PS 1920 The Harmony and Dissonance of Harmonization: A Comparison of Four Globally Harmonized System (GHS) Carcinogen Categorizations with NTP, US EPA, and IARC Classifications

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The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) was developed to harmonize classifying and labeling of chemicals internationally. GHS was developed through the cooperation of the International Labour Organization, the Organization for Economic Cooperation and Development, and the United Nations Sub-Committee of Experts on the Transport of Dangerous Goods. The intent was a harmonization of the categorization process, not necessarily a harmonization of the categorization result, leaving the door open for organizations to interpret and apply the data differently. This study compared the carcinogen categorizations by four organizations that have compiled GHS categorizations (the European Union (CLP Annex VI), Safe Work Australia, Japan METI, and German IFA (GESTIS)) for 100 chemical substances. These GHS categories were compared to NTP, EPA and IARC carcinogen classifications. Overall there was broad agreement on carcinogenicity, but out of 100 substances, there were disagreements among the four GHS categorization compilations for 41 substances. Of the 28 substances that at least one of the carcinogen classification agencies (NTP, EPA and IARC) ranked as known human carcinogens (or equivalent), 14 were categorized by the GHS-ranking agencies as a GHS carcinogen category 1B or 2 (presumed or suspected carcinogen). Of the 69 substances that at least one of the NTP, EPA or IARC classified as possible or probable carcinogen (or equivalent), 14 of the substances were classified by at least one of the GHS-ranking agencies as not classifiable or insufficient data. This analysis demonstrates that the harmonization of process does not always lead to harmonization of decision. Understanding the advantages and pitfalls of carcinogen classification is important for interpretation of hazards. The findings and conclusions in this report are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

PS 1921 Impact of Different Criteria for Identifying Endocrine-Disrupting Substances under the EU Biocidal Products Regulation

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The potential impact of three different schemes for identifying endocrine-disrupting (ED) substances was assessed on the basis of publicly available toxicological information. One-hundred forty seven assessment reports (ARs) for 108 different biocidal active substances (ASs) have been published until 31 January 2014. These public ARs were examined for indications of ED properties in the toxicological hazard section. According to the BPR interim criteria, one of the 108 ASs "shall be regarded" as ED substance. In addition, four ASs "may be regarded" as ED substances, according to the interim criteria. Thus, ED interim criteria are met by 5 out of 108 = 4.6% of all ASs for which an AR is available. If this proportion is extrapolated to the entirety of ASs in the review programme, a total of eleven ASs are expected to meet the criteria to "may be regarded" as ED substance. Following an evaluation scheme proposed by UK and Germany, three ASs have been identified as ED substances of regulatory concern. This is equivalent to 2.8% of all ASs for which an AR is available. Seven ASs is the extrapolated number of ASs that will be affected by the application of these proposed criteria to the complete review programme. The ED classification scheme likely to be proposed by the EU Commission features three categories. One AS was placed in Category I (known or presumed ED), one AS was placed in Category II (suspected ED), and five ASs were identified as Category III substances (some evidence for ED).
It should be kept in mind that these classifications are only based on the limited toxicological information from the public ARs.

PS 1922 Threshold of Toxicological Concern and Its Use in Agrochemical and Chemical Risk Assessment

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The threshold of toxicological concern (TTC) approach has been put forward as a tool for assessing substances of unknown toxicity present at low levels in human diet and potentially other routes of exposure. The TTC concept is based on the principle of establishing generic threshold levels of human exposure for all chemicals, below which there is a very low probability of an appreciable risk to human health. In theory the TTC approach can be used to evaluate the safety of any chemical if its structure is known and a robust estimate of human exposure can be made. However, it is important to note that: It is generally accepted that the TTC approach is not suitable for certain chemical classes. It is not proposed as a replacement or alternative to testing procedures required for regulatory approval. To be applied successfully the method of determining the level of human exposure needs to be as accurate and robust as possible. The underlying principles of the TTC concept continue to be challenged and scrutinised to ensure their applicability for existing and new areas of risk assessment. The TTC approach as either a pragmatic risk assessment tool or prioritisation tool is already established in several areas of chemicals risk assessment: Evaluation of chemicals in food contact materials by the United States Food and Drugs Administration (FDA). Evaluation of food flavouring agents by the European Food Safety Authority (EFSA) and FAO/WHO Expert Committee on Food Additives (JECFA). Impurities in pharmaceutical products by the European Medicines Agency (EMEA) and FDA. Other areas where application of the concept is currently under consideration are: The evaluation of the toxicological relevance of pesticide metabolites for dietary risk assessment. For waiving toxicity testing based on exposure estimates under the EU Registration, Evaluation, Authorisation and Restriction of Chemicals (REACh) legislation. The evaluation of components in cosmetics (SSCP, 2008) and consumer products. This poster focuses on proposals for its use in the EU under REACH and the authorisation of plant protection products under Regulation (EC) No 1107/2009.

PS 1923 Evaluating and Providing Risk Context for Water Contaminants with Minimal or No Toxicity Data

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The Minnesota Department of Health (MDH) is tasked with determining human health risks from exposure to contaminants in drinking water. In conducting this work, MDH relies upon standard risk assessment methodologies to derive health-based guidance. Traditional risk assessment methods, however, require chemical-specific toxicity data in order to develop numerical guidance. Advancement in analytical methods has led to the detection of many unregulated contaminants. These contaminants often have little or no publically available toxicological data, making it difficult to sufficiently evaluate the chemical using traditional risk assessment methods. To develop appropriate public health responses, MDH, with funding provided through the State of Minnesota Clean Water Fund of the Clean Water, Land and Legacy Amendment, identified risk-based methods that could be used to provide risk context for chemicals with minimal toxicity data. MDH worked with partners to critically review and test a range of published "generic" screening methods (e.g., threshold of toxicological concern), extrapolation methods and computational tools. Initial findings identified three toxicological endpoints for which available methods and tools may not be sufficiently protective: genotoxic carcinogenicity; cholinesterase inhibition and endocrine disruption. This finding, along with method testing results, was used to develop a systematic decision framework for evaluating contaminants in water. The framework provides a stepwise assessment process starting with chemical-specific structure and conservative benchmark values and progressing to more in-depth assessment depending upon the availability of toxicity information and predictive models (e.g., QSAR, biological, and hybrid models). MDH plans to use this decision framework to prioritize research needs and provide risk context for contaminant occurrence data, including chemical-specific drinking water guidance when possible.

PS 1924 Mode of Action and Adverse Outcome Pathways: Distinguishing a Difference via Case Study Analysis

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Mode of action (MOA) and adverse outcomes pathways (AOPs) are two approaches proposed to facilitate the incorporation of pathway-based evidence into regulatory decisions. Although both describe biological response pathways (BRP), MOA aims to identify causally linked key events through evidence evaluation ac-

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