

PS 2459 Inhalation Health Effects Testing of Isobutanol Gasoline Blend: A Promising New Biofuel

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Isobutanol is a high-value molecule offering several advantages over existing transportation biofuels. Isobutanol blended with gasoline at 16% is currently under development as a new automotive biofuel in the US. To evaluate the potential health effects from exposure to isobutanol gasoline blend when dispensed at the pump, a battery of GLP whole-body inhalation studies using Sprague-Dawley rats was conducted in accordance with US EPA fuel testing requirements, described in Section 211(b) of the Clean Air Act and its Alternative Tier 2 Rule. Testing included the following guideline studies: 90-day subchronic toxicity with neurotoxicity, neuropathology, glial fibrillary acidic protein (GFAP) measurements across 8 brain regions, and 4-weeks recovery; 28-day immunotoxicity; 28-day genotoxicity; one-generation reproductive toxicity; and embryo-fetal developmental toxicity. To approximate the hydrocarbon composition of fugitive emissions to which humans are potentially exposed during refuelling, light-end hydrocarbon emissions were generated from the whole fuel heated to 130°F and condensed to form a vapor condensate (VC) test substance. Isobutanol levels in the VC were 2–3%. In all studies rats were exposed to re-vaporized test substance at target concentrations of 0 (air control); 2,000; 10,000; and 20,000 mg/m³, the latter being 50% of the lower explosive limit of the VC. Exposure frequency and duration were tailored to study design. The only treatment-related finding in the 90-day study was light hydrocarbon nephropathy in male rats, a known effect specific to male rats and not relevant to humans. No treatment-related findings were seen in neuropathology, GFAP, neurotoxicity, immunotoxicity, genotoxicity, or developmental toxicity. The no-observed-adverse-effect level (NOAEL) for these endpoints was 20,000 mg/m³. In the reproductive study transient changes in body weight gain and food consumption were seen in high-dose paternal and maternal animals. These effects occurred at hydrocarbon exposure levels several orders of magnitude above conditions typically experienced at dispensing pumps during refueling (<1 mg/m³, 5 min). Based on these results, inhalation exposure to light-end hydrocarbons emitted from 16% isobutanol gasoline during refuelling is unlikely to present a unique health hazard to humans.

PS 2460 A New E-Cigarette Aerosol pH Technique with Improved Toxicological Relevance

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In the past, the determination of pH-values of mainstream cigarette smoke was controversial both in terms of analytical methodology and interpretation of the results in terms of nicotine addiction and other toxicological effects. The controversy has continued with the introduction of e-cigarettes (e-cigs) and related devices and the e-liquids (e-liqs) used with them, but there is one main difference. The aerosol generated by e-cigs does not contain carbon dioxide and other acids generated from combustion of the tobacco. Since there are no products of combustion, e-liq pH should equal e-cig aerosol pH. This is not the case. E-liquids contain little or no water, and must be diluted with water to achieve the dilute aqueous solution needed for accurate pH measurements and possible use of the Henderson-Hasselbalch equation. However, dilution of mentholated and highly flavored e-liquids results in cloudy mixtures. Attempts to measure the pH on undiluted e-liq is technically incorrect as e-liquids pick up water from ambient drawn in by users puffing on the devices, sometimes increasing water concentration as high as 10%, and there may be precursors of volatile acids in e-liquids that are activated by the e-cig heater assembly. Thus, pH determinations should be conducted on the undiluted aerosol emitted by the e-cigs. Health Canada Test Method T-113 has been used for e-cig aerosols, but T-113 specifies a modified pH electrode and sampling chamber that is atypical of the human mouth. These disadvantages can be overcome by using nonstandard pH electrode is a glassmouth such that the active portion of the electrode is in the smoke stream. One example system is based around a Hanna Instruments HI-99171N Leather and Paper pH Meter and probe. Without an aerosol stream, resting pH ≈7, with the aerosol (4-sec 55-mL puff every 30 sec) from popular brand 1, pH ≈7.2 and from popular brand 2 (known to contain organic acid), pH ≈6.8; nicotine at 50 mg/mL in PG, pH ≈7.6. These values are lower than obtained with other techniques and indicate that likelihood of adverse health effects from high pH may have been overestimated. Placement of water or synthetic saliva in bottom of glassmouth permits a second check on the pH values and change in water and/or saliva pH during and after vaping.

PS 2461 Microbiological Prevention in the Concentration of Bacterial Pathogens on the Athletic Equipment in the Heal Complex at Paine College

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Background: *Staphylococcus aureus* is a gram positive bacterium and a commonly acquired hospital pathogen. *S. aureus* is normally found in moist, warm areas of the human body such as armpits, crotches, and the upper respiratory tract. Delayed detection of *Staphylococcus aureus* can lead to a more severe infection known as Methicillin resistant *Staphylococcus aureus* (MRSA). MRSA was originally found in hospitals or health care facilities. However, MRSA has now branched to the community, known as Community Associated Methicillin Resistant *Staphylococcus aureus* (CA-MRSA). MRSA is a difficult infection to treat because of its resistance to antibiotics of the penicillin family. If this infection is not treated, it can become systemic and lead to organ failure. Recent reports show that *Staphylococcus aureus* was present on the frequently used athletic equipment utilized by students and athletes on campus. Methods: Research was conducted in the HEAL Complex to monitor changes in *S. aureus* concentrations in the athletic weight room after a MRSA bundle (informative presentation and signage postings throughout weight room) was presented to the athletic department in an effort to raise awareness about risk of infection. Over seven sample periods, athletic equipment was swabbed using sterile cotton swabs. After being re-suspended in 10% sterile saline, they were subcultured in triplicates for each equipment piece. Samples were grown on Mannitol Salt Agar and incubated for 3 days at 37°C. Colonies were counted. Results: Some athletic equipment such as the treadmill, incline, bench, and crunch saw a sharp decrease in *S. aureus* concentrations over the sample period. However, the biceps equipment had an overall increase. While not a strong linear relationship ($R^2=0.01$), a downward trend in *S. aureus* concentrations was detected following the MRSA bundle presentation. Conclusion: The results of this project suggest that the introduction of a MRSA bundle was successful in decrease the concentrations of *Staphylococcus aureus* athletic equipment.

PS 2462 Identification of Compounds That Modulate Retinol Signaling Using a Cell-Based qHTS Assay

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all-trans Retinoic acid (atRA) is the most abundant natural metabolite of retinol (vitamin A). Physiological levels of atRA are maintained by the retinol signaling pathway (RSP), which controls the biosynthesis and catabolism of atRA. atRA regulates transcription of genes that are essential for embryonic development. Chemicals that interfere with the RSP can cause abnormal intracellular levels of atRA and therefore are potential developmental toxicants. To assess chemicals for the potential to adversely affect embryonic development by interfering with retinol signaling, we have developed a cell-based RARE (Retinoic Acid Response Element) reporter gene assay that can be used to identify disruptors of the RSP. To validate the RARE assay in a quantitative high-throughput screening (qHTS) platform, we screened the Library of Pharmacologically Active Compounds (LOPAC) in both agonist and antagonist modes. The screens detected known RSP agonists, demonstrating assay reliability. In addition, the screens identified novel RSP agonists including kenpaullone, niclosamide, PD98059 and SU4312, and RSP antagonists including Bay 11-7085, LY294002, 3,4-Methylenedioxy-β-nitrostyrene (MNS), and a set of topoisomerase inhibitors (camptothecin, topotecan, amsacrine hydrochloride, and idarubicin). These compounds were further evaluated in the P19 pluripotent cell and were found to affect the expression of the Hoxa1 gene that is essential for body patterning during development. These results show that the RARE assay is an effective qHTS approach for screening large compound libraries to identify chemicals that have the potential to adversely affect embryonic development through interference with retinol signaling.

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

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