the risk is considered acceptable; otherwise, additional Risk Management Measures (RMM) must be implemented. These requirements pose particular challenges for complex substances with unknown or variable compositions. In this paper we use a hydrocarbon solvent, white spirit, as an example to illustrate how complex substances and uses can be assessed for risk. Hydrocarbon solvents were divided into groups (categories) of substances based on physical/chemical properties and compositional elements. Representative substances in each category were identified as the basis for DNEL determination. A series of adjustment factors were applied in the calculation. Exposure assessments were made using a set of generic exposure scenarios (GES) which incorporated predicted exposures reported by ECETOC Targeted Risk Assessment. GESs were established following a control banding process in which DNELs and volatility were grouped as high, medium or low. Newly-developed computer-based tools helped automate RCR calculations and ensured appropriate RMMs were applied and uniform communications made to users via safety data sheets.

## PS 1902 What Is an Acceptable Risk of Cancer Due to Occupational Exposure to a Carcinogen?

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It is widely accepted that there is no completely "safe" dose of a genotoxic carcinogen, and that there is some excess risk of developing cancer from any non-zero exposure. The excess risk from low exposures may be vanishingly small, but it is generally presumed to be greater than zero. Since it is not feasible to totally eliminate all exposures to suspect carcinogens in the workplace, some target or acceptable risk level is needed for purposes of establishing occupational exposure limits for carcinogens. Target risk levels for carcinogen exposures in the general population are usually set quite low, in the range of 1 in 10,000 to 1 in 1,000,000 lifetime excess risk. In the occupational setting, the 1980 U.S. Supreme Court "benzene" decision implied that a 1 in 1000 lifetime excess risk is a significant risk, while a 1 in 1 billion risk is not. The Court noted that it is the responsibility of the relevant government agency to determine what it considers to be a "significant" risk. A review of international policies for developing occupational exposure limits for carcinogens reveals a range of acceptable lifetime excess risks of up to 4 in 1000 (Netherlands) to 1 in 100,000 (Sweden). By comparison, the lifetime fatality rates in occupations generally thought of as low risk, such as the wholesale and retail trade sector and the services sector, has been reported to be in the range of 1-2 per 1000 workers. Taken together, these data suggest that lifetime excess cancer risks in the range of 1 in 100,000 to perhaps 1 in 1000 may be acceptable in the occupational setting. *The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.*

## PS 1903 Comparison of Inhalation Occupational Exposure Limits (OELs) and European Worker's Inhalation-Derived No-Effect Levels (DNELs) for Volatile Organic Compounds

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The European Chemical Agency (ECHA) previously released manufacturer/importer REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) chemical registration files, making available the Derived No Effect Levels (DNELs) for hundreds of substances. The DNEL is defined as "the level of exposure above which humans should not be exposed" and needs to reflect the likely route(s), duration and frequency of exposure. Specifically, worker DNELs are levels intended to protect workers during manufacture. Typically, DNELs are developed by Industry using ECHA's guidance; the registrant has the final decision on the selection of the key studies, endpoints of concern, and the assessment factors to account for sources of uncertainty. By comparison, currently accepted occupational exposure limits (OELs), such as permissible exposure limits (PELs) or threshold limit values (TLVs) developed by the Occupational Safety and Health Administration (OSHA) and the American Conference of Industrial Hygienists (ACGIH), respectively, may have been derived using different methods, some of which incorporate economic and technical feasibility concerns and/or health-based assessment. In addition, these other occupational values may have been based on different toxicological data and endpoints. Because the worker DNELs may potentially be used as guideline levels for worker exposures in Europe and have the potential to become de facto OELs in other regions due to the global extent of REACH, a comparison analysis between the long-term inhalation DNELs for the worker population and OELs developed within Europe and by OSHA and ACGIH was completed for several volatile organic compounds (VOCs) of toxicological concern. This analysis showed that in most cases the long-term inhalation worker DNELs for VOCs that were used for comparison were equivalent to or lower than the accepted OELs. This is consistent with our previous findings in which the same analysis was conducted on metal substances.

## PS 1904 Characterizing Risks from Exposure to Hazardous Air Pollutants: Consideration of Health Risks from Acute Exposure

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Section 112 of the Clean Air Act establishes a two-stage regulatory process to address emissions of hazardous air pollutants (HAP) from stationary sources. In the first stage, the EPA is required to develop technology-based standards for categories of sources. In the second stage, EPA is required to assess the health and environmental risks that remain after implementation of the technology-based standards. If additional risk reductions are necessary EPA must develop standards to address these remaining risks under the Risk and Technology Review (RTR) Program. The potential risks due to acute inhalation exposure to HAP is one of the factors considered in RTR assessments. The acute risk assessment methodology is tiered and iterative in nature, and designed to identify and eliminate from further consideration those sources of emissions (i.e., industrial facilities) for which we have confidence that no acute health effects of concern will occur. Available health effect reference values from various sources are considered in the characterization of potential risks due to acute inhalation exposure to HAP. Consideration of a reference value in a regulatory decision requires a critical evaluation of the available acute health effect reference values in the context of the available toxicity database. This presentation includes specific HAP examples to illustrate the critical elements considered when selecting appropriate reference values to be used in risk assessments that support regulations (e.g., biological relevance to humans, methods used to derive a given reference value). The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

## PS 1905 Reanalysis of Angina Study Cited by US Environmental Protection Agency As Primary Basis for National Ambient Air Quality Standards on Carbon Monoxide

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The Environmental Protection Agency has never changed the National Ambient Air Quality Standards (NAAQS) for carbon monoxide (CO) adopted in 1971 but it has changed their basis. In a 2011 review, EPA rejected all epidemiological evidence and gave "primary consideration" to one controlled exposure study of men with angina. EPA commissioned this in 1983 from the Health Effects Institute (HEI) to "replicate and extend" studies done by Dr. Wilbur Aronow in the 1970s after an audit could not find his records. HEI's Multicenter CO Study Team, Allred *et al.*, evaluated the effect on men with angina of exercising in clean air after 1-hour CO exposures producing average carboxyhemoglobin (COHb) levels of 2.2% and 4.4%. Results were published thrice: in *HEI Research Report 25* and *The New England Journal of Medicine* in 1989 and *Environmental Health Perspectives* in 1991. HEI, like Aronow, discarded its CO study archives but it published enough individual data to reanalyze all the primary results and reconstruct most of the published figures and summary tables in all 3 versions. Over 100 errors and inconsistencies were found in the methods, results and conclusions. Some defy laws of toxicology, cardiology and statistics, including flat and flip-flopping dose-response curves; misinterpreting venous COHb as a measure of cardiac exposure; finding adverse effects only as COHb fell during exercise in air but never as it rose during CO exposure; and deriving p-values from permutation tests of trimmed means that exactly match t-tests, which should only happen in the limit. Most critically, the study's 3 centers could not replicate Aronow's results or each other's. Conclusions about significant risks posed to men with angina by 2-4% COHb are contradicted by results showing no correlation between CO exposures 1.5-10 times the 1-hour NAAQS of 35ppm and the onset of angina or ECG changes (Pearson r<.03). Given that men with angina are demonstrably not at risk from CO, EPA should lower the NAAQS to protect fetuses who epidemiology studies show are most at risk from exposure to current ambient CO levels.

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