2376 US Consumer Product Safety Commission Approaches to Estimating Chemical Exposures from Consumer Products

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US Consumer Product Safety Commission (CPSC) is responsible for regulating thousands of consumer products used in homes and schools that contain a wide range of chemicals. The general approaches for understanding the risks associated with chemical exposures from products are outlined in the CPSC Chronic Hazard Guidelines. The guidelines have been used to develop a range of exposure and risk assessments that address many consumer products, including recent examples such as drywall, wood products, children's products, and products containing nanomaterials. These products may be manufactured domestically, and may be composed of recycled and/or novel materials. The CPSC staff is also exploring new approaches for identifying and prioritizing the potential implications of emerging technologies such as wearable technology, 3D printing and nano-enabled products.

2377 Determining a No Effect Level for Selection of a Point of Departure for Risk Assessment of an Irritant Aerosol Using a 3D *In Vitro* Assay

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Use of new technologies is essential to address increasingly complex risk and hazard characterization. The 3D *in vitro* model of the human respiratory tract is a new tool for assessment of aerosol toxicity potential and accurate endpoint selection. MucilAir is an *in vitro* model of the human airway epithelium and provides a structurally and functionally accurate representation of the respiratory tract. When used in conjunction with computational fluid dynamics (CFD) model derived estimates of respiratory surface concentrations it can accurately predict the outcome of repeat dose inhalation exposure for human risk assessment. Inhalation of chlorothalonil, a fungicide, causes respiratory tract irritation and associated lesions in acute and repeat dose inhalation studies in rats. As irritant responses to inhaled chlorothalonil occur locally in the respiratory tract the toxicity of chlorothalonil is particularly amenable to modeling *in vitro*. Five sets of MucilAir tissues, each derived from a different human donor, were exposed to a commercially available chlorothalonil formulation for 24 hrs. Irritancy endpoints (trans-epithelial electrical resistance, lactate dehydrogenase release and resazurin metabolism) were assessed. Results indicated a good concordance of response across endpoints and that a high concentration of chlorothalonil was required to induce a significant irritant response irrespective of donor. To derive points of departure for risk assessment, benchmark dose (BMD) modelling of MucilAir data was conducted to calculate 10% deviation from background (BMD_{10}) and associated lower 95% confidence limit (BMDL) values. BMDL values were typically in the 50 - 100 g/L range across donors and endpoints. CFD modelling of tissue level concentrations indicate that BMDL estimates significantly exceed probable tissue level exposure concentrations in the human upper respiratory tract.

2378 Effects on Pulmonary Host Defense following Acute Exposure to Diesel Emission Particulate and Crystalline Silica in Combination

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During hydraulic fracturing operations, workers are exposed to respirable crystalline silica (SIL; MIN-U-Sil®5) and diesel exhaust (DE), which, when combined, may increase risk for adverse respiratory health effects. The goal of this study was to investigate effects of acute pulmonary co-exposures to SIL and DE particulate (DEP; NIST SRM 2975) *in vivo* on host defense using a model of respiratory infection. Rats were exposed by a single intratracheal instillation (IT) of phosphate-buffered saline (PBS) as vehicle or one of the following doses of particles: 50 µg DEP, 233 µg SIL, 233 µg of carbon black (CB; Printex® 90), SIL and DEP combined (50 µg DEP/233 µg SIL or 233 µg DEP/233 µg SIL), or 233 µg SIL/233 µg CB combined (control for particle load). One week following particle exposure, rats were inoculated IT with ~$5x10^5$ cfu *L. monocytogenes*. At 1, 3, 5, 7 and 14 days post-infection (d.p.i.), bronchoalveolar lavage fluid (BALF) and cells were collected to assess pulmonary injury, inflammation, and immune response. Left lung was harvested and cultured to determine bacterial clearance. A previous study of acute SIL and DEP particle exposure showed that at 1 wk after exposure, the time point coinciding with bacterial inoculation in the current study, DEP and SIL in combination increased lung injury and inflammation as compared to DEP only or vehicle control. For the 233 µg SIL and all combination groups, lung injury, neutrophils and lymphocytes were increased in the lung as compared to PBS, 50 or 233 µg DEP, or 233 µg CB groups. Clearance of bacteria from the lung of rats exposed to the 233 µg DEP/233 µg SIL combination group showed a trend for increased bacterial clearance at 1 d.p.i., with increased clearance at 3 d.p.i when compared to PBS, 50 or 233 µg DEP, and 50 µg DEP/ 233 µg DEP SIL groups. When comparing the 233 µg CB/ 233 µg SIL combination group with the 233 µg DEP/233 µg SIL combination group, there were no differences in bacterial clearance or parameters of injury, inflammation, or immune response. The data suggest that the high particle doses in combination enhanced the innate immune response to infection, and that effects on host defense following acute exposure to a combination of DEP and SIL particles were more likely related to particle load than composition of DEP at the doses and time points examined.

2379 An Alternative Approach for Evaluating the Human Health Risk from Exposure to an Irritant Aerosol

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Modernizing strategies for evaluating human health risk from pesticide exposure requires new approaches that increase our ability for an integrated evaluation of exposure and hazard. Accurate and relevant risk evaluation based on actual inhalation exposure scenarios and target site-specific respiratory surface concentrations is one such strategy to describe human health risks. Exposure data that includes measured aerosol characteristics of non-volatile pesticide formulations provides an improved input to exposure models. To improve target site-specific dosimetry, previously developed computational fluid dynamics (CFD) models for the rat and human were used to calculate surface concentrations of deposited aerosol formulations in discrete regions of the respiratory tract using a Lagrangian (stochastic) aerosol transport approach coupled with the CFD airflow model under realistic exposure conditions. By incorporating the physical/chemical properties of the formulation, the resulting CFD model predictions of airway deposition are transferable to multiple pesticide compositions or active ingredients for formulations with similar properties. For formulations that typically produce aerosols >10 µm mass median aerodynamic diameter (MMAD), the majority of human respiratory tissue exposures are to the anterior nasal cavity including the vestibule, which alone accounts for 69, 86, and 97% of total deposition of inhalable aerosols at 15, 20, and 30 µm MMAD, respectively. Resulting surface concentrations of active ingredients (formulation-specific) at these aerosol sizes can vary widely, ranging from ng/cm^2 in areas of greatest deposition in the nose to pg/cm^2 or less in the larynx with very little aerosol penetration to the lung. We used the calculated surface concentrations of active ingredients in high deposition areas as a dose metric to directly compare with similar target tissue deposited doses in animal bioassays as well as applied doses from *in vitro* studies using primary human respiratory epithelial cells grown in 3D cultures. Both methods provide points of departure (POD) for benchmark dose (BMD) modeling of the response and human equivalent exposure concentrations for establishing exposure.

2380 Effects of Acute Inhalation of Crude Oil Vapor on Pulmonary Function

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Workers in the oil and gas industry are routinely exposed to hydrocarbon vapors and volatile organic compounds (VOCs). Exposures occur while oil workers open the "thief hatch" of oil tanks during manual measurement or removal of crude oil samples. The effects of crude oil vapor (COV) inhalation upon the pulmonary system are unknown, and several aspects of its possible effects on the lungs were investigated in this study. Rats were placed in whole body chambers and exposed to a single 6 h inhalation exposure of 300 ppm total VOCs produced from Deep Water Horizon surrogate crude oil at a temperature of 75° F. Control animals were exposed to air and endpoints were measured at 18 h and 28 d post-exposure. Total VOCs, benzene, toluene, ethylbenzene and xylene concentrations were monitored and regulated during inhalation exposures to maintain COV concentration constancy. In anesthetized rats, vapor had no effect upon basal lung resistance (R_L), basal dynamic compliance (C_{dyn}) or reactivity to inhaled methacholine


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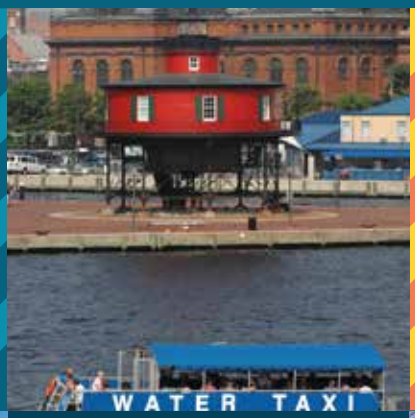

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