both hazard level and exposure level, the MOM model was assessed as more suitable for risk warning than the EPA model for 1-BP occupational health hazard risk assessment in China.

## 1533 A Systematic Approach to Organize 182 Toxic Air Contaminants by Target Organ: A Risk Assessment Tool

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The Oregon Department of Environmental Quality (DEQ) recently adopted health-risk based regulations for industrial point source emissions of toxic air contaminants. The new regulations require industrial point sources to assess health risks that their emissions may pose to neighbors. The risk assessment process for noncancer effects includes summing hazard quotients for toxic air contaminants that affect the same target organ or organ system. The Oregon Health Authority (OHA) and DEQ developed a spreadsheet that lists target organs and organ systems for all 182 toxic air contaminants regulated under the new regulations. The spreadsheet lists chronic and acute noncancer targets separately. OHA and DEQ created criteria for including a target organ or organ system for each chemical and sought feedback from an external technical advisory committee. The committee had expertise in toxicology, risk assessment, and development of chemical-specific toxicity reference values. OHA and DEQ used summarized information from the US Environmental Protection Agency, Agency for Toxic Substances and Disease Registry, and the California Environmental Protection Agency's Office of Health Hazard Assessment to populate the spreadsheet according to the *a priori* established criteria. For each chemical, the spreadsheet includes the source of information for each target organ and notation about the quality and certainty of information linking the toxic air contaminant to each target organ. The spreadsheet displays a breakdown of uncertainty factors, species tested, and duration of exposure for the critical studies used to derive toxicity reference values for each toxic air contaminant. OHA and DEQ anticipate that this publicly available spreadsheet will be a useful tool for assessing noncancer risks for emissions sources in Oregon and may be useful for risk assessors outside of Oregon as well.

## 1534 Application of 3R Principles to Dog Studies for Agrochemicals: Building the Case for Eliminating the Dog as a Required Species?

L. Murphy, K. Stebbins, R. Rasoulpour, and C. Terry. *Corteva Agriscience, Indianapolis, IN.*

A core requirement for global pesticide registration is a 90-day toxicity study in a non-rodent species, for which the dog is usually chosen (USEPA 1998, EU 2010/63, OECD 1998, JMAFF 2000). To establish toxicologically relevant dose levels for the 90-day dog study, palatability and 28-day toxicity studies are conducted first. There are no published guidelines for conduct of these preliminary studies, so there is significant opportunity to refine the design and minimize animal use. A combined palatability/28-day study design, using the same animals, is now our standard. The preferred route of exposure is via diet as it is the least invasive route of administration and is more relevant for human health risk assessments. Significant differences in palatability can exist for herbicides and insecticides, and this combined study design considers options and alternatives for each active ingredient. For the herbicide florpyrauxifen benzyl, with no palatability or toxicity issues, the combined study evaluated 500 mg/kg/day in 2 female dogs for 7 days. On day 8, 2 males were offered 500 mg/kg/day for 21 days and 2 dogs/sex/dose were offered 1000 mg/kg/day until day 28. This approach reduces animal use as only two dose levels are tested, and control animals are not needed. Any potential treatment-related effects are compared to pre-exposure measurements of food consumption, body weight and clinical observations on the study animals. The insecticide, sulfoxaflor, presented challenges due to reduced palatability and tolerability with food consumption and body weight effects. Palatability was evaluated using alternatives, such as addition of bacon or peanut butter flavoring, pelletizing the diet, and gelatin capsule administration with the option of supplemental canned diet to encourage food consumption. The combined palatability/28-day study has reduced the use of dogs up to 83% compared to traditional toxicity testing designs and eliminated animal stress indicative of maximum tolerated dose exposures. Further refinements could include consideration of re-homing animals, if termination at study conclusion is not necessary. In addition, animal enrichment opportunities are of critical importance and include consideration of provided toys, minimum daily exercise, and expanded housing space to accommodate regular companionship of group animals. These refinements represent initial, but key steps towards an animal-free toxicity testing future.

## 1535 Evaluation Framework to Qualitatively Assess the Health Effects of New Tobacco and Related Products

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Many new tobacco and related products (TRP) have emerged on the market, with unknown health risks. Here, we present an evaluation framework containing all factors and relations between them that contribute to the TRP's health effects. As an example, we evaluated the JUUL, a very popular e-cigarette. Factors that determine attractiveness, addictiveness and toxicity of TRP were defined based on previous assessments, literature, and expert discussions, resulting in an evaluation framework. Relations between factors were evaluated, which was supported by literature. Relevant publications on JUUL were used to evaluate all factors. Results: Our framework can be used to identify aspects of TRP that require specific attention for public information or product regulation. In addition, it can gauge attractiveness for specific user groups, while considering exposure. Aspects of concern for JUUL are its attractive and discrete shape, user-friendly prefilled pods, high aerosol nicotine levels, and liquids containing nicotine salts instead of free-based nicotine. Our framework will aid in identifying the key risk factors contributing to increased risk of adverse health effects for a product in a qualitative manner. In case of JUUL, the addictiveness and especially attractiveness are sufficiently high to have a large potential impact on population health due to its contribution to use and hence exposure, even if the amounts of toxicants in the emissions should be lower than for other e-cigarettes. As results can change over time due to changes in use and product modification, market research and monitoring is crucial. Our framework and the tests we recommend can be used for risk assessment of TRP. Since all factors presented contribute (in)directly to the, attractiveness, and addictiveness and toxicity of TRP, policy makers are advised to consider these factors as a possible target for future product regulation. In addition to the identified aspects of concern for the JUUL, we advise to consider regulation of the many JUUL compatible pods, JUUL knock off devices, and e-liquid brands selling high-nicotine products.

## 1536 Evolving the Use of Respiratory Irritation as a Health Endpoint in Occupational Risk Assessments

E. Frank, T. Niemeier, and C. Whittaker. *NIOSH, Cincinnati, OH.*

The effects of occupational irritant exposures are of major importance to public health. Approximately 40% of the exposure limit values for agents listed in the current NIOSH Pocket Guide are estimated based on exposure thresholds for respiratory irritation. Respiratory irritation signs and symptoms include rhinorrhea (runny nose), coughing, and airway obstruction and accompanying exposure levels can coincide with sensory irritation responses in other tissues such as stinging and burning in the eyes and skin. Inhalation and dermal exposure to irritants is highly relevant to the use of solvents, catalysts, cleaners, fragrances, and many other agents extensively utilized in workplaces and industrial processes. Despite this, existing guidelines to assess and characterize irritation hazards are limited by inadequate testing methods, poor mode-of-action knowledge, and outdated risk characterizations. NIOSH is responding to these gaps with coordinated efforts across the agency and collaborating partners to meet scientific needs in the following specific areas: 1) Assessing the relationship between sensory irritation responses and traditional respiratory toxicity endpoints in animals (i.e., respiratory depression, airway histopathology, corrosion, inflammatory activation); 2) Investigating the utility of *in vitro* tests for generating irritation toxicity data using primary tissue and cultured cell lines: 3) Developing updated protocols for evaluating irritation toxicity data and integrating existing hazard information to derive exposure limit values, including recommended exposure limits, short-term exposure limits, and ceiling/immediately-dangerous-to-life-and-health (IDLH) values; and 4) Investigating the toxicological mechanisms targeted by irritants and working towards a consistent understanding of the adverse outcome pathways involved. These efforts will address occupational health needs by increasing the prevalence, quality, and utility of irritation toxicity data and improving the efficiency and accuracy of risk assessments for irritation hazards. In addition, these outcomes will be of scientific benefit to consumer product safety, environmental health in industry-adjacent communities, and numerous other public health needs arising from exposure to chemical irritants.

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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 59th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 15–19, 2020.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 542.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 580.

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