarettes (AZUR) display formaldehyde level of 0.01-0.02 µg/cig. Analytical results show that the formaldehyde yields of these products are slightly higher (125-263 µg /cig) than traditional Canadian cigarette of comparable tar values.

In conclusion, the results indicate that toxic emissions of cigarette-like or modified cigarette products that are perceived or presented as less hazardous are, in fact, similar to toxic emissions of traditional Canadian cigarettes, and thus are susceptible to produce the same health hazards such as cancer, respiratory diseases, etc. than smoking any other cigarettes. These data provide evidence required for the Tobacco Control Programme to address emerging risks posed by novel products.

2.23 Trend of Nicotine Levels in Canadian Cigarettes (1968-2005)

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SUMMARY: This study evaluates the nicotine levels in Canadian cigarettes (1968-2005) and determines whether nicotine contents and nicotine emissions follow the same trend. This study confirms that the amount of nicotine in unburnt tobacco is not the key variable influencing the nicotine delivery; cigarette design characteristics have a larger influence.

OBJECTIVES: The Canadian *Tobacco Reporting Regulations* (TRR) requires the manufacturers to report every year the levels of 25 chemical constituents found in tobacco and 40 chemical emissions found in tobacco smoke. In addition, Health Canada performs emissions testing on various cigarette brands in order to have additional data. This study evaluates the trend of nicotine levels in Canadian cigarettes between 1968 and 2005, and determines whether nicotine contents and nicotine emissions follow the same trend.

DESIGN: In this study, the data of over 400 cigarette brands, representing the Canadian market, was studied for their nicotine content in whole tobacco (HC Method T-301), as well as nicotine and tar in mainstream smoke (ISO smoking conditions, HC Method T-115). The ratio nicotine/tar and percentage of nicotine transferred from the tobacco to smoke were calculated.

OUTPUTS/RESULTS: Results indicate that the nicotine content in whole tobacco increased by 122% (9-20 mg/g tobacco) between 1968 and 2005. A decrease of nicotine (1.3-0.9 mg/cigarette, 31%) and tar (22-10 mg/cigarette, 55%) in mainstream smoke is observed. In addition, the ratio nicotine/tar increased by 83% (0.06-0.11) while the percent of nicotine transferred from the tobacco to smoke decreased by 56% (16%-7%). Despite a dramatic increase in nicotine content in the unburnt tobacco, a slight decrease in nicotine emissions under ISO smoking conditions is observed. Therefore, other cigarette design characteristics are responsible for this trend rather than the nicotine content itself. The main physical characteristics that can have an impact are: tobacco weight, filter efficiency, paper porosity and ventilation holes.

IMPACTS/OUTCOMES/CONCLUSIONS: This study confirms that the amount of nicotine in unburnt tobacco is not the key variable influencing nicotine delivery under ISO smoking conditions. Cigarette design characteristics have a larger influence on nicotine delivery than nicotine content.

2.24 The Mutagenic Activity of High-Energy Explosives, Contaminants of Concern at Military Training Sites

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SUMMARY: The genotoxicity of energetic materials such as TNT, tetryl, RDX and HMX has not been rigorously tested. We found that both TNT and tetryl are clearly mutagenic in Salmonella. Testing of RDX and HMX is in progress. Additional research examining the mutagenic activity of contaminated soils from military training sites is underway.

OBJECTIVES: To evaluate the mutagenic activity of energetic compounds (i.e., high explosives) that commonly occur in contaminated soils at military training sites.

DESIGN: The Salmonella reverse mutation assay, and the Muta™Mouse in vitro transgene mutation assay were employed to examine selected energetic compounds. Salmonella strains TA98 (i.e., frameshift mutations), TA100 (i.e., base-pair substitution mutations), and the metabolically enhanced strain YG1041 (TA98 background), with and without exogenous metabolic activation (S9) were employed to assess TNT and tetryl. These compounds were also examined using the Muta™Mouse assay. Both assays are currently being employed to examine RDX and HMX, as well as contaminated soils from military sites (e.g., CFB Petawawa).

OUTPUTS/RESULTS: Initial results indicate that TNT elicited a significant positive response in *Salmonella* strains TA98 and YG1041 without S9, generating potencies of 0.68±0.05 and 1.01±0.05 revertants/µg TNT, respectively. However, TNT failed to induce a positive response in TA100, or in TA98 and YG1041 with S9. Tetryl exhibited considerable mutagenic activity in all strains with and without S9. The mutagenic potencies ranged from 0.92±0.07 to 17.04±0.4 revertants/µg tetryl, with the highest values obtained with TA98 and YG1041 without S9. Initial testing using the Muta™Mouse assay was inconclusive, and samples are currently being re-evaluated.

IMPACTS/OUTCOMES/CONCLUSIONS: Results to date indicate that TNT is a direct-acting frameshift mutagen. In contrast, tetryl exhibits both frameshift and base-pair substitution mutagenic activity with and without metabolic activation. Preliminary results suggest that testing of other energetic materials, as well as contaminated soil samples from military training sites (e.g., CFB Petawawa), is warranted in order to accurately assess the mutagenic hazards posed by these complex environmental matrices.

2.25 Design of the National Radon Database in Support of a Canadian Radon Map

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SUMMARY: Over the last few decades, Health Canada has conducted many surveys of the radon concentration in Canadian houses. Unfortunately most of the records are scattered and not easily accessible. This work aims at building a state-of-the-art database regrouping all the available records of radon measurements in Canadian homes and offices.

OBJECTIVES: To develop a complete, robust and easily expandable database regrouping all the available records (both from governments and private companies) of radon measurements in Canadian homes and offices. The primary application of the database will be its use in the development of the Canadian radon potential map.

DESIGN: The National Radon Database is designed in Microsoft Access and is using all the utilities of modern relational databases. Furthermore the database is built to be easily expandable and web-based forms are being developed (also using MS Access) to access, maintain and update the database. The starting point of the database is the work done by Huixia Jiang, Jan Zielinski and Jing Chen in 2006, who built records of most of the radon measurements in a "spread sheet type" database.

OUTPUT/RESULTS: At this stage the development of the database is well underway. Although more data need to be added and some data cleaning is necessary, the database presently regroups more than 15 000 radon measurements taken at ~ 6000 locations scattered (albeit in a non-uniform way) across Canada. Preliminary charts, graphs, and tables derived from and obtained with the database will be displayed in the presentation.

IMPACTS/OUTCOMES/CONCLUSIONS: It is now generally accepted that radon exposure is the second cause of lung cancer behind smoking resulting in as many as 2000 deaths every year in Canada. Since it is impossible to measure the radon concentration in every Canadian house, it is essential to develop tools to predict the risk factor associated with a given house and/or region. Of particular interest would be a national map indicating the radon potential of each region. The National Radon Database will be one of the essential building blocks for the creation of such a map.

2.26 Evaluation of Current Evidence for Human Exposure to Mycobacterium avium subsp. paratuberculosis (MAP) and its Association with Crohn's Disease (CD)

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SUMMARY: A qualitative analysis of scientific literature on potential sources of human exposure to MAP through food and evidence for a cause-effect relationship between MAP and CD. The conclusions and recommendations of the analysis could be used to develop strategies to reduce the risk of exposure to this potential human pathogen.

OBJECTIVES: MAP is a known cause of Johne's disease (JD) of both domestic and wild ruminants and has been implicated as a possible cause of CD in humans. The objective of this risk profile is to qualitatively assess the risk of human exposure to MAP in Canada and the potential role of this microorganism in the development of CD and other human diseases. The document could provide grounds for the development of risk management (RM) options aimed at reducing the risk of human exposure to MAP.

DESIGN: Selected scientific publications pertaining to MAP, JD and CD were critically evaluated and documented in a risk profile. The document was peer-reviewed by experts in relevant fields.

OUTPUTS/RESULTS: Canada has the highest rates of CD reported in the world to-date. Foods derived from cattle appear to be significant sources of human exposure to MAP. Presence of viable MAP has been demonstrated in surveys of commercially pasteurized retail milk and cheese in both Europe and N. America. Other potential environmental/zoonotic sources of MAP include beef, produce and water. In spite of the fact that an increasing number of recent studies support the role of MAP in the etiology of human disease, a scientific consensus on the cause-effect relationship has not been reached.

IMPACTS/OUTCOMES/CONCLUSIONS: Although data regarding the sources of MAP are limited, it can be concluded that Canadians are likely being exposed to this organism through the food supply. The document identifies knowledge gaps and recommends research to answer questions related to human exposure to MAP in Canada. As a result of the outcomes of the risk profile, an Expert Advisory Group on MAP has been established with the aim to develop and prioritize potential RM options. This risk profile will ensure all relevant information is considered during the development of RM options.

2.27 Dermal Exposure to Environmental Contaminants as Assessed by In Vitro Absorption Tests with Human Skin: Cold Storage at Issue

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SUMMARY: Human skin tissue is commonly stored frozen for use in laboratory tests to determine skin permeability to soil contaminants. Our results suggest that freezer storage decreased skin permeability to some chemicals. More tests are needed to ensure that such tissue storage artefacts do not adversely affect health and safety regulations.

OBJECTIVES: To explore the possibility that storing human skin tissue frozen for use in *in vitro* tests may decrease skin permeability and adversely affect hazard/risk assessment of dermal exposure to soils from Federally designated contaminated sites.

DESIGN: Human skin surgical waste obtained from the Ottawa Hospital was tested fresh and after 30 and 60 days freezer storage (- 22°C) to six ^{14}C-radiolabelled environmental contaminants (Benzo[a]pyrene (B[a]P), ethylene glycol, methyl parathion, naphthalene, nonyl phenol. and toluene). Dermal absorption was assessed *in vitro* using Bronaugh flow-through diffusion cells and Liquid Scintillation Counting. Informed consent was obtained from patients donating skin tissue and ethics approval was obtained from the Ottawa Hospital Research Ethics Board and the Health Canada Research Ethics Board.

The amount of ^{14}C-activity present in the receiver solution pumped under the skin to simulate blood flow and that remaining absorbed into skin was used to assess skin permeability.

OUTPUTS/RESULTS: With the total % absorption expressed as the sum of both that detected in the receiver solution and that remaining in the skin there was a significant difference ($P < .05$) between fresh controls and freezer stored skin for only one (toluene) of the six chemicals tested. However with % absorption expressed as that in the receiver solution alone, a trend was seen with less absorption for controls *versus* frozen skin for all six chemicals that was significant for two chemicals (B[a]P and toluene) at both the 30 and 60 day storage times.

IMPACTS/OUTCOMES/CONCLUSIONS: The data suggest that the common practice of using freezer-stored human skin may decrease skin permeability as measured by standard *in vitro* tests. This could lead to underestimating dermal exposure to soil contaminants. More testing is needed for chemicals with diverse structural properties (e.g., molecular size, fat solubility).

2.28 National First Nations Environmental Contaminants Program (NFNECP): Overview and Key Findings of the 2000-2006 Community-Based Research Projects

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SUMMARY: The NFNCP funded 32 community-based research projects from 2000 to 2006. This study provides an overview of project findings concerning environmental contaminants and environmental health issues within First Nations communities.

OBJECTIVES: To compile results and review outcomes from the community-based environmental research projects funded through the NFNECP from 2000 to 2006.

DESIGN: The NFNECP was launched in 1999 to help First Nations assess the extent of their exposure to environmental contaminants and the potential for associated health risk. Research questions are primarily determined by the communities in order to investigate and address their environmental concerns. 32 NFNECP projects were reviewed in order to extract and synthesize information related to environmental contaminants in participating First Nations communities. This poster will report on overall outcomes and primary contaminants of concern.

OUTPUT/RESULTS: Most of the research projects quantified levels of contaminants in different media and compared it to the relevant safety guidelines. A large proportion of research projects (19/32) investigated levels of contaminants in traditional foods such as fish and game. Other media such as water (13/32), sediments (8/32), and soil (6/32) were also studied. A few research projects (5/32) conducted analyses on human biological samples such as hair, blood and urine. The primary contaminants studied, in order of frequency were; mercury, lead, arsenic, cadmium and PCBs. Mercury analyses were conducted in 19/32 projects in a variety of media, showing that mercury is an important environmental concern among these First Nations. Dietary surveys were conducted in 12/32 of the projects.

IMPACT/OUTCOMES/CONCLUSION: The review and synthesis of NFNECP project results and findings could help inform decision-making at the policy level regarding environmental contaminants and food safety in First Nations communities. It is important to further investigate the presence of contaminants in various first Nations traditional foods as they fall outside federal and provincial inspection processes. This program provides a unique opportunity for knowledge transfer leading to an increased awareness and understanding of environmental contaminants by the general First Nations population, researchers, and decision makers alike. Through the participation of community members and the integration of traditional practices into science, it also results in capacity-building in the field of First Nations environmental health.

2.29 Assessment of Uncertainty Using Co-Located Duplicate Sampling: First Step for Spatial Data Interpretation in the Windsor, Ontario Exposure Assessment Study

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SUMMARY: Factors and sources affecting measurement uncertainty in the Windsor, Ontario Exposure Assessment Study were investigated by assessing variations in particulate matter (PM) mass measurements and elemental analyses using co-located duplicate samples and comparison of two analytical approaches.

OBJECTIVES: To investigate and understand the overall uncertainty associated with both gravimetric and elemental measurements in order to provide data of known quality for interpretation of the spatial distribution of airborne metals.

DESIGN: Co-located duplicate 24-hr personal, indoor and outdoor samples were collected using the R & P Chempass® multi-pollutant sampler. Sampling bias was estimated using relative percent difference (RPD%) of the co-located duplicated samples. Elemental concentrations were determined and compared using ED-XRF and ICP-MS. Filter samples were digested after direct measurement of ED-XRF using an ultrasonication digestion method and 4:1 HNO_3+HF followed by ICP-MS determination. The gravimetric analysis was performed using Health Canada's custom-designed buoyancy-corrected Archimedes M3™ Facility.

RESULTS: PM concentrations of 24 sets (48 samples) of indoor and personal PM_{10} filters, and 9 sets (18 samples) of outdoor $PM_{2.5}$ filters displayed the following ranges (medians): 2.2 – 40.7 (11.0) $\mu g\ m^{-3}$; 8.0- 48.3 (11.9) $\mu g\ m^{-3}$; and 17.1- 42.3 (21.6) $\mu g\ m^{-3}$, respectively. The gravimetric analytical results reveal that the variations in PM mass measurements for same-day sampling are insignificant compared to real temporal or spatial variations: 92%, 100% and 96% of indoor, outdoor and personal co-located duplicate samples respectively pass the quality criteria (RPD $\leq$ 20%). Uncertainties associated with XRF elemental measurements of S, Ca, Mn, Fe and Zn pass the quality criteria for 78% to 100% of the duplicate samples. Inadvertent introduction of metal contamination is found to be one of the main causes for variations in metal determination.

CONCLUSIONS: Sampling and analytical procedures for indoor PM_{10}, personal PM_{10} and outdoor $PM_{2.5}$ assessed using co-located duplicate samples show that the data are highly reliable. While the uncertainty associated with sampling and analysis of PM is insignificant compared to temporal variability and spatial (indoor/outdoor/personal) variability, uncertainty associated with elemental measurements must be assessed on an element-by-element basis.

2.30 Emission and Constituent Analysis of Counterfeit and Illicit Cigarettes Found in Canada

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SUMMARY: The chemical profile of smoke and whole tobacco of counterfeit and illicit cigarettes is compared to the one of cigarettes found on the Canadian market. Significant differences of tar level in smoke and metals in whole tobacco are noted. The reasons for these differences are discussed.

OBJECTIVES: For various reasons, Canadian smokers may turn to illicit and counterfeit cigarettes. Consumers and regulators are unaware of the level of toxicants emitted by these products.

The purpose of the study was to characterize and compare illicit and counterfeit cigarettes with legal Canadian cigarettes. Illicit and counterfeit cigarettes are expected to have different emission and constituent profiles compared to brands available on the Canadian market.

DESIGN: The levels of 26 smoke emissions obtained using ISO and Health Canada modified smoking conditions were measured. In addition, the analysis of whole tobacco (metals and alkaloids) was performed.

RESULTS: Results indicate that the tar level of two samples of illicit cigarettes packaged in plastic bags was significantly larger than the level typically observed for Canadian cigarettes using ISO smoking conditions. The levels of aminobiphenyls, aminonaphthalenes and tobacco specific nitrosamines were also larger than levels observed for Canadian cigarettes, even when considering their large tar levels. In addition, formaldehyde and hydrogen cyanide levels determined under ISO smoking conditions of counterfeit cigarettes were significantly different than levels of the genuine brands. Difference in ventilation of the counterfeit and genuine brands was noted.

The tobacco's metal content (e.g., lead, cadmium, chromium, etc.) of counterfeit and illicit cigarettes was larger than in brands on the Canadian market. The tobacco's metal content is related to the soil where it is grown and the difference observed suggests a different origin.

CONCLUSION: The differences of chemical composition of whole tobacco and emissions indicate that different tobacco is used in illicit cigarettes packaged in plastic bags, counterfeit cigarettes and Canadian cigarettes. The origins of the samples studied being unknown, the analysis provided an indication of what is available in Canada.

2.31 The Potential for Pathogen Cross-Contamination of Foods with Gloved Hands: Experiments with Feline Calicivirus as a Surrogate for Human Enteric Viruses

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SUMMARY: The United States Food Code prohibits bare hand contact of ready-to-eat foods to prevent pathogen transmission. The food industry has adopted the use of gloves as barrier protection. Thought to eliminate the risk of spread of pathogens, the possibility of cross-contamination of foods via gloved hands essentially remains unexplored.

OBJECTIVES: The objectives of our study were to determine the potential of gloved hands in the cross-contamination of food contact surfaces using a quantitative and standardized test protocol and to assess the importance of ethanol-based solutions in the reduction of foodborne pathogen spread.

DESIGN: Each disk (1 cm diameter) of brushed stainless steel, representing hard food contact surfaces, received 10 µL (~1000 PFU) of feline calicivirus (FCV) in a soil load. The inoculum was touched for 10 seconds at a pressure of 0.5 kg/cm^2 with either a bare or gloved fingerpad while the inoculum was still wet or after it had been allowed to become visibly dry. After a time lag of 10 seconds, fingerpads were either eluted or placed in contact with a sterile metal disk at the pressure and contact time mentioned above then eluted. The extent of acquisition and transfer was calculated using plaque assays. The effect of 75% ethanol as a treatment to interrupt virus spread was also investigated.

OUTPUTS/RESULTS: Neither bare nor gloved fingerpads transferred any detectable levels of FCV from the disks with dried inocula. In contrast, both gloved and bare fingerpads could transfer approximately 2-5% from the wet inocula. The use of 75% ethanol (1 ml) on blue-nitrile or clear-vinyl gloves for a contact time of 10 or 30 seconds only reduced the virus by approximately 1 $\log_{10}$ pfu/mL.

IMPACTS/OUTCOMES/CONCLUSIONS: While gloving by foodhandlers is essential, this is the first report demonstrating that gloves themselves could readily acquire, retain and transfer pathogens. Our findings demonstrate the impact of glove use in the spread of viral pathogens as well as the ineffective nature of 75% ethanol to interrupt virus spread. In this context, wearing gloves alone does not guarantee food safety; proper personal and food hygiene practices must be implemented to ensure a safe food supply.

2.32 Pre- and Post-Natal Exposures to Soy Isoflavones do not Augment Azoxymethane-Induced Colon Carcinogenesis in F1 Generation Male Sprague-Dawley Rats

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SUMMARY: There is substantial evidence suggesting that soy isoflavones do not have any beneficial effect or conversely cause adverse effects in relevant experimental animal models of colon cancer. In our study, we aimed to assess the effects of life-time exposure of dietary soy isoflavones, including in utero and in post-natal stages, on colon cancer. Our results suggest that life-time exposure to soy isoflavones do not augment colon cancer in male Sprague-Dawley rats and at low doses reduces the size of colon tumors.

OBJECTIVES: There is substantial scientifically paradoxical evidence suggesting that soy isoflavones either have no or adverse effects in experimental colon cancer models. Hence, our study aimed to study the effects of life-time exposure of dietary soy isoflavones in a well established animal model of colon cancer.

DESIGN: Briefly, male pups born to Sprague-Dawley rats exposed (including during pregnancy and lactation) to soy isoflavones at either no (0 mg), low (40 mg) or high (1000 mg) doses per Kg body weight in their diet were weaned and remained to receive their respective parental diets until the end of the study. Weaned rats received s.c. injections of azoxymethane, a colon-specific carcinogen at 15 mg per Kg body weight once a week for two weeks. After 26 weeks, the rats were euthanized and the incidence and growth coordinates of colon pre-cancerous lesions (commonly called aberrant crypt foci) and tumors were determined. Colon tumors were assessed for changes in the gene and protein expression of estrogen receptor (ER)-í, the main candidate purported to be involved in soy isoflavone-induced cellular signalling. Furthermore, using DLD-1 human colon adenocarcinoma cells *in vitro*, ER-í mediated cellular and molecular responses of soy isoflavones were studied.

RESULTS: The number and growth features of pre-cancerous lesions were not affected by soy isoflavones. In comparison to the Control, soy isoflavones, at either dose did not affect tumor incidence (100% in all groups) or multiplicity. The low dose of 40 ppm significantly ($p<0.05$) decreased tumor burden, and average tumor size per tumor-bearing rat and average tumor size per group compared to the Control. Our results also indicate that ER-í crucial in mediating the growth suppressive effects of soy isoflavones *in vitro* and *in vivo*.

CONCLUSIONS: Our results demonstrate that life-time dietary exposure to soy isoflavones do not enhance colon cancer in male rats. Conversely, soy isoflavones at low doses assist in reducing the size of colon tumors. Whether colon carcinogenesis in female rats is affected by dietary soy isoflavones exposure at specific stages of menarch remain to be explored. These pre-clinical observations

are of significance to human health in determining the paradoxical effects of soy isoflavone consumption thought to be influenced largely by dose and type of soy isoflavones, and parameters such as gender, target organs and ER status.

2.33 Canadian House Dust Study Part I: Selection of Methodologies

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SUMMARY: The Canadian House Dust Study is a four-year collaboration between researchers and risk assessors, which aims to collect representative indoor environmental information from 800-1000 urban homes across Canada. This poster describes how the study was designed to address data gaps in risk assessment identified by both HC and PHAC.

OBJECTIVES: To obtain a statistically robust estimate of background levels of chemical and bacterial contaminants in urban household dust across Canada.

DESIGN: A three stage stratified sampling design was developed to obtain a random and representative sample of Canadian cities with population greater than or equal to 100 000. Based on existing information on the variability of metal concentrations in Ottawa households, it was determined that sampling of 800 to1000 homes in 13 cities across Canada was required in order to get a reasonable bound on the error of estimation. Sampling methodologies include collection of an integrated vacuum sample (VDI 4300 Pt 8); bacterial swipe samples from kitchens, bathrooms, pet feeding areas and entryways; and settled dust wipe samples (ASTM E-1728) from living rooms, bedrooms, kitchens and entryways. Vacuum dust samples are air-dried for 24 hours and sieved to the <80 micron size fraction for subsequent determination of a wide range of inorganic and organic constituents.

OUTPUTS/RESULTS: Thirteen cities were randomly selected for sampling: Richmond, Vancouver, Regina, Calgary, Burlington, Hamilton, Cambridge, Barrie, Thunder Bay, Sudbury, Gatineau, Montreal, and Halifax. As of June 2007, sampling has been completed in Burlington (79 homes), Hamilton (120 homes), and Cambridge (83 homes), and sample preparation and analysis is underway.

IMPACTS/OUTCOMES/CONCLUSIONS: Health Canada's Federal Contaminated Sites Program requires baseline indoor dust data to compare with indoor dust data from contaminated sites, while the Public Health Agency of Canada requires baseline information on presence/absence of bacteria in urban Canadian households. At the end of four years, this study will provide nationally representative information on chemical and bacterial constituents of urban household dust to address data gaps in risk assessment identified by both organizations.

2.34 Human Health Risk Assessment as a Scientific Tool in Federal Environmental Assessments

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SUMMARY: The use of human health risk assessment (HHRA) as a scientific tool for evaluating human health impacts in environmental assessments (EAs) conducted under the Canadian Environmental Assessment Act (CEAA) was investigated to determine the current state of practice and the need to develop Health Canada (HC) policy and guidance.

OBJECTIVES: Human health impacts are often evaluated as part of the EA process to determine if changes in environmental factors (e.g., air quality, water quality, etc) from a development project are impacting human health. HC's Environmental Assessment Division provides expertise and guidance to other departments on the determination of human health impacts under CEAA. The study objective was to investigate the use of HHRA in federal EAs across Canada and determine the relevance of current HC policy and guidance.

DESIGN: A representative sample of Environmental Impact Assessment documents, including screenings, comprehensive studies and panel reviews, submitted to HC under CEAA were reviewed. The type and level of HHRA used was assessed to determine: 1) qualitative vs. quantitative analysis; 2) level of analysis (i.e., simple screening, pathway specific HHRA, multi-media HHRA); 3) type of methodology (i.e., jurisdiction); and, 4) input parameters (i.e., source). HC policy and guidance documents on HHRA were also examined to determine current policy and regulatory context.

OUTPUTS/RESULTS: The study showed that HHRA use in federal EAs across Canada ranges widely from simple screening assessments to detailed quantitative multi-media pathway HHRA. Methodologies and input assumptions (e.g., receptor and exposure characteristics, Toxicological Reference Values) varied widely with many different jurisdictions being used. A review of HC policies and guidance documents indicates a lack of clear direction on use of HHRA in federal EAs.

IMPACTS/OUTCOMES/CONCLUSIONS: The study confirms the continued importance of HHRA as a scientific tool in evaluating human health impacts in federal EAs. The study also suggests that EAs would benefit from standard HC guidance for use of HHRA in EAs as a means of increasing consistency and scientific defensibility of the evaluation of human health impacts across Canada.

Session B: Interactions Between Health and the Environment, Protection of Human Health and the Envrionment, Alta Vista Salon, November 9, 2007

2.35 A Re-Evaluation of the Scientific Basis for the Reduced Regulatory Requirement Polymer Definition for New Substances

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SUMMARY: We have determined that the Reduced Regulatory Requirement Polymer criteria of the New Substances Notification Regulations, defining polymers that are presumed to be of 'low concern' to human health and the environment do, in fact, describe new polymeric substances that have little inherent toxicity.

OBJECTIVES: The New Substances Notification Regulations (Chemicals and Polymers) require that all new substances, including polymers, be assessed by Health Canada and Environment Canada for risks they may pose to the environment and to human health. The Regulations establish a definition for a class of polymers that have high number average molecular weights, limited percentages of low molecular weight oligomers, are chemically stable and have limitations on certain reactive and cationic chemical groups. Polymers that meet these criteria are believed to exhibit low inherent toxicity because of limited bioavailability and low reactivity, and are subject to reduced data requirements for regulatory submissions. This work aims to identify whether these criteria are truly indicative of polymers that are of 'low concern'.

DESIGN: In this study we have conducted a retrospective analysis of the more than 3000 Reduced Regulatory Requirement (RRR) Polymers assessed by Health Canada and Environment Canada to identify those for which some toxicological, ecotoxicological, physical-chemical and environmental fate studies have been conducted.

RESULTS: A substantial majority of the results of acute toxicity, ecotoxicity, skin and eye irritation, skin sensitization and genotoxicity studies for RRR polymers of diverse chemical classes suggest that these polymers are devoid of significant toxicological activity. Although some exceptions do exist, such as certain fluoropolymers, these constitute only a small minority. Data from this subset of polymers were used to suggest if there were any polymers or chemical classes of polymers having toxicological activity that is inconsistent with the perceived 'low concern' nature of the RRR polymer class.

CONCLUSIONS: The assessment of the available data for polymers meeting the RRR criteria has shown that they are generally associated with having low toxicological activity. Where exceptions exist, the polymers belong to classes whose toxicity is well characterized and reduced data requirements do not hinder risk assessment.

2.36 Fetal and Early Life Origins of Adult Chronic Disease: A New Public Health Paradigm?

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SUMMARY: There is mounting epidemiologic evidence to suggest that particular perinatal events, such as disturbances of fetal nutrition and growth, prematurity, low birth weight, certain infant feeding practices and patterns of growth after birth, may increase the risk for adult onset of chronic diseases such as cardiovascular disease, obesity and diabetes.

OBJECTIVES: To describe the mounting evidence for the 'developmental origins of chronic disease' hypothesis and its implications for future research/public health policy.

DESIGN: This poster presents a synthesis of some of the existing literature on the Developmental Origins of Chronic Diseases hypothesis. Relevant articles in journals pertaining to human and animal physiology, nutrition, medicine, obesity, pediatrics and epidemiology were referenced. This topic has begun to gather exceptional global momentum (there is now a learned International Society for Developmental Origins of Health and Disease which has sponsored international congresses on an annual or biannual basis since 2001). The objective of this poster presentation is to raise the consciousness among decision makers, scientists, policy analysts and programmers working in the federal health portfolio of this relatively new (15 years) and fascinating area of research. The Developmental Origins research has potential policy implications that include, but are not limited to: chronic disease prevention, optimal maternal nutrition, importance of pre-conception health of girls and young women, and the possible influences on health in later life of birth weight, infant feeding practices and infant growth patterns.

OUTPUTS/RESULTS: Fetal nutrition refers to the availability/delivery of nutrients, oxygen and hormones to the developing fetus. Disruptions to fetal nutrition, including hypoxia and excessive exposure to certain maternal hormones, occurring at critical periods of fetal life, can result in physiological changes that lead to permanent structural and functional adaptations called "programming". Fetal programming occurs at the gene, cell, tissue, organ and system levels, and may result in altered cell number, organ structure, hormonal set points, and gene expression that predispose the fetus to cardiovascular, metabolic and endocrine diseases in adulthood. It is thought that programming occurs not only for the fetus' immediate survival advantage, but also in preparation for a nutritionally disadvantaged environment after birth. However, adequate or excessive nutritional support during postnatal life enables catch-up growth that may create metabolic conflicts, predisposing the adult to an increased risk of chronic disease.

IMPLICATIONS FOR RESEARCH AND PUBLIC HEALTH POLICY: Research on infant feeding practices and the early programming of appetite; lifecourse approach to epidemiological studies to understand disease risks associated with adverse early developmental environments and their interaction with neonatal, childhood, adolescent and adult lifestyles; optimal balance of micro- and macro-nutrients

during pregnancy; effects of maternal nutrition acting at different stages from conception to adulthood.

It may be possible to mitigate some of the negative consequences of a sub-optimal intrauterine environment by ensuring optimal growth during infancy and childhood. New WHO Global Child Growth Standards describe how children up to age 5 should grow. For the first time there are standardized BMI charts for infants and children. The new standards are based on the premise that the breastfed baby is the norm for healthy growth among infants.

2.37 A Temporal, Multi-City Model to Estimate the Effects of Short-Term Exposure to Ambient Air Pollution on Health

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SUMMARY: As a means of evaluating whether efforts to control air pollution have actually resulted in public health improvements, we propose two multi-year estimators that use current plus several previous years of data to estimate current year risk, and assess trends in these estimators over time.

OBJECTIVES: Countries around the world are expending significant resources to improve air quality, in part, to improve the health of their citizens. Are these societal expenditures achieving what governments hope? Are they improving public health? We consider these issues by tracking the risk of death associated with outdoor air pollution exposure over both space and time in 24 of Canada's largest cities over the 17 year period from 1984 to 2000. The risk of exacerbating heart and lung diseases, as measured by hospital admissions, can also be tracked over space and time.

DESIGN: We propose two multi-year estimators that use current plus several previous years of data to estimate current year risk. The methods have an advantage that there is no need to adjust the health risk estimate for a selected year even if new data for years after the selected year become available. The estimators are derived from sequential time series analyses using moving time windows (windows of 3, 5, 7 and 9 years were evaluated). To evaluate the statistical properties of the proposed methods, a simulation study with three scenarios of changing risk based on the Canadian data is conducted.

RESULTS: The annual average daily concentrations of ozone appeared to be increasing over the 17 year period while those of NO_2 are decreasing. However, the proposed method returns different time trends in public health risks. Evidence for some monotonic increasing time trend in the annual risks for ozone is weak ($p=0.3870$) but somewhat stronger for NO_2 ($p=0.1082$). In particular, an increasing time trend becomes apparent when excluding year 1998 that reveals lower risk than proximal years, even though concentrations of NO_2 are decreasing. The simulation results validate the two proposed methods producing estimates close to the pre-assigned values.

OUTCOMES/CONCLUSIONS: Despite decreasing ambient concentrations, public health risks related to NO_2 appear to be increasing. Further investigations are necessary to understand why the concentrations and adverse effects of NO_2 show opposite time trends. Applying the proposed method to morbidity data is also necessary to confirm the time trend.

2.38 Disinfection of Noroviruses on Surfaces

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SUMMARY: Surface contamination is one important medium by which noroviruses are spread. Unfortunately, human noroviruses do not grow in cell culture, and thus we cannot directly determine their infectivity. We have used a mouse norovirus, the most genetically similar surrogate available to date, to determine norovirus resistance to common disinfection agents.

OBJECTIVES: To define disinfection procedures required for the inactivation of norovirus on surfaces, using the murine norovirus (MNV-1) and feline calicivirus (FCV) as surrogates.

DESIGN: Brushed stainless steel discs inoculated with 1 X 10^6 particles of MNV-1 or FCV were left untreated, or covered with ethanol, bleach, or activated hydrogen peroxide. The virus was recovered from the discs at various time points and infectivity was determined by plaque assay using tissue culture cells susceptible to infection with MNV-1.

RESULTS/OUPUT: The MNV-1 surrogate demonstrated a considerable amount of resistance to treatment with the various disinfectants. Initial results indicate that nearly 50% of the virus survived exposure to 1000 ppm bleach for 10 minutes. Slightly higher rates of virus inactivation were obtained when the virus was exposed to 75% ethanol for 10 minutes. Increasing the bleach concentration to 5000 ppm resulted in =90% inactivation of the virus in 5 minutes. Experiments with hydrogen peroxide are underway.

IMPACTS/OUTCOMES/CONCLUSIONS: The inactivation profiles of the MNV-1 surrogate are different than those obtained with the previously accepted surrogate, FCV. This study shows that surrogates must be carefully selected for inactivation studies. The outcome of these studies will be useful in developing standards for norovirus inactivation in various settings. Human noroviruses are Category B bioterrorism agents, however MNV-1 and FCV have not been shown to infect human.

2.39 Machine Learning for Compliance Verification of the Comprehensive Nuclear-Test-Ban Treaty

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SUMMARY: Health Canada conducts explosion detection for the Comprehensive nuclear-Test-Ban-Treaty by monitoring the radioactive noble gases in the atmosphere. Synthetic nuclear explosion data-based on Nevada test site measurements along with environmental background data are used as training datasets to establish an optimal classification model employing state-of-the-art technologies in artificial intelligence.

OBJECTIVES: Since January 1959, Health Canada has been active in the measurement of radioactive fallout on air filters, to ensure the health and well being of Canadians. This work has evolved to include an active role in achieving a comprehensive ban on the testing of nuclear explosions. Compliance verification of the Comprehensive Nuclear-Test-Ban Treaty (CTBT) employs noble gas monitoring of four radioisotopes of radioxenon, namely, ^{131m,133m,133,135}Xe. The activity concentrations of these isotopes can help distinguish normal operating emissions from a nuclear reactor and from a nuclear explosion. In locations where nuclear reactor emissions are easily measured, classification of these two sources becomes difficult. Machine learning (ML) is employed to overcome this difficulty. This form of artificial intelligence utilises algorithms to classify data.

DESIGN: Radioxenon measurements from Health Canada's radioxenon monitoring stations are combined with synthetic data based on publicly available Nevada Test site measurements to establish an optimal classification model employing state-of-the-art technologies in ML. We conducted a preliminary study involving ML algorithms including Naïve Bayes, Neural Networks, Decision Trees, k-Nearest Neighbors, and Support Vector Machines, that revealed that any noise, uncorrelated features, and interactions in extracted weapon signals will cause difficulties for induction algorithms. Further study into improving these algorithms and the synthetic data set is on going.

RESULTS: Classification results for modern machine learning technologies were compared to a classical linear discriminator approach, and it was found that the modern techniques can discriminate anthropogenic sources from explosions as well as the linear discriminator. These modern approaches have better performance in cases where the linear discriminator breaks down.

IMPACTS: Greater accuracy in discriminating a nuclear explosion from regular anthropogenic sources of radioxenon is achieved. These algorithms can be used by Canada's National Data Centre and by the Comprehensive Test-Ban Treaty Organization, to better identify radioxenon sources and hence make policy decisions.

2.40 North Korean Nuclear Test of October 9th, 2006: The Utilization of Health Canada's Radionuclide Monitoring Network and Environment Canada's Meteorological Modeling

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SUMMARY: Health Canada conducts explosion detection for the Comprehensive nuclear-Test-Ban Treaty by monitoring the radioactive gases in the atmosphere. Health Canada's radionuclide monitoring system was able to detect radioxenon at Yellowknife, which Environment Canada's meteorological models have shown that it was most likely from the North Korean test of October 9th, 2006.

OBJECTIVES: Since January 1959, Health Canada has been active in the measurement of radioactive fallout on air filters, to ensure the health and well being of Canadians. This work has evolved to include an active role in achieving a comprehensive ban on the testing of nuclear explosions. After the announcement on October 9th, 2006 of the North Korean nuclear explosion, work intensified to verify this claim. In compliance verification of the Comprehensive nuclear-Test-Ban Treaty (CTBT), there are 4 technologies (seismic, hydroacoustic, infrasound, and radionuclide), of which, the only "smoking" gun is the radionuclide detection technology. This technology coupled with meteorological modelling, can determine the source location of the event.

DESIGN: Radioxenon measurements from Health Canada's monitoring stations, combined with seismic timing information, and meteorological modeling can determine the source of Xe-133. The use of atmospheric transport models was employed. Historical and real time monitoring data on the size and distribution of releases from Chalk River Laboratories, which is the major anthropogenic background to Yellowknife are studied. Careful review of other large Xe-133 measurements at Yellowknife with meteorological modeling was used to understand the October 2006 measurements of radioxenon.

OUTPUTS/RESULTS: The use of atmospheric transport models and the use of historical and real time monitoring data on the size and distribution of releases from Chalk River Laboratories allowed us to conclude with a fair degree of certainty that the Xe-133 detected at Health Canada's Yellowknife station, could be attributed to a release from the October nuclear test in North Korea.

IMPACTS/ CONCLUSIONS: Health Canada and Environment Canada have demonstrated that radioxenon detection combined with meteorological modelling is a viable technology for treaty verification.

2.41 Assessing Human Health Impacts in Environmental Assessment

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SUMMARY: This study examines how Health Canada's scientific expertise in air and water quality, country foods, noise, radiation and electromagnetic fields is used to meet departmental obligations under the Canadian Environmental Assessment Act and assess the impacts of development projects on health.

OBJECTIVES: The Environmental Assessment Division (formerly Environmental Health Assessment Services), Safe Environments Programme, was created in 1992, when the *Canadian Environmental Assessment Act (CEAA)* was enacted. The objectives of the study were to review the types of expertise and advice HC provides regarding the health impacts of development projects and how this advice and expertise is used in environmental assessment.

METHODOLOGY: The study reviewed HC's role in providing scientific expertise by reviewing previous HC input to a regionally and sectorally representative sample of environmental assessments processes. The sectors represented were:

Hydro-electric Energy
Mines and Minerals
Nuclear Energy
Transportation
Fossil Fuel Energy
Remediation of Contaminated Sites

The review examined: (1) areas of expertise the HC provided input for each case study; (2) when the input was provided (e.g., development of Terms of Reference, review of Environmental Impact Statement, etc.); (3) the types of input provided (request for additional information, suggestions of guidelines, corrections, recommendations for mitigation, etc.); and, (4) how HC input was incorporated into the final EA document i.e., comprehensive study reports and panel reports. HC guidance and policy documents on the provision of scientific expertise were also reviewed.

OUTPUTS/RESULTS: The outputs are an overview of how HC contribution to scientific expertise for EA has evolved. It also considered its current state of practice and provided an analysis of how possible developments in EA knowledge and process may impact HC's provision of scientific expertise.

IMPACTS/OUTCOMES/CONCLUSIONS: The review clarifies HC's current role in providing scientific expertise for the federal EA process. It also provided an analysis of current and future trends in the provision of and demand for health related scientific expertise.

2.42 Severity of Murine Innate Immune Response Differentiates Potentially Harmful From Safe *Pseudomonas* Strains

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SUMMARY: The safety of bacteria intended for use in biotechnology was tested by spraying them into the lungs of mice. Illness symptoms and early immune effects were monitored over a week and this information was used to rank the bacterial strains for potential health concerns.

OBJECTIVES: *Pseudomonas* is an opportunistic pathogen causing acute and chronic infections. It has also been used for various industrial biotechnology applications, and several strains are listed on the Domestic Substance List (DSL) of the *Canadian Environmental Protection Act* (CEPA). Since there are both clinical concerns and biotech interests, our objective is to use immune-specific markers and assays to assess potential toxicity/pathogenicity of biotech *Pseudomonas* strains.

DESIGN: Strains identified *in vitro* as potentially hazardous (*P.aeruginosa* (Pa) ATCC#s 31480, 700370, 700371; *P.fluorescens* (Pf) ATCC#s 13525) were further tested by endotracheal instillation of Balb/c mice for up to one week. Mice were examined/monitored for physical symptoms, bacterial clearance and tissue/blood indicators (granuloycte infiltration, cytokines, acute phase proteins and immunoglobulin levels).

OUTPUTS/RESULTS: At 2 h exposure, physical effects were limited to Pa-exposed mice showing slight lethargy and ruffled fur. These symptoms receded, but for Pa31480, symptoms of piloerection, lethargy and slight muscle atrophy transiently appeared at 48h. Bacterial counts in the lung, trachea and esophagus were erratic over time, suggesting possible cycling between colonization and clearance. Pa strains caused elevations in pulmonary granulocytes at 2h, and again at 48h (4-6X). Pulmonary pyrogenic cytokines (IL-1ί, IL-6, TNF-a) were elevated between 2-48h with Pa exposure and serum cytokines were also significantly elevated between 48 and 96h. At one week, all cytokine levels were comparable to controls. For Pa31480, serum amyloid A was elevated by >50-fold at 48h.

IMPACTS/OUTCOMES/CONCLUSIONS: A ranking of the most problematic strains was established. Pa31480 was the most hazardous, and Pa700370 and Pa700371 also showed immune-related effects. In contrast, Pf13525 did not appear to cause any deleterious effects with the tests used here. These data will be used for filling gaps towards regulatory safety assessment of strains intended for biotechnology applications.

2.43 Is the Prevalence of Chronic Conditions Increasing in Canada?

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SUMMARY: This study examines changes in prevalence of chronic conditions in Canada over the last decade using data from two national health surveys (the 1994/95 cycle of NPHS and the 2005 cycle of CCHS).

OBJECTIVES: To examine changes in prevalence of chronic conditions over the last decade; understand how the ageing population and increased incidences of chronic conditions may have contributed to the rising health care costs; and identify population groups that preventive programs should target.

DESIGN: With data from national health surveys (1994/95 NPHS, and 2005 CCHS), age-specific and age-adjusted prevalence, and number of cases are estimated for ageing-related chronic conditions (hypertension, diabetes, cancer, heart disease, stroke and cataract). Descriptive analysis by sex, region, race and other population characteristics are also performed to pinpoint demographic factors that are most likely associated with the increases in prevalence.

OUTPUTS/RESULTS: Preliminary results show that prevalence of almost all conditions studied (except cancer) increased significantly over the last decade. Age-adjusted prevalence of hypertension rose from 9.86% in 1994/95 to 15.31% in 2005 among the population aged 15 and over (3.46% to 4.93% for diabetes, and 2.91% to 4.5% for cataract at the same time period). Prevalence of hypertension among seniors aged 65 to 80 increased from less than 30% in 1994/95 to over 40% in 2005. Prevalence of diabetes among individuals aged 60 to 65 more than doubled in the last ten years, rising from 5% to 11%. A large increase is seen in cataract prevalence among seniors aged 65 to 75. A significant increase in diabetes and hypertension is also observed among younger Canadians, which should be an alarming concern to all parties involved with health care.

IMPACTS/CONCLUSIONS: Increased prevalence of chronic conditions combined with an ageing population imposes an enormous burden to the health care system. Effective preventive programs targeting the right population groups are urgently needed to reverse the increasing trend in prevalence of chronic conditions.

3.01 Well Defined "Healthy Lifestyle" Reference Groups are Needed in the Design of Clinical Evaluations of New Drugs in Type 2 Diabetes

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SUMMARY: Exercise and dietary interventions are core treatments in type-2 diabetes, yet they often fail, due to lack of patient compliance. Innovative IT tools are used for the motivation of diabetic patients and the monitoring of diet and exercise, and provide optimized evaluation of new drugs. The discussion may impact on regulations for clinical trials in diabetes, particularly in remote communities.

OBJECTIVES: Exercise and dietary interventions are core therapeutic measures in the treatment of rising lifestyle-related diseases, particularly type-2 diabetes, yet they have suffered from lack of standardization and compliance, as patients tend to prefer substitution with pharmaceuticals. Difficulties in risk/benefit assessment of drugs usually lie in the choice of a reference group with which to compare the efficacy and safety of a new product. The objective of this work is to review current approaches in the design and management of clinical trials in type-2 diabetes, and to assess the availability and validity of innovative tools for optimized evaluation of the efficacy and safety of new drugs intended for treating type-2 diabetes.

METHODS: Internal reviews of the Clinical Trial Applications to the Canadian regulatory authority were performed in the field of anti-diabetic drugs since year 2000. As well, a comprehensive literature search focused on available quantitative measures used for the introduction and follow-up of lifestyle interventions, and on the availability and validity of using novel approaches such as emerging technologies in clinical trials.

RESULTS: Diabetes related Clinical Trial Applications (CTA) to Health Canada have been rising faster than all other CTA since year 2000. Reference groups comparing standardized healthy lifestyle interventions to the addition of a new drug are no longer implemented. Dietary recommendations are poorly documented and monitored, at best, by patients' self-questionnaires.

Reports on the use of information technology (IT) tools for easy quantification of dietary measures, exercise interventions, and long-term compliance (built-in time-logs) are increasingly available, as well as the evaluation of their validity.

CONCLUSIONS: Well-defined “healthy lifestyle” reference groups supported by IT tools, would not only optimize the benefit/ risk evaluation of anti-diabetic drugs, but also would trigger knowledge transfer and the design of policies and recommendations needed for the regulation of type-2 anti-diabetic drugs.

3.02 A Novel System (iCropTheBug) for Collecting, Concentrating, Capturing and Transferring Immunomagnetic Particles

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SUMMARY:

OBJECTIVE: Develop an immuno-magnetic system to safely, simply and rapidly collect, concentrate, capture, and transfer immuno-magnetic beads (IMB) used to isolate and detect food and environmental pathogens. The performance of the new system was compared to the Pathatrix (Matrix MicroScience Limited, UK).

DESIGN: The *i*CropTheBug system consists of: an IMB collector (IBMCOL); an IMB concentrator (IBMCON); and an IMB "pipettor" (IBMPIP). The devices were developed between our laboratory and Filtaflex Ltd. The system procedure is: i) add 100 µl antibody-conjugated IMB to 250 ml food homogenate in a 500 ml Erlenmeyer flask and incubate at room temperature for at least 15 min to capture target microorganisms on IMB; ii) place the flask on the IBMCOL for 1 min to draw the particles to the bottom of the flask; iii) place the flask on the IBMCON and run for 5-10 min (dependent on size, weight, magnetism, etc, of the IMB) to concentrate them in a pellet in the middle of the flask; and; iv) with the IBMPIP, transfer the pellet to an Eppendorf tube for cleaning followed by plating, DNA extraction, etc. Two types of particles: - Bug-Trap™ BT1-50 (GenPoint, Norway) (BT) and; MagaBeads®-Streptavidin CTM-CM019 (Cortex Biochem, USA) (MB) were used in comparing the performance of the *i*CropTheBug and Pathatrix systems. Spinach was spiked with *Shigella flexneri* and enriched in *Shigella* and Shiga broths. IMB were added to 250 ml of distilled water or spinach suspension. IMB were captured by the two systems and transferred to pre-weighed 200µl PCR microtubes containing 200 µl of 95% ethanol, collected with a magnet and rinsed again with 95% ethanol. After overnight drying (airflow hood) the weights of beads were determined by reweighing the tubes on an analytical balance. A haemocytometer was used to screen for the presence of beads from microtubes when there was no visible pellet.

RESULTS: The average weight of BT beads captured by the *i*CropTheBug system from 250 ml of distilled water was 3.5 times higher than by the Pathatrix (0.7 *vs* 0.2 mg). The capture of MB beads from water samples by *i*CropTheBug was 0.4 mg, but zero by the Pathatrix system, even by using the haemocytometer. For BT, while the Pathatrix system captured 0.2 mg from spiked spinach in both *Shigella* and Shiga broths, yields by the *i*CropTheBug system were 7.0 and 8.5 times higher for these broths (1.4 and 1.7 mg), respectively. For MB, the Pathatrix captured no beads from spiked spinach in *Shigella* broth and only 0.1 mg of beads from Shiga broth while the *i*CropTheBug system yielded 1.1 mg of beads from *Shigella* broth and 1.2 mg from Shiga broth (i.e., at least 10 times higher). The weight of the captured beads increased notably with spiked spinach (1.1 mg to 1.7 mg) compared with the nominal weight of the added beads (BT: 0.75 mg/100 µl and MB: 1.0 mg/100 µl, respectively), presumably due to adsorbed spinach components and captured bacteria.

CONCLUSIONS: These preliminary results demonstrate excellent capture of BT or MB magnetic particles from food and water samples by the iCropTheBug system. The system is easy to use, faster than Pathatrix, occupies little space and appears ideally suited to use in the field (e.g., on-site water analysis) as it requires only a 9V DC power source.

3.03 Consensus on Terminology for Psychoactive Pharmaceutical Products Abuse

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SUMMARY: Psychoactive therapeutic substances can be abused or lead to addiction. Research in this area and consensus around concepts and terminology is lacking. An international group of experts identified the most appropriate terminology to use in surveillance and research on psychoactive pharmaceutical 'abuse' and defined key concepts and indicators.

OBJECTIVES: Identify the most appropriate terminology to use in the conduct of surveillance activities and research on psychoactive pharmaceutical 'abuse' and to define key concepts and indicators.

DESIGN: Health Canada convened an international group of experts who developed a framework for defining the terminology using the following dimensions: patterns of use (dose, route, duration/frequency), use in combination with other psychoactive substances, disregard of precautions, degree of guidance/supervision (e.g., ongoing re-evaluation of risk/benefit), purpose (non-therapeutic vs. therapeutic) and source.

OUTPUTS/RESULTS: Results of the workshop included a consensus on definitions for abuse, dependence and addiction.

IMPACTS/OUTCOMES/CONCLUSIONS: These definitions are informing the development of indicators for inclusion of psychoactive pharmaceuticals in surveillance initiatives, such as the new Canadian national drug use survey that is currently under development.

3.04 Approaches for Meeting the Regulatory Clinical Data Requirements for the Market Authorization of [18F]-Fluorodeoxyglucose (FDG), a Radiopharmaceutical for Diagnostic Imaging with Positron Emission Tomography (PET) in Various Cancer Indications

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SUMMARY: [18F]-Fluorodeoxyglucose (FDG) has a long history of safe use as an investigational diagnostic radiopharmaceutical in various cancer settings. To avoid duplication of available literature evidence, approaches have been taken to reduce the clinical data package in marketing applications of FDG to support a per-disease indication within the current regulatory framework.

OBJECTIVES: Describe the approaches taken in meeting the clinical data requirements for the market authorization of FDG (a Schedule C drug) under the current regulatory framework, and suggest additional approaches.

DESIGN: An analysis of the available evidence on the investigational use of FDG and of the regulatory requirements as interpreted by the policy, *Regulatory Requirements for Positron-Emitting Radiopharmaceuticals (PERs)*, was carried out.

RESULTS: FDG with PET has a significant history of investigational use in cancer imaging at over 25 institutions in Canada. Because of the short half-life ($t_{1/2}$=110 min) of FDG, each institution produces its own product or obtains a product from a nearby supplier. Several reports suggest that FDG is safe and efficacious in many cancer settings. The current regulatory framework for market authorization requires original clinical trial data for each FDG product and for each indication.

However, in order to account for the published studies of safety and efficacy, each FDG marketing application under a New Drug Submission (NDS) may fulfill the regulations with:

1) A bridging clinical trial in a specific cancer setting with a sufficient sample size in order to allow a meaningful statistical comparison of sensitivity and specificity with literature values, and/or

2) A retrospective analysis of data from the sponsor's own open-label experience, and

3) Acceptable quality and chemistry & manufacturing data.

Based on the sponsor's clinical data and published literature, a request to broaden the indication on a per-disease basis can be considered. For example, a bridging study in solitary pulmonary nodule may support other uses under 'lung cancer'.

CONCLUSIONS: The approach described suited the two initial NDSs for FDG. However, significant duplication may result as additional FDG products and/or indications seek market authorization. The feasibility of using the abbreviated regulatory framework, and of relying solely on published data to support additional indications, could be explored in the future.

3.05 A Determination of Inter-Rater Agreement in Assessing the Quality of Research Papers

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SUMMARY: A research instrument was developed to evaluate the methodological quality of published research papers. The reliability of evaluations conducted by two reviewers on 63 papers was examined. Reviewer agreement was only 65% demonstrating that the questions within the instrument should be improved to be used with a broader application.

OBJECTIVES: In the winter of 2005, a systematic review was undertaken to assess alternatives for trans fat in the Canadian diet as a component of work that supplemented the recommendations produced by the Trans Fat Task Force. A portion of this work involved the development of a study appraisal tool to assess the methodological quality of the papers gathered from a literature review used to support these recommendations.

DESIGN: An eight-page study appraisal tool was developed based on a review of existing checklists/scales/research for the assessment of both randomized and non-randomized studies. This tool was developed to further remove any ineligible papers and to appraise study quality. Applying pre-selected inclusion/exclusion criteria, 63 papers were assessed. The appraisal tool addressed issues of internal validity (14 questions; e.g., sample size, appropriate statistical tests, etc.) and clinical applicability (7 questions; e.g., population appropriateness). Each paper was independently assessed by two reviewers, an overall assessment (Good, Fair, Poor quality) of all appraised studies was determined and the inter-rater agreement was calculated using Kappa Statistics (K) and percentage agreement.

RESULTS: The kappa value for the inter-rater agreement of assessing the overall quality rating of each study was K= 0.14 (poor inter-rater agreement) with a 65% agreement. The relatively poor agreement between the reviewers was likely a reflection of the subjective nature of the process and the need to refine the tool to better reflect methodological quality. Five of the questions regarding internal validity and two questions related to clinical applicability had no influence on the quality appraisal of papers.

IMPACT/CONCLUSIONS: In order for the tool to be utilized with a broader application, further work needs to be conducted to refine the questions related to internal and external validity so that they truly assess methodological quality.

3.06 Evaluation of Subsequent Entry Biologics in Health Canada: Issues and Challenges from Clinical Perspectives

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SUMMARY: This study identified the challenge and issues in evaluation of the clinical data of subsequent entry biologics submissions in Health Canada. Impact of varies options to deal with the challenges/issues were discussed. Advances in the research of biologics and policy initiatives may provide a good opportunity for regulatory guidance development.

OBJECTIVES: Patent expirations for biologics provide opportunities for introducing subsequent entry biologics (SEB) in Canada. This study is to report the challenges and issues in the evaluation of clinical data required to support marketing authorization of SEBs in Canada.

DESIGN: The current regulatory guidelines/practices in evaluating clinical data for SEB submissions in different jurisdictions have been reviewed. The common challenges and issues in evaluating the clinical data were identified. Various options dealing with these challenges and issues were suggested.

RESULTS: The current regulatory practice in evaluating clinical data of SEB submissions in Canada is outlined in an SEB factsheet published on the Health Canada website. Because a regulatory guidance document is still under development, for now, clinical data from SEB submissions will be evaluated utilizing the new drug submission (NDS) pathway.

A reduced clinical data package, rationale for data extrapolation and clinical indications as compared with the reference used in trials are the most challenging issues in the evaluation of clinical data of SEB submissions. It should be emphasized that although the number of clinical trials conducted may be reduced to a certain extent, the quality of a pivotal trial, including the number of patients enrolled, should be appropriate to demonstrate the similarity of SEBs to the reference biologics from both efficacy and safety perspectives.

It is our opinion that advances in biologics research, SEB regulations in other jurisdictions, and the new policy initiatives in BGTD would provide a good opportunity to develop practical guidance for regulating SEBs in Canada.

CONCLUSIONS: Clinical reviewers are facing scientific and regulatory challenges in the evaluation of clinical data from SEB submissions. These challenges would impact on the timely approval of application for marketing authorization of SEBs and on the consistency of the standards for granting authorizations.

3.07 Seniors' Falls in Canada: Predictors, Prevalence and Consequences

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SUMMARY: Injuries sustained in unintentional falls are a serious public health issue for Canada's seniors. With longitudinal data we explore the characteristics of those seniors who suffer a fall, and of those seniors for whom a fall is most health altering.

OBJECTIVES: This study examines falls among Canadian seniors (aged 65+) in order to identify those most at risk of suffering falls, and those most at risk of declining health subsequent to a fall.

DESIGN: Using the personal / household (94/95 to 04/05) and health institutions (94/95 – 98/99) components of the longitudinal National Population Health Survey (NPHS) we follow all seniors in the survey, with special attention to those who suffered falls in any cycle. How did those suffering falls differ from the general population of seniors? What are the health impacts after a fall? Several measures of health, common risk factors, and use of health services are explored.

OUTPUTS/RESULTS: Logistic regressions of the NPHS longitudinal data on seniors are used to establish a profile of seniors who fall. Next, among those who suffered falls, determinants of subsequent health status are identified. Several predictor variables differentiate those who suffered a fall from those who did not, and differentiate the health consequences of a fall.

IMPACTS/OUTCOMES/CONCLUSIONS: As the population ages, we can expect a significant increase in injurious falls. Longitudinal analysis allows for the identification of predictive factors, prevalence, and consequences of seniors' falls. By sharing this knowledge, policy makers, researchers, and other stakeholders can contribute to the development of effective fall prevention policies and interventions, and to the reduction of trauma, disability and premature death from falls among Canadian seniors.

3.08 Success Factors in First Nations Communities

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SUMMARY: The First Nations and Inuit Health Branch is exploring factors that create and sustain successful and healthy First Nations communities to inform future policy directions with an approach that builds on the strengths of First Nations communities.

OBJECTIVE: To identify characteristics and/or indicators which constitute a "successful" community from a First Nations perspective to inform policy directions with an approach that builds on strengths.

This project uses oral interviewing as a method of knowledge translation for data collection. Twelve Indigenous leaders in health in Canada were asked to share their impressions about what constitutes a "successful community" and provide examples of such communities. Interviewees were selected from a list developed by the Assembly of First Nations, First Nations and Inuit Health Branch (Health Canada), and Kishk Anaquot Health Research. Participants were asked the following standardized questions: Which communities would you identify as "successful"? Why? Are successful communities random or predictable, and why? Can successful communities be created? If so, how? If not, why not? Responses were tabulated and analysed to identify commonalities and differences.

Although much of the data are qualitative and anecdotal, points of divergence and convergence between data sources are possible and the sampling strategy attempted to ensure representation from regions, and all operational levels (i.e., community, regional and national).

Responses can be grouped into three categories: Relationship, Institutions and Leadership. *Relationship*, for example, identifies a community environment, which is collaborative and has a strong identity. *Institutions* include the concept that community members respect and participate in local institutions. *Leadership* identifies a community, which is proactive in planning toward a long-term vision. This list will inform future research to validate findings.

This research is intended to be the first step in the development of a tool to effectively measure key indicators of success in First Nations communities. Next steps include the development of case studies of identified "successful" communities to identify key success factors. This information can inform health policy that will support the development of these success factors in First Nations communities.

3.09 Human Papillomavirus (HPV) and Cervical Dysplasia in the Northwest Territories (NWT)

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SUMMARY: Women in the NWT attending routine clinics for Pap tests will be invited to participate in HPV/DNA test and a risk factor questionnaire. The resulting analysis of HPV prevalence and risk factors for cervical dysplasias will help guide government and community development of more effective cervical cancer screening programs.

OBJECTIVES: To determine the prevalence of HPV infection and cervical dysplasia in women of the NWT; to determine the impacts of the HPV sub-types infection and demographic and behavioural risk factors on the prevalence of cervical dysplasias; and provide evidence for policy makers, community leaders and local public health professionals in NWT to plan and implement more effective cancer control programs.

DESIGN: Women over the age of 15 in the NWT who attend routine clinics for Pap smears will be invited to participate in this cross-sectional study. A consent form and a risk factor questionnaire will be filled by the participants. Sample collection will be incorporated into the routine Pap testing done by local physicians or community health nurses. The HPV/Gene test will be performed by the National Microbiology Laboratory in Winnipeg using the Luminex assay. Data management and analysis will be performed by CCDPC, PHAC.

OUTPUTS: A descriptive analysis of socio-demographic characteristics will be performed. The prevalence of HPV infection and dysplasia will be calculated with 95% confidence intervals. Multivariate logistic regression analyses will be used to explore associations between outcomes and explanatory factors. Population attributable risk fraction will be calculated to measure the impact of explanatory factors to the prevalence of HPV.

IMPACT: This study will contribute to our knowledge of HPV prevalence in women living in the NWT. The results may be useful in developing strategies aimed at preventing HPV infection and reducing the burden of illness associated with high risk HPV infection. This study is expected to demonstrate that more effective cervical cancer screening programs can be developed with the use of HPV testing in combination with the conventional Pap testing.

FUNDING: A total of $610,000 dollars was granted from the Department of Indian and Northern Affairs through a NSERC/IPY peer review process.

3.10 Indigenous Community Engagement in Health Impact Assessment

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SUMMARY: The Environmental Research Division of First Nations and Inuit Health Branch promotes Health Impact Assessment (HIA) within a legislated Environmental Impact Assessment (EIA) process. The presentation will outline the importance of HIA/EIA integration and highlight a number of challenges in carrying out this integration from an indigenous perspective.

OBJECTIVES: Building capacity within Indigenous communities to carry out research in support of Health Impact Assesment; thereby leading to beter decison-making.

DESIGN: Environmental Impact Assessment (EIA) is seen as part of a global strategy to meet Sustainable Development (SD) needs at the local, regional and international level. EIA is a legislated process in over 100 countries around the world. Health Impact Assessment (HIA) is a holistic and innovative approach to impact assessment, which clearly places human beings at the centre of considerations about development, while seeking to ensure the durability of the ecosystem of which they are an integral part. HIA is an attempt to bridge the disciplinary specialization and distinct world views, presently reflected in human health risk assessment (identification of hazards and subsequent analysis of exposure and risk) and the more holistic community health model (determinants of health).

Training and capacity building is needed; in particular with small, remote Indigenous communities. The Environmental Research Division (ERD) of FNIHB, HC, has focused on improving community engagement in HIA by promoting community-based research (questions developed by the community, research conducted by the community, results disseminated and used by the community for decision-making). Because the research is done by Indigenous communities they have greater capacity to develop and disseminate their own culturally sensitive information (Traditional Knowledge) on the health impacts of a development project, thereby leading to better evidence-based decision making.

RESULTS: Health Canada has become a world leader in HIA and the department has been involved in capacity building internationally. ERD is now focusing capacity building on small remote Indigenous communities so that they too can participate fully in decision-making.

CONCLUSIONS/IMPLICATIONS: ERD's efforts to enhance indigenous peoples understanding of HIA/EIA integration and environmental research will lead to inclusive rather then exclusive research and to better decision making.

3.11 Assessment of Government Policies and Guidelines to Improve the Uptake of Science in Health Policy

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SUMMARY: Good science is necessary to accurately diagnose an issue, to support one course of action over another, to evaluate a chosen policy option and to review the evidence of policy effectiveness and efficiency. Gaps in science guidelines have been identified that may limit implementation and performance of science into policy.

OBJECTIVE: to review federal government policies related to science policy to determine:

1) If there are any gaps in the main science policy documents that may support the belief of a gap in the federal science/policy practices; and
2) What strategies could be applied to address the gaps and improve the science/policy interface.

METHODS: A review of 34 federal science policy documents, using standard criteria, was conducted to address the first question posed in the objective statement. A review of the evidence-based policy literature was also completed and particular attention paid to case study reviews that could be used to identify possible strategies to improve the use of science in evidence-based policy.

RESULTS: The guidance documents reviewed did meet the majority of the criteria, however, there are gaps in implementation guidance and especially evaluation. System standards need to be set and reinforced with a view to developing a learning environment built on continuous quality improvement principles. Twelve key recommendations have been determined towards an employable strategy to more fully utilize science in the service of health policy.

A science based department's ability to provide science evidence is also necessary in order to respond to pressures for greater transparency and accountability in decision-making. It is often stated that a "gap" exists at the interface of science and policy that hinders our ability to produce, disseminate and uptake the science required for health policy related activities. These results suggest there may be areas of science policy that could be improved to further implementation and performance of science in health policy.

3.12

WITHDRAWN

3.13 Integrating Patient and Consumer Voices in Evidence-Based Decisions About Risk and Benefits

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SUMMARY: Healthy Products and Food Branch (HPFB) is developing more open and transparent regulatory approaches that integrate public input, including qualitative information, as a source of important evidence in our assessment of the risks and benefits of health products, resulting in strengthened regulatory decisions. (e.g., advisory bodies or public forums re: breast implants or Cox 2.)

OBJECTIVE: As drug regulation worldwide changes in response to advances in pharmaceutical sciences, drug development, and changes in public expectations, the HPFB is modernizing its approach to regulating therapeutic products and food under a "Blueprint for Renewal". Public involvement is integral to this modernization. To successfully implement its *Review of Regulated Products: Policy on Public Input,* HPFB is developing methodologies to identify the need for broader input, assess different kinds of evidence, and will increase information available to support informed participation.

DESIGN: Given the horizontality and complexity of regulatory environments, regulators managing risks related to food and health products increasingly rely on broader external expertise and experience to arrive at quality decisions.

Public and stakeholder involvement can also enhance public trust and confidence in the regulatory system.

"Government of Canada's Cabinet Directive on Streamlining Regulation" (2007) emphasizes "open, meaningful, and balanced consultations at all stages of the regulatory process"*.*

To support the inclusion of public input, HPFB is developing methodologies to assess and integrate different kinds of qualitative and quantitative evidence, for a more complete evidence picture.

RESULTS: The Policy on Public Input's emphasis on the contribution of a range of perspectives and evidence to the risk-benefit assessment represents an important step in the modernization of the regulatory system.

There is broad acceptance of the Branch's mandate to seek public input as part of regulatory decision-making and that public input is relevant to the legislated criteria of safety and effectiveness.

CONCLUSION:
-External input strengthens our decisions and our accountability to Canadians.
-Informed participation relies on increasing the amount and kind of information (about regulatory processes; information used to make decisions; or regulated products) available to the public.

-Methodologies to incorporate broader evidence from public input will become increasingly important to regulators assessing risks and benefits throughout a regulated product's life cycle.

3.14 Determination of Deoxynivalenol in Soft Wheat by Immunoaffinity Column Clean-up and HPLC-UV Detection: Interlaboratory Study

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SUMMARY: Deoxynivalenol (DON) is a naturally-occurring mycotoxin common in North American grains. The current Canadian guidelines are under review. To support the current or revised guideline, an analytical method was successfully validated by an international collaborative study. The method was determined to be fit for use as an official method.

OBJECTIVES: Validate an analytical method for deoxynivalenol (DON) in soft wheat by international collaborative study. Transfer the method to Canadian Food Inspection Agency and other stakeholders for compliance testing in support of existing guidelines and anticipated revisions to the guideline levels for DON.

DESIGN: Soft wheat samples, naturally contaminated with DON at five levels, were analysed as blind duplicates by twelve laboratories in eight different countries using the subject method. Blank wheat materials were spiked in duplicate with DON for recovery assessment. The analytical portion of the sample was extracted with water. The sample extract was centrifuged, filtered, passed through an immunoaffinity column for clean-up and evaporated. The residue was dissolved in mobile phase (water + methanol [90.5 + 9.5, v + v]). The separation and determination of DON was performed by reverse-phase HPLC, with detection by UV absorption at 220 nm.

OUTPUTS/RESULTS: Statistical analyses of the results from all five contamination levels and spiked samples met the repeatability, reproducibility, and recovery criteria for DON outlined by the European Community and AOAC International.

IMPACTS/OUTCOMES/CONCLUSIONS: Results from this collaborative study indicate that the method met the within- and between-laboratory precision for soft wheat, is fit for use as an official Health Canada method, and can be used for regulatory purposes. The method will be submitted for inclusion in Health Canada's compendium of methods for chemical analysis of foods.

3.15 Measuring Efficiency and Effectiveness in Healthcare Sector: Issues and Challenges

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SUMMARY: This paper provides a survey of recent development of efficiency and effectiveness measurement on public health spending. It outlines a conceptual framework in which efficiency analysis can be carried out in healthcare sector, and identifies the challenges and data gap for future research.

OBJECTIVE: This paper aims to provide a framework for efficiency analysis by conducting a critical review of recent development in efficiency and effectiveness measurement in the healthcare sector.

DESIGN: We review in considerable detail the conceptual and measurement issues on measuring efficiency, describe various approaches found in the literature, and examine possible ways forward for more accurate measurements in the health care sector, with a particular attention on the measurement opportunities and challenges in the Canadian context. Based on the literature, we propose a framework for efficiency analysis at various levels of the health care system.

OUTPUTS: We suggest that the health system performance could be evaluated and compared at different levels. At the system level, measuring and explaining health outcomes and cost-effectiveness should be given priority, although output measurement within the system of national accounts also needs to be improved. At disease level, although health outcome indicators such as quality-adjusted life years have been used, other indicators are needed to better reflect the impact of preventive care policy. Since it is easier to obtain a high quality output indicator for homogenous segments of the health care system, output measures are suggested to be used for efficiency measurement at sub-sector level. Through the critical literature review, we find that these approaches are complementary, but significant data gaps exist.

CONCLUSIONS: Measuring efficiency and effectiveness of health care is of great importance for policy making. The limited number of studies, controversial methodologies, and existence of data gap all call for further research to improve the measurement in the health care sector. In the meantime, policy makers should be aware of the limitations and uncertainty of different techniques employed for efficiency measurement, particularly in cross-country comparisons.

3.16 A North American Standard for the Analysis of Norovirus Genotypes

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SUMMARY: To control spread of norovirus infections, we need to identify when an outbreak spreads from a single source. This is only possible if all testing labs use the same typing methodology. To achieve this, a collaborative project has been initiated to determine a standardized protocol for use across North America.

OBJECTIVES: To compare two separate protocols and identify the most sensitive and reproducible method for norovirus genotyping and recommend its implementation across North America.

DESIGN: A panel of 100 norovirus samples has been prepared by Health Canada and Centers for Disease Control and Prevention (CDC) coordinating labs. This panel has been tested using “Region C” and “Region D” protocols in the two coordinating labs. The panel will be shipped to nine public health laboratories across North America for the same testing. Data from the participating labs will be received and analysed by October 2007.

RESULTS/OUPUT: Preliminary results obtained by the two coordinating labs indicate that the “Region D” typing system is more sensitive than “Region C”, identifying 83% of strains compared to 69% for “Region C”. However, four strains were identified by “Region C” and not by “Region D”.

IMPACTS/OUTCOMES/CONCLUSIONS: The “Region D” protocol is tentatively identified as the most sensitive; this awaits confirmation in the large collaborative study. There may be some merit to a two-step procedure, where “Region D” is preferentially recommended, with “Region C” reserved for typing samples not successfully identified by “Region D”.

3.17 Extending the Evidence Base to Enhance the Quality of Regulatory Safety Review of Health Products

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SUMMARY: This paper describes a project to develop tools to assist evaluators of regulated marketed products (health and food) in implementing HPFB's Policy on Public Input. These tools will be used for integrating qualitative and quantitative data in regulatory safety review, in cases where completion of evidence requires public input.

ABSTRACT: Drug regulation worldwide is changing in response to advances in pharmaceutical sciences, drug development, and changes in public expectations. Health Products and Food Branch (HPFB) is reviewing its own approach to regulating therapeutic products and food, and consequently, legislative, regulatory, and policy frameworks are being modernized under a "Blueprint for Renewal".

Integral to this modernization is public consultation and transparency at all stages of the regulatory process, as emphasized in a 2007 Government of Canada Cabinet Directive on Streamlining Regulations. The effective management of risks related to food and health products relies on public and stakeholder confidence. In the case of some products where scientific uncertainty is high, effective risk management may also depend on the knowledge and experience of stakeholders as product consumers, in support of quality regulatory decision-making.

*HPFB's Review of Regulated Products: Policy on Public Input*articulates circumstances where the Branch may identify a need for evidence from external sources in addition to that provided by product sponsors in a typical submission for safety review. The Branch is developing methodologies to assess and integrate different kinds of evidence on specific health products, where reviewers may benefit from supplementing existing scientific knowledge with real-world experience of the risks and benefits arising throughout a drug's life cycle. OCAPI, charged with overseeing implementation of the Policy, initiated a project to investigate the perspectives of on-the-ground regulatory actors with an early opportunity to refer products for input: Branch review staff. This paper addresses the sub-theme through its attention to reciprocal relations between knowledge users and generators; articulating lessons from public engagement; and recognizing the value of the contribution stakeholders can make to a scientifically sound risk-benefit analysis of regulated products.

OBJECTIVES: 1) Develop instruments to support implementation of a policy on incorporating input from public (external) sources into regulatory safety review. 2) Establish cross-Branch communications to ensure tools and guidance respond to the needs of those regularly using them.

DESIGN: A four-stage method was developed:

1. Iterative documentary review (international best practices; literature on comparative validity measures for qualitative data; relevant Branch initiatives and instruments).
2. Questionnaire investigating evaluators' perspectives, with findings informing development of a draft implementation tool.
3. Evaluator focus groups to gather feedback on the draft tool and fine-tune remaining steps of the project.
4. Refinement of tool for piloting within the Branch.

RESULTS: Stage 3 is completed. Early analysis shows that evaluators recognize their compliance with the Policy is dependent on a flexible, multi-phase tool (checklist, decision tree, standard operating procedure, scenarios, additional guidance) with support within each directorate. Innovative suggestions were recorded and are being incorporated into the implementation strategy.

CONCLUSIONS: Variations in practices and culture across directorates may impact on the 'Branch-wide' nature of transformation of review. While some generalized tools will be valuable in early implementation, it is expected that customization of guidance and instruments per directorate will likely ensure smooth implementation.

3.18 A Microsimulation Model to Measure Impacts of Policy Changes in Federal/Provincial Health Insurance Schemes

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SUMMARY: Cost and effectiveness issues have generated a need for changes in the program elements of certain non-essential health coverage targeting underprivileged populations. To compare and contrast different proposed changes, we developed a microsimulation model “The Gupta Model”. The model quantifies the impacts of hypothetical plans on both the target population and government expenditures.

OBJECTIVES: This model has three closely related objectives. The first is to estimate federal/provincial costs for pharmaceutical and dental coverage under new hypothetical model options and existing options. The second is to perform ‘what if’ analysis on program options to enable a short list of feasible alternatives. The third is to conduct an impact analysis of such options to reduce the cost burden for the government with a minimum impact on health outcomes of the vulnerable individuals/families.

DESIGN: The Gupta model requires comprehensive individual data on the health expenditure and utilization. Due to the lack of several required variables in the available data, data gaps were filled by merging two different large complex administrative claim data systems and then simulating non-claimants to obtain a list of all eligible clients of that population. Demographic information and family structure of the claimants and non-claimants were simulated using a Monte Carlo technique to further enhance this merged database. The model incorporates existing federal/provincial and hypothetical pharmaceutical and dental coverage, and conducts simulations on this comprehensive database to identify policy options that optimize benefits for the population in question while minimizing cost.

OUTPUTS/RESULTS: This model is applied to a synthesized health utilization and expenditure dataset to assess the impacts of possible changes on federal/provincial health insurance schemes. These allow selection of a short-list of feasible alternatives to assure the continuing sustainability and efficiency of such programs for those underprivileged populations.

IMPACTS/OUTCOMES/CONCLUSIONS: The Gupta model provides policy makers with a robust tool to identify gaps in pharmaceutical and dental insurances and the need for policy action to minimize health risk to some underprivileged populations in Canada. This robust tool can be easily generalized to specific health programs for underprivileged populations in other countries such as Australia or the US.

3.19 Toward a Monitoring Network: A Technical Workshop for Pharmaceuticals and Personal Care Products in the Environment

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SUMMARY: Further research is needed to determine the potential impact to non-target organisms of pharmaceuticals and personal care products found in the Canadian environment. In 2004, Health Canada, Environment Canada, the Canadian Water Network, Agriculture and Agri-Food Canada, and the Ontario Ministry of the Environment sponsored a second workshop to examine in greater detail three areas of research (analytical methods, sampling, and effects), and to recommend strategies to achieve the 2002 research agenda.

A large number of substances contained in pharmaceuticals and personal care products (PPCPs) have been detected globally in the environment. Human waste (sewage) and current livestock and aquaculture production practices, combined with increasing sales of PPCPs are contributing to the increasing environmental exposure of these substances. Further research is needed to determine the potential for these substances to cause a variety of physiological responses in non-target organisms. In addition, the indirect impact on human health and the direct impact on the environment need to be examined further.

In an effort to enhance collaboration on issues related to PPCPs and the environment, Health Canada and Environment Canada brought together a group of international experts in this field in March 2002 to assess the information gaps and to propose a prioritized research agenda to address the identified gaps.

In follow up to the 2002 workshop, in March 2004, Health Canada, Environment Canada, the Canadian Water Network, Agriculture and Agri-Food Canada, and the Ontario Ministry of the Environment sponsored a second workshop to examine in greater detail three areas of research (analytical methods, sampling and effects) and to recommend strategies to achieve the 2002 research agenda.

The title of this workshop was “Toward a Monitoring Network: A Technical Workshop for Pharmaceuticals and Personal Care Products in the Environment”. The development of a monitoring network would help to further understand the potential risks of PPCPs in the environment. This workshop provided a forum to discuss PPCPs within a cross-jurisdictional, national and international perspective. Its main objectives were to focus on analytical methodologies and capacity, sampling protocols, bioassays, measuring effects, and building on existing partnerships.

The proceedings of this workshop have been published as a government report. The major conclusions and recommendations will be presented as well as a tabulated summary of research priorities.

3.20 The Canadian Listeriosis Reference Service: Surveillance for Listeria monocytogenes in Canada, 1995 – 2003

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7 CPHLN, the Canadian Public Health Laboratory Network, is a nationally minded, proactive forum of public health laboratories

SUMMARY: Listeria monocytogenes is capable of growing at refrigeration temperatures, and thus is of major concern in extended shelf life, refrigerated foods. It is thought that as much as 80 to 90% of human listeriosis cases are linked to the ingestion of contaminated food.

OBJECTIVES: In Canada, listeriosis has recently been re-added to the list of nationally notifiable diseases (since its removal in 1999). Provincially, listeriosis has remained reportable, though it has only been reportable in Quebec since 2003. Canadian cases and outbreaks of illness caused by *L. monocytogenes* between 1995 and 2003 were tracked and characterized by serotyping, and pulsed-field gel electrophoresis (PFGE).

DESIGN: In 2001, the Canadian Listeriosis Reference Service (LRS) was created with major goals to include investigation of listeriosis cases and maintain a national collection of isolates. The LRS is creating a comprehensive molecular epidemiological database of all Canadian isolates for use as a resource for outbreak investigations, research and other microbiological investigations. PFGE profiles are being established and stored for clinical, food, environmental, and possibly animal strains. Other activities for the investigation into the ecology, behaviour, and characterization of *L. monocytogenes* includes ribotyping, multi-locus sequence typing (MLST), variable number of tandem repeats (VNTR), multi-locus virulence sequence typing (MLVA), microarray-based technologies and sequence-based typing schemes. Most isolates were obtained from blood and cerebrospinal fluid. A total of 557 listeriosis cases were reported to provincial/territorial and/or national notifiable disease systems during the study period.

OUTPUTS/RESULTS: The average annual incidence rate of reported listeriosis remained below 0.35 cases per 100 000 nationally. The overall male:female ratio of the 555 cases where gender data was available was approximately 1:1. Serotype 1/2a predominated in isolates from patients in Canada, followed closely by serotypes 4b and 1/2b.

IMPACTS/OUTCOMES/CONCLUSIONS: A retrospective analysis of PFGE data uncovered several clusters potentially representing undetected outbreaks, suggesting that prompt and comprehensive prospective PFGE analysis coupled with real-time epidemiological investigations may lead to improved outbreak detection

and control. The molecular epidemiological data, timely coordination and exchange of information should help to reduce the incidence of listeriosis in Canada.

3.21 Development of Canadian Standards for Working with Foodborne Viruses: The Microbiological Methods Committee's (MMC) Technical Group on Virology

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SUMMARY: Known and emerging enteric viral agents such as noroviruses, hepatitis A, and hepatitis E are increasingly incriminated in foodborne disease. A pressing need exists to develop more efficient, reliable and rapid methods to capture, concentrate and detect viruses in food matrices, as well as aiding in policymaking and regulatory-based activities.

OBJECTIVES: A technical group was created to standardize methodologies for detection and characterization of foodborne viral pathogens and develop guidelines for validation of novel methodologies. To compare disparate methodologies, the use of the feline calicivirus (FCV) as an internal control for all isolation and detection methods targeting RNA viruses is proposed.

DESIGN: Plaque forming units (PFU), tissue culture infectious dose ($TCID_{50}$) and reverse transcription-polymerase chain reaction (RT-PCR) units were used to titre stocks of FCV. This study was also an example of the methodology required for validating viral isolation procedures, including three different viral stocks each tested in triplicate by two different laboratories.

OUTPUTS/RESULTS: There was no significant difference between the titres of the three stocks assayed in triplicate using the $TCID_{50}$ or the PFU approach. Variability between replicates was used to assess differences between the titration methods. Two labs each performed plaque assays in triplicate and there was a maximum 3.5 fold difference between the titres. The $TCID_{50}$ assay had greater variability, with titres ranging from 1.8×10^6 units/mL to 1.3×10^8 units/mL. Statistical analyses suggest that the PFU assay is more sensitive at detecting variability between stocks, being more precise than the $TCID_{50}$ method, which demonstrated significantly more variability than the PFU method. This indicates that plaque assays may be a better indication of FCV titre for use as a control in viral extraction methods. FCV will be useful as a control when validating current and emerging isolation, nucleic acid extraction and downstream amplification methods.

IMPACTS/OUTCOMES/CONCLUSIONS: The true potential impact of foodborne gastroenteric and hepatic viruses on public health remains uncertain. The use of standardized, continual and active surveillance in Canada will enable quantification and mitigation of this risk. This work will be essential for developing risk assessments for virally acquired foodborne illnesses in Canada.

3.22 Working Conditions of Nurses and Absenteeism: Is There a Causal Relationship? An Empirical Investigation of National Survey of the Work and Health of Nurses

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SUMMARY: We used 2005 National Survey of the Work and Health of Nurses to investigate the causal relationship between the working conditions and illness- and injury-related absenteeism of Registered Nurses (RNs) and Licensed Practical Nurses (LPNs) working full-time. Our empirical findings suggest the existence of such a relationship.

OBJECTIVES: Investigate the causal relationship between the working conditions and illness- and injury- related absenteeism of full-time Registered Nurses (RNs) and Licensed Practical Nurses (LPNs).

DESIGN: Using 2005 National Survey of the Work and Health of Nurses (NSWHN), we estimated Negative Binomial regression models separately for RNs and LPNs with *absenteeism* as the dependent variable, which we defined as the number of days missed due to illness or injuries. The regressors included in the model are working conditions, work settings, and shift type/length along with socio-demographic variables.

OUTPUTS/RESULTS: Among the working conditions variables (various scores computed by Statistics Canada for the NSWHN), only *depression scale score* is statistically significant for RNs but *role overload score, effort-reward imbalance score* are also significant for LPNs with expected signs. Higher *depression scale score* leads to higher absenteeism for both RNs and LPNs. For LPNs, higher *role overload score* leads to higher absenteeism but higher *effort-reward imbalance score* (higher reward for a given effort) leads to lower absenteeism. For LPNs, those working in *long-term care facility*, *community health setting* and *other* are likely to have lower absenteeism than those working in hospitals, and those working *12-hour* shift are likely to have higher absenteeism than those working *8-hour* shift. Those working *evening* shifts are likely to have higher absenteeism than those working *day* shifts for both RNs and LPNs. For RNs, those working *mixed* shift are also likely to have higher absenteeism. Absence of chronic conditions leads to lower absenteeism for both RNs and LPNs. Male RNs or LPNs are less likely to be absent than their female counterparts.

IMPACTS/OUTCOMES/CONCLUSIONS: These results have implications for decision makers generally and health human resource policy makers specifically. The importance of exploring and implementing innovations in promoting healthy workplaces for Canada's nursing human resources is underlined given the evidence related to healthy work environments and decreased absenteeism.

3.23 Triangulation of Drug Use Data: Comparisons of General Population Surveys with Drug Seizure Information

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SUMMARY: Our understanding of drug use behaviours are typically derived from general population surveys. These surveys provide a rich source of information; however, they underestimate the actual levels of use. This project will compare the data from past surveys with seizure data to corroborate trends in survey-based estimates.

OBJECTIVE: (1) To explore multiple data sources on illicit drug use patterns within the Canadian population; and (2) to confirm the validity of trends in survey-based estimates of the prevalence of illicit drug use by comparing these trends with those associated with seizures from police and custom officers.

DESIGN: Data from several data sources will be examined to estimate illicit drug use across time and location. The National Alcohol and Other Drugs Survey (NADS; 1994), the Canada's Alcohol and Other Drugs Survey (CADS; 1994), and the Canadian Addiction Survey (CAS; 2004) provide estimates within the general population. Provincial school- based student surveys provide estimates for school-aged youth. Details of drug seizures will be gleaned from the Drug Analysis Service (DAS) Laboratory Information Management System and from the Controlled Drugs and Substances Database (CDSD). Information will be compared across time and region on several indicators of drug use in Canada. Matched-sample comparisons will be utilized when available. In-depth analyses will be computed on the general population data and linkages to drug seizure cases will be examined. Finally, the presentation will address methodological considerations when working with this type of data.

RESULTS: Preliminary analyses indicate that survey-based trends of illicit drug use within the general population are quite similar to trends observed with drugs seized by Canadian police and custom agents. Therefore, more in-depth analyses of survey based data and data collected from drug seizures will be conducted to identify if similar patterns will be observed amongst these different data sources. This will enable us to better estimate the prevalence of drug use within the Canadian population.

CONCLUSIONS: The data from general population surveys have great potential as an important and complementary source of information to drug seizure data that can be used for identifying emerging drug trends. Through the triangulation of these data platforms, a more robust assessment of drug use patterns in Canada can be estimated.

3.24 Studies on the Infectivity Distribution of Bovine Spongiform Encephalopathy (BSE) in the Small Intestines of Pre-Clinical Cattle for Definition of Specified Risk Materials (SRM)

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SUMMARY: The aims of this international collaborative study are to determine when and where the abnormal prion protein (PrPres) can be detected in the small intestine of young cattle orally challenged with BSE and if the tissues are infective. The results will be used in assessing the current federal SRM policy.

INTRODUCTION: To establish public health protection measures for BSE risks it is important to precisely define the tissues of infected BSE cattle that can transmit the disease. These tissues are defined in the *Food and Drugs Act* as specified risk materials (SRM) and are banned for use in food.

In Canada, only the distal ileum of the small intestine from cattle of all ages is defined as SRM. In clinically affected BSE cattle BSE was detected only in the distal ileum by biochemical tests and by conventional mouse bioassay. However, the sensitivities of those laboratory techniques are quite limited and no data are available for intestinal tissues from cattle in the early incubation phases of BSE.

OBJECTIVES: In cattle up to 24 months of age that are orally challenged with BSE:

- to determine the time after post exposure to BSE that abnormal prion protein (PrP^{Res}) can be detected and is infective in the distal ileum and jejunum of the small intestine; and
- to estimate quantitatively using biochemical tests the rates of increase of PrP^{Res} concentrations in the distal ileum and jejunum.

DESIGN: For this three-year study the small intestine tissues were collected at post mortem from two control animals and from 22 cattle that were orally challenged with 100 grams of BSE infected brain inoculua at 4 to 6 months of age. The tissue samples included jejunum, distal ileum and the ileocaecal junction from cattle which were culled after 4, 8, 12, 16, 20 and 24 months post exposure respectively. Biochemical tests used to detect PrP^{Res} include immunohistochemistry (IHC -two different monoclonal antibodies); western blot (WB), and two commercially available ELISA tests. To determine infectivity a bioassay using a transgenic mouse model (Tgbov XV) is used.

RESULTS: Preliminary results from the biochemical tests planned for fall 2007.

OUTCOMES/CONCLUSIONS: The systematic approach of this study will allow mapping of the exact temporal and spatial emergence/distribution of PrP^{res} in the

small intestine of young cattle, in particular in the gut associated lymphoid tissues (GALT).

Results will be used in evaluating the current definition of SRM.

3.25 Estimating the Temporal Relationship Between PrPRes Detection and Incubation Period in Experimental Bovine Spongiform Encephalopathy (BSE) of Cattle

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SUMMARY: This international collaborative study examines tissues from sequential kill, time course cattle pathogenesis studies to obtain guidance on estimates of the age at which the central nervous system tissues and associated structures should be removed from cattle at slaughter to protect human and animal health from exposure to BSE infection.

OBJECTIVES: To examine cattle tissue structures, that are both currently defined in Canada as specified risk materials (SRM) and some that are not and to determine at which stage of BSE incubation they are or are not infected with the BSE agent.

To correlate, compare, and evaluate BSE test methodologies (including sensitivity and specificity) that are currently in use in Canada or in use internationally for detection of the marker for the BSE agent in tissues, abnormal prion protein (PrP^{res}).

DESIGN: The cattle bioassay pathogenesis experiments included age matched controls; used varied oral doses of pooled brain inoculums; recorded observational data for all animals' lifetime in the experiment; and had sequential time period culls from the study by incubation age.

The earliest that challenged cattle were removed and tissues collected for analysis was at 2 months post exposure (p.e.) and the latest 89 months p.e. For this study 11 neural tissue structures from each animal were collected, fixed and frozen. For each cattle tissue selected, a known infection or control starting point and end point of the source animal was recorded. For comparative purposes the tissue samples underwent BSE testing with two tests currently being used in Canada and two others that are being used internationally.

RESULTS: Initial preclinical detection of PrP^{Res} was invariably by IHC in the brainstem. The earliest was 30 months p.e. in high dose (100 g challenge). The earliest in low dose (1 g challenge) was 44 months post exposure.

Little overall difference in the timing of detection of PrP^{Res} in brain and spinal cord.

Significant difference in the estimated time p.e of detection between the 1g and 100g dosed cattle.

By IHC applied to rostral medulla, 50 percent of cases would be detected in low dose cattle at 1.7 months before clinical onset and 9.6 months in high dose cattle.

OUTCOMES/CONCLUSIONS: The results from this study have been peer reviewed and accepted by a panel of international BSE experts. HC TSE Science and Policy Teams are reviewing current BSE risk management policies and the SRM legislation in light of these study results.

3.26 Relating Eating Well with Canada's Food Guide to Food Consumption and Nutrition Surveys

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SUMMARY: The objective was to update a methodology to assess nutrition surveys against the CFG guidance. Foods were classified into CFG groups and assigned a FG serving size. Total number of servings will be calculated and compared with CFG recommendations. This approach will provide valuable information on dietary compliance of Canadians.

OBJECTIVE: To update methodology to assess dietary adherence of the Canadian population against the guidance provided in Canada's Food Guide (CFG) since a new version of CFG was released in 2007.

DESIGN: The classification of foods and recipes into CFG groups as well as Food Guide (FG) serving size assignments was developed using the guiding principles and thresholds from work previously conducted with the Canadian Nutrient File (CNF). The classification and FG servings were revised to meet the 2007 CFG principles. To extend the classification decisions made for CNF foods to foods and recipes reported in national nutrition surveys, a number of additional steps were required. Reported foods were coded either as basic foods or as recipes with ingredients. Each recipe was examined to determine whether it should be classified as one single food guide group (ex: breaded pork chop) or if each component should be classified into different food guide groups (ex: lasagna). Once all food and recipes were assigned to a FG group, the number of servings had to be calculated. In the updated methodology the number of servings were calculated for all food groups by dividing the grams consumed by the FG servings size.

OUTPUT/RESULT: This updated methodology will be used to evaluate the Canadian Community Health Survey (CCHS 2.2) data in regard to compliance to the new CFG.

CONCLUSION: This approach will provide valuable information on dietary compliance of Canadians to the guidance provided in the 2007 CFG.

3.27 A Probabilstic Approach to Information Synthesis for Informing Nutrition Policy as Applied to Healthy Eating and Prostate Cancer

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SUMMARY: The development of an adequate scientific evidence base for policy development requires the synthesis of data and information from many different sources. We integrate and extend methods from epidemiology, biostatistics and risk assessment to synthesize information for policy development in nutrition, addressing concerns over dairy product intake and prostate cancer.

OBJECTIVE: To develop an integrated, systematic, probability based approach to the synthesis of scientific literature in support of the development of nutrition policy, particularly as it relates to chronic disease prevention. Concern over dairy product intake and prostate cancer provides a concrete example.

DESIGN: Systematic review methods, commonly applied to evidence based medicine, were used to identify meta-analyses in the current literature examining the association between dairy products and prostate cancer. Statistical results from these studies were combined with food consumption data and integrated in a probabilistic risk assessment model. Possible changes in dietary intake of dairy products for the Canadian population corresponding to various policy scenarios were simulated and the corresponding risks quantified.

OUTPUTS/RESULTS: Ten meta-analysis were identified in a systematic review, examining a variety of study populations, study designs and dietary exposures. Statistically significant results were reported in some individual meta-analyses. Descriptive information of all studies was provided. Results were combined using stochastic modelling techniques to compensate for variability and uncertainty across information sources. The simulations demonstrated that an increase of one serving of non-liquid dairy products daily (as is sometimes recommended) resulted in a negligible increase in prostate cancer risk.

IMPACTS/OUTCOMES/CONCLUSIONS: As addressing increasingly complex health issues, including chronic, multifactorial diseases becomes more of a focus of health policy, it is essential that research methods be developed to synthesize a wide range of information. Different from much systematic review work that focusses on scientific inquiry, this study utilizes statistical methods to summarize and integrate evidence from a safety perspective, in support of risk management decisions and the policy development process.

3.28 Transitions in Living Arrangements of Seniors: Empirical Findings from Canadian NPHS Longitudinal Data

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SUMMARY: This paper examines transitions in living arrangements decisions of the elderly individuals using Canadian National Population Health Survey (1994/95-2004/05). Transitions from independent to intergenerational and institutional living arrangements are analyzed. The paper provides several policy implications in order to respond to aging of Canadian population.

OBJECTIVES: Like other developed countries, Canada's population is becoming aged, and this aging has implications for health system costs. This paper explores the role publicly-provided homecare and social support services, self-reported health and other factors play in the decision of transiting from independent to intergenerational and institutional living arrangements of seniors.

DESIGN: We use a discrete-time hazard rate multinomial logit modeling framework and account for unobserved individual heterogeneity. The data for this study come from the first six cycles (1994/95-2004/05) of the National Population Health Survey, a nationally representative longitudinal health survey of Canadians, conducted by Statistics Canada. In this paper, we use responses of individuals who were aged 65 or above in the 1994/95 survey.

OUTPUTS/RESULTS: We find that the model that accounts for unobserved individual heterogeneity is the preferred econometric model to analyze transitions in living arrangements decisions. After accounting for unobserved individual heterogeneity and compared to the independent living arrangement, we find that: a) provision of homecare services reduces the probability of institutionalization by about 41%, but its effect on intergenerational living arrangements is statistically insignificant; b) access to and availability of social support services reduces the probability of institutional living arrangements in the range of 38-51%; c) higher levels of functional health status measured by HUI scores reduces the probability of transiting to both intergenerational and institutional living arrangements by more than 96%; d) a decline in self-reported health status increases the probability of institutionalization by about 42%, but does not affect intergenerational living arrangements; e) the hazard of transiting to both intergenerational and institutional living arrangements increases with the duration of survival; and f) Demographics and household income also affect transitions in living arrangements decisions.

IMPACTS/OUTCOMES/CONCLUSIONS: Our empirical findings suggest that provision of homecare services, social support services and healthy life-style contribute positively towards independent living and reduce institutionalization.

3.29 The Financial Burden of Prescription Drug Costs: Some Empirical Evidence from Canada

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SUMMARY: In Canada, the costs of prescription drugs are financed by a complex mix of public and private sectors. Some 20% of total prescription drug expenditure is financed through out-of-pocket expenses. This study examines how insurance status and socio-economic characteristics explain financial burden of drug expenditure and derive health policy implications.

OBJECTIVES: Prescription drug is one of the non-insured health care services under *Canada Health Act*. The objective of this study is to examine the financial burden of prescription drug expenses among adults and seniors in Canada.

DESIGN: The data for this study come from the comprehensive PHARMASIM database developed at the Microsimulation Modelling and Data Analysis Division of Health Canada. We use a two-component finite mixture method, which is more suitable to capture presence of latent heterogeneity in the data and has the natural interpretation of two classes characterized by high- and low financial burden. We conduct analysis of out-of-pocket expenses for Canadian adults aged 18 years and above as well as for seniors.

OUTPUTS/RESULTS: Our results suggest that the two-component finite mixture method is the superior econometric method compared to the ordinary least squares regression. We find that the predicted mean out-of-pocket drug expenses are $374 and $47 for the two latent classes for adults, and $790 and $144 for seniors. After controlling for provincial fixed-effects and latent heterogeneity, having insurance coverage is an important determinant of out-of-pocket drug expenses for adults. For instance, adults covered under both public and private insurance incur $1,147 and $184 in two latent classes. Household income, age, gender, marital status, educational status and immigration status are statistically significant determinants of out-of-pocket drug expenses and the results differ across the two latent classes for adults. We find that the results substantially differ for seniors and we offered plausible explanations of our results.

IMPACTS/OUTCOMES/CONCLUSIONS: Our study find that a number of socio-economic factors explain the financial burden of prescription drug consumption among adults. Because of the generosity of prescription drug coverage for seniors, a number of socio-economic and demographic differences that we found in the adult sample are largely absent in the senior sample.

3.30 Communicating Uncertainties to the Public: Case Study of a Vapour Intrusion Project in Valcartier, Québec

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SUMMARY: Communicating information to the public on health risks posed by contaminants in the environment involves providing factual information on the measured concentrations, as well as interpreting this information. This presentation describes the challenges of communicating health risks in the face of significant scientific uncertainties and a history of public distrust.

OBJECTIVES: The presence of an extensive trichloroethylene (TCE) plume in the Valcartier (Québec) regional aquifer creates the potential for migration of TCE into homes and other buildings through cracks and other openings in the building foundations. In 2006 and 2007 Health Canada, National Defence, and the Direction régionale de santé publique de Québec collaborated in conducting a vapour intrusion research project, with two primary objectives: (1) to assess the degree to which vapour intrusion of TCE is occurring in the Valcartier region; and, (2) to communicate the health implications of potential TCE intrusion to residents and those working at the military base and research facility.

DESIGN: The field work, consisting of groundwater, soil gas, subslab air and indoor air testing, was carried out by Golder Associates during two seasons – fall and winter. Winter is generally considered to create “worst-case” conditions with respect to vapour intrusion, because of reduced ventilation in homes, and the negative pressure indoors created by heating. The study targeted 22 buildings in the Valcartier sector. Municipal representatives and federal employees were invited to information sessions on the project, and generally welcomed the initiative.

RESULTS: Indoor air in all buildings was found to meet proposed air quality recommendations. Nonetheless, the results suggested that some vapour intrusion could be occurring in some of the buildings tested.

IMPACTS/OUTCOMES/CONCLUSIONS: Vapour intrusion of volatile substances at contaminated sites is an emerging area of research, with considerable uncertainty with respect to the environmental and hydrogeological factors influencing the phenomenon. At Valcartier, communication of results and conclusions of the vapour intrusion project proved challenging in the face of significant scientific uncertainty. This presentation will describe lessons learned with respect to both the phenomenon of vapour intrusion and risk communication.

3.31 A Focus on Gender with Regards to Alcohol and Other Drug Use

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SUMMARY: Using data from the Canadian Addiction Survey (2004), analysis was conducted to determine which factors significantly impacted substance use and whether there were similarities or differences observed for men and women. These findings will allow for gender specific programs and campaigns to be developed.

OBJECTIVE: Obtain key demographic characteristics disaggregated by sex in order to uncover similarities and differences between females and males with regard to alcohol and other drug use.

DESIGN: The results are based on the Canadian Addiction Survey (CAS) 2004, a random digit dialling telephone survey of 13 909 Canadians aged 15 years old and over living in the 10 provinces (the Territories are not included) dedicated to alcohol and other drugs.

OUTPUTS/RESULTS: When examining alcohol use, similarities were observed with regard to age and province of residence. However, marital status predicted drinking behaviour differently. For example, previously married women were significantly more likely to drink than married women; this was not observed in men. Depending on the outcome observed, educational attainment impacted drinking behaviour both similarly and differently. For example, heavy monthly and weekly drinking were impacted by education in men; this was not the case for women.

When examining illicit drug use, similarities exist with regard to age, province and income. However, marital status impacted women's use of illicit drugs more than men's and education impacted the use in men but not for women. The household location had an opposite effect with regard to past-year cannabis use. Women living in non-rural areas were more likely to use cannabis, whereas, men living in non-rural locations were less likely to have done so.

IMPACTS/OUTCOMES/CONCLUSIONS: The demographic characteristics impacting the use of alcohol and drugs by men and women are different, depending on the outcome. These findings increase our knowledge with regard to differences in substance use and will allow for tailored approaches to develop appropriate and targeted prevention campaigns or treatment programs. It also raises additional questions to further research as to why these demographics differ among women and men.

3.32 Canadian Community Health Survey Cycle 2.2, Nutrition (2004)--Income-Related Household Food Security in Canada

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SUMMARY: Using the Canadian Community Health Survey Cycle 2.2 (CCHS 2.2) Share File, descriptive analyses of the food security data from 33 346 Canadian households were undertaken to estimate the prevalence of food insecurity among Canadian households at the national and provincial level.

Food security is an important public health issue in Canada and a key social determinant of health. For many Canadians, the ability to access safe and nutritious food on a consistent basis is a challenge.

OBJECTIVES: Key objectives of the study were to: (i) describe income-related food insecurity in Canadian households; and, (ii) describe a new approach to interpreting the food security data from a standard multiple-indicator measure of household food security.

DESIGN: Using the Canadian Community Health Survey Cycle 2.2 (CCHS 2.2) Share File, descriptive analyses of the food security data from 33 346 Canadian households were undertaken to estimate the prevalence of food insecurity among Canadian households. The food security questions included in the CCHS 2.2 were adapted from the 18-item Household Food Security Survey Module (HFSSM) developed in the United States; new approaches to determine adult and child food security status and to derive household status were employed.

OUTPUTS/RESULTS: In 2004, more than 1.1 million households (9.2%) experienced income-related food insecurity at some point in the previous year. Prevalence of food insecurity was higher in households with certain characteristics, including: household income in the lowest (48.3%) or lower middle (29.1%) income adequacy categories; social assistance (59.7%) or workers' compensation / employment insurance (29.0%) as their main source of income; not owning their dwelling (20.5%); female-led lone parent households (24.9%); and Aboriginal households off-reserve (33.3%).

IMPACTS/OUTCOMES/CONCLUSIONS: These findings have implications beyond the health care sector, highlighting relationships between food security and social determinants of health. The results provide important information for guiding policy, program and research decisions and will serve as an important reference on household food security in Canada in 2004.

3.33 National Health Products (NHPs) Research Program: Building Research Capacity in the Community and Knowledge Transfer in a Regulatory Environment: Critical Success Factors, Impact and Lessons Learned

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SUMMARY: Research and knowledge-based development in NHPs was supported directly and through the development of community infrastructure and partnerships, to facilitate regulatory decisions and informed choice by consumers. Strategic partnerships and focus on building an environment conducive to strengthening of research capacity and information exchange are key to effective knowledge translation.

OBJECTIVES: Through support of community initiatives and partnerships, bridge knowledge gaps and generates evidence-based information supporting regulatory processes and informed decision-making by consumers.

DESIGN: The NHP research program was based on four activity pillars: capacity building, support for the conduct of research, development of community infrastructure and partnerships and knowledge transfer, as identified through a national consultation process. An evaluation of the program used telephone interviews, program documentation review, expert panel reviews and selected literature review to assess impact and draw lessons learned. A five-year review provided additional information on overall performance and legacy of the program.

OUTPUTS/RESULTS: A total of 64 projects and just over $3M in funds were supported. Five collaborative agreements were negotiated with CIHR who contributed over $1.2 million to these initiatives. Results include support for development of national research networks and smaller networks, training and mentoring opportunities, publications in peer reviewed journals, presentations at North American and international venues and funding of research in areas of NHP safety, efficacy and quality.

IMPACTS/OUTCOMES/CONCLUSIONS: Rather than being focused on supporting a few large research projects, the research Program placed emphasis on community capacity and partnership building with NHP stakeholder groups. This led to a number of outcomes notably: partnership with the CIHR was important in raising legitimacy and profile of NHP research as well as building on existing opportunities; collaboration with partners in the research community helped to build a critical mass of researchers and infrastructure; enhanced sharing of information occurred across sectors through support for multi-disciplinary initiatives; support for the creation of a NHP research community, including established national research networks assisted in the implementation of a science based NHP regulatory framework; and ultimately an environment where informed decision making by consumers was in part supported.

3.34 Dietary Vitamin D and Calcium Intakes of Canadians: Data from CCHS 2.2

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SUMMARY: Canadian Community Health Survey (CCHS) 2.2 (2004) data suggest a low prevalence of inadequate vitamin D intake among Canadian males and a low prevalence of inadequate calcium intakes among Canadians males and females. The primary dietary source of vitamin D and calcium in the Canadian diet is 2% milk.

OBJECTIVES:

1-Identify groups of Canadians likely to have a low prevalence of inadequate vitamin D and calcium intake.
2-Identify major food sources of vitamin D and calcium in the Canadian diet.

DESIGN: The vitamin D and calcium median intakes were derived from the 24-hour recalls of the Canadian Community Health Survey 2.2 (n=27 424). Nutrients intakes were compared to the Adequate Intakes (AIs; recommended average daily intake) by Dietary Reference Intake age-sex groups. Top food sources of vitamin D and calcium were identified using one day intakes.

RESULTS: Canadian children, male adolescents and male adults 19-50 years likely have a low prevalence of inadequate vitamin D intake as their median intakes exceeded the AIs. Females 14-50 years, and males and females over 50 years exhibited median vitamin D intakes below the AIs. Males and females ≥19 years, displayed median vitamin D intakes of 5.4 g/day and 4.4 g/day, respectively.

All age groups (9 years +) in both sexes (except men 19-30 years) had median calcium intakes below the AIs. Males and females ≥19 years, displayed median calcium intakes of 868 mg/day and 752 mg/day. Milk (2% fat), fish and milk (1% fat) contributed respectively to 21%, 17% and 10% of total vitamin D intake. For calcium, milk (2% fat), high-fat cheeses and low-fat cheeses contributed respectively 15%, 11% and 9% of the total intake.

CONCLUSION:

1) These data estimate a low prevalence of inadequate vitamin D intake among males and a low prevalence of inadequate calcium intakes among males (except 19-30 years) and females. The AI has limited uses in assessing nutrient intakes of groups because of insufficient evidence to establish the distribution of requirements. Findings should thus be interpreted with caution.

2) 2% milk contributes the most to vitamin D and calcium intakes in diets of Canadians.

3.35 Differing Paradigms/Mutual Interest: Achieving a Federal - First Nations Partnership in a National On-Reserve Survey

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SUMMARY: First Nations have adopted a research paradigm consistent with their traditional - indigenous knowledge and the Regional Health Survey was developed using that perspective. This presentation details how different perspectives on data governance between Federal and First Nations could be maintained, while data was collected/shared in a mutually satisfactory way.

OBJECTIVES: To provide details on a unique Federal - First Nations partnership in the collection and management of First Nations' health data for research, policy, and program planning.

DESIGN: The First Nations Regional Longitudinal Health Survey (RHS) is a national sample (n=22 602) of on-reserve First Nations in 238 communities across Canada. This large-scale survey was implemented over a five-year cycle between 2001 and 2006, requiring ongoing federal resourcing and negotiation of two differing paradigmatic approaches to data governance. A naturalistic inquire was conducted detailing the way in which the federal government and First Nations accommodated these differing perspectives.

RESULTS: First Nations' experiences with research and data collection are markedly different from that of the general Canadian population. This historical context helped shape current First Nations principles of information stewardship and their interactions with funding partners. The successful outcome of the RHS revolved around the recognition that two fundamentally different paradigms existed and these two perspectives could be maintained by each party, while important health data was collected and shared in a mutually satisfactory and beneficial way.

IMPACTS: Prior to the RHS, relatively little reliable First Nations on-reserve health data existed. RHS data fills a critical gap in the overall understanding of First Nations health status in Canada.

3.36 Statistical Analysis of Health System Utilization, Use of Diagnostic Testing, and Perceptions of Quality and Satisfaction with Health Care Services of Official Languages Minority Communities (OLMC)

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SUMMARY: Official Languages (OL) minority and majority communities of Canada were compared in terms of their health service utilization and perceptions of quality and satisfaction with health care services. Certain differences are significant and will be presented.

OBJECTIVES: Determine whether individuals in the official language minority communities differ in terms of their health service utilization and perceptions of quality and satisfaction with health care services from that of the majority community.

DESIGN: The Canadian Community Health Survey (CCHS 2005) and Health Services Access Survey (HSAS 2005) are used for analysis. Each respondent was assigned to the OL minority or majority group based on three CCHS questions: Language respondent can converse in; First official language learned and still understood (mother tongue); Language spoken most often at home.

Quebec and Canada outside of Quebec were analyzed separately. Logistic regression analysis was performed to identify the odds of health system utilization, disease prevention and detection, and health service indicators, based on official language status while controlling for age, sex, urban/rural area, self-rated health, chronic conditions, education, employment, and household income.

RESULTS: The analysis does not reveal significant overall differences between OL minorities and majorities, although certain differences are significant. Some results are:
Quebec Anglophones are about:
37% less likely to rate the quality of health care as excellent or good compared to Francophones.

45% less likely to be satisfied with the way health care is provided compared to Francophones.

93% more likely to report difficulties getting specialist care than Francophones.

Outside of Quebec Francophones:
Were less than half as likely to receive health care services compared to Anglophones.

About 2.6 times more likely to rate the quality of community based care as excellent or good and they are about 2.4 times more likely to be satisfied with way community based care provided compared to Anglophones.

IMPACTS: The analysis provides baseline data for the evaluation of the Contribution Program to Improve Access to Health Services for OLMS.

3.37 Addressing Sex and Gender in Systematic Reviews: A Challenge for Knowledge Transfer and a Case for Integrating Sex and Gender Based Analysis (SGBA)

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SUMMARY: Transferring knowledge about sex and gender-based differences, is essential for sound regulatory, policy and clinical decision-making, but our study showed sex and gender-based analysis was limited in systematic reviews. We make a case for routine inclusion of SGBA in systematic reviews.

OBJECTIVE: The purpose of this enquiry is to determine whether and how sex and gender is addressed in systematic reviews (SRs) using sex and gender-based analysis (SGBA). SRs are used as synthesized evidence for regulatory, policy and clinical decision-making in health, and are a key method of translating research knowledge into policy and practice. SGBA is an analytic approach used to show which population subgroups are included or excluded. We consider whether SRs provide sufficient information of the effects of interventions for subgroups, and are adequate for knowledge translation.

DESIGN: We reviewed the literature and relevant grey literature, with regard to sex and gender-based analysis in SRs. We randomly sampled Cochrane SRs on cardiovascular interventions because it is an area that contains known evidence of treatment and outcome differences in men and women, and the large number of reviews lends itself to this analysis. Using a set of questions adapted from existing SGBA tools, we determined whether sex and gender were addressed and, if so, how.

OUTPUT/RESULTS: Our findings showed that SGBA was limited. Data were often not collected or not analyzed, despite implications for quality assurance, equity, or potential for harm in subgroups. For knowledge translation, evidence may be assessed as incomplete if it cannot be shown to incorporate the interests of subgroups that include men and women, boys and girls.

IMPACTS/OUTCOMES/CONCLUSIONS: There is a need for increased capacity-building for SGBA in health research and SRs. We propose that systematic reviewers report what is known and *not* known about sex and gender to raise awareness of the problems created by non-specific group analyses, and to build a

robust base for future work. We make recommendations with regard to protocol design and methodology for systematic reviews. SGBA in SRs is a challenge, but without it, the quality of evidence used for knowledge translation will continue to be insufficient.

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Salle de conférence – Hôtel Marriott

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 – 2e 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 – 3e étage

Victoria Ballroom Gallery/Mézzanine de la salle de bal Victoria
Salon Rideau Salon
Salon Dalhousie Salon
Salon Wellington Salon