

a variety of types of environmental data sets, there are differences in the way censored data are handled, distributional type is determined, and 95% UCL calculation method is selected. These differences can, in some cases, lead to substantial differences in the 95% UCL value derived. Skewness of the sample data was found to be an important factor in determining the conservatism of the 95% UCL estimates, and affected the two software tools differently. The 95% UCL software tools are a convenient means to calculate exposure point concentrations, but should not be treated as "black boxes." Existing tools have strengths and weaknesses that need to be understood in order to apply them properly in the calculation of exposure point concentrations for contaminated sites.

### 1623 A GLUTARALDEHYDE RISK ASSESSMENT USING BENCHMARK DOSES: DECISIONS, DECISIONS, DECISIONS!

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The objective of this study is to describe a quantitative risk assessment for inflammatory responses associated with glutaraldehyde exposure, using benchmark dose (BMD) methods, and to evaluate the impact of alternative assumptions on the estimated risk. These alternatives included the choice of which data set to use as a basis for BMD estimation, which toxicological endpoint(s) should be selected for extrapolation to humans, how the toxicologically-based BMDs should be scaled to humans, which statistical models in the BMD suite should be used, and how the different BMDs should be synthesized into a recommendation for human occupational exposures. Two NTP data sets were considered (13-week and 2-year), as well as RD<sub>50</sub> data. A total of 119 BMD models were fitted to various toxicological endpoints for male and female mice and rats in the two NTP studies. Within data set/endpoint combinations, different dose-response models were fit and a model-averaged BMD was obtained. BMDs based on squamous epithelial inflammation were chosen for extrapolation to humans; these ranged from 50-130 ppb in female rats and from 56-93 ppb in female mice suggesting that the BMD is not critically dependent on the choice of target species. Adjusting for 8-hr occupational exposures as opposed to 6-hr exposures in the NTP study reduces the rat BMD range to 38-98 ppb. The rat BMDs were then extrapolated to humans on the assumption of equal effects at equal exposure concentrations, regardless of species. A 32-fold uncertainty factor was applied, yielding an occupational exposure range of 1-3 ppb. This exposure range is intended to be protective against respiratory irritation due to chronic exposures to glutaraldehyde; however, it is not known whether it will also protect workers from respiratory sensitization.

*Disclaimer: The findings and conclusions in this abstract have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.*

### 1624 DEVELOPMENT OF SHORT-TERM, SUBCHRONIC AND CHRONIC ORAL REFERENCE DOSES (RfDs) FOR MICROCYSTIN-LR.

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Microcystins are monocyclic heptapeptide toxins produced by several species of cyanobacteria (blue-green algae), including members of *Microcystis*, *Anabaena*, *Nodularia*, *Nostoc* and *Oscillatoria*. Human exposure to microcystins may occur through the consumption of contaminated drinking water, ingestion of contaminated surface water during recreational activities or through the use of blue-green algae dietary supplements. Microcystins are potent hepatotoxins, primarily due to their preferential uptake into the liver via the bile acid transport system. The primary mechanism of action of microcystins is well known and involves the inhibition of serine/threonine protein phosphatases PP1 and PP2A leading to hyperphosphorylation of cytosolic and cytoskeletal proteins and subsequent hepatocyte disruption and hepatotoxicity. Additionally, microcystins have been shown to induce a number of other cellular alterations ranging from lipid peroxidation to apoptosis. At least 80 microcystin structural variants have been identified though the most commonly detected and best studied variant is microcystin-LR. In 1999, the World Health Organization (WHO) established a provisional "Tolerable Daily Intake" (TDI) for microcystin-LR of  $4 \times 10^{-5}$  mg/kg-day. New repeated-dose experimental animal toxicity data have been generated by several laboratories since the WHO provisional TDI was published in 1999. Here, following a thorough literature review and the evaluation of all available toxicity information, oral Reference Doses (RfDs) for short-term (up to 30 days), subchronic (up to 10% of the average lifespan) and chronic (up to lifetime) exposure durations were derived for microcystin-LR using current US Environmental Protection Agency methodology.

### 1625 COMPARATIVE ECOLOGICAL RISK ASSESSMENT FOR A NEW ALUMINUM SMELTER IN ICELAND.

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Protection and maintenance of local populations and communities of plants and wildlife is gaining importance in corporate decision-making regarding industrial development. During the facility design phase for an aluminum smelter in East Iceland, it became necessary to determine if a wet (seawater) scrubber system should be installed to reduce overall sulfur dioxide emissions. In this case, predictive risk assessment was used to determine whether there would be a consequential difference in the level of risk to human and ecological receptors from constituents in air emissions from the aluminum smelter either with or without wet scrubbers. Benchmark exposure concentrations corresponding to negligible ecological risk were established for avian, mammalian, and plant receptor groups based on the toxicity literature. These benchmark exposure concentrations were then converted to concentrations in air and compared to air modeling predictions to develop risk estimates. Benchmark air concentrations were derived using plant uptake models for fluoride and PAH, and food-web modeling for birds and mammals. Spatially and temporally explicit exposure models were developed for all receptors based on predicted concentrations of constituents in air, and population-level effects were modeled for plant (lodgepole pine, heather, and mosses/lichen), bird (ptarmigan) and mammalian (wood mouse) receptors. The results of this work revealed that exposures under both scenarios are likely to be much lower than concentrations corresponding to risk thresholds and that overall risk was lower for a smelter operating without wet scrubbers. Thus, although mass loading of sulfur dioxide (and other constituents) would be reduced using wet scrubbers, corresponding risk to ecological receptors would actually be higher because of higher exposure-point concentrations in air.

### 1626 CANCER POTENCIES AND DAILY INTAKE LEVELS FOR SIX INDUSTRIAL CHEMICALS.

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Cancer potencies for six carcinogens (C.I. Direct Blue 218; 2,4-hexadienal; pyridine; bromoethane; propylene glycol mono-t-butyl ether; and N-methylolacrylamide) were estimated based on data from National Toxicology Program (NTP) rodent studies. Each of these chemicals was chosen for assessment of cancer potency because they are industrial chemicals (solvents, chemical intermediates, etc.) for which exposures of workers, consumers, and/or the general population are likely to occur. Based on a review of mechanistic data, the dose-response relationship was assumed to be consistent with linearity at low dose for all six chemicals, and a linearized multistage model was used to estimate cancer potency. The cancer potency estimate corresponds to the upper 95 percent confidence bound on the linear term of the multistage model fit to the tumor response data, adjusted to account for body size differences between humans and animals. One of the chemicals (N-methylolacrylamide) induced tumors at multiple sites (liver, lung and hardierian gland) in mice. In this case, cancer potency was taken to be the sum of potencies associated with the three types of tumors in the male (most sensitive sex) mouse. Because of the statistical uncertainty in individual estimates of potency for each site, the linear terms were summed statistically, using Monte Carlo techniques. The upper 95 percent confidence bound on the summed linear terms was taken as the cancer potency estimate for N-methylolacrylamide. The cancer potency estimates range from greater than 1 (mg/kg-d)-1 for pyridine down to just over 0.01 (mg/kg-d)-1 in the case of C.I. Direct Blue 218. Daily intake levels corresponding to lifetime cancer risks of one in a million vary from several micrograms per day for the least potent carcinogens down to hundredths of a microgram per day for pyridine, the most potent of these six carcinogens.

### 1627 VALUE OF INFORMATION APPROACH FOR DEVELOPMENT OF MODELS OF THE DEVELOPING NEOCORTEX AFTER EXPOSURE TO LOW DOSE RADIATION FROM INTERNALLY DEPOSITED RADIONUCLIDES.

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Low dose radiation exposures during particular gestational periods can result in permanent neuronal perturbations and can lead to abnormalities in behavior and mental activity. Multiple mechanisms underlie these effects including radiation-induced cell death among neuronal precursors in the proliferative regions of the neocortex. We developed a computational model based on diverse data sets to describe the extent and pattern of cell death in the neocortex and the altered patterns of mi-

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# Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46<sup>th</sup> Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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