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Two New HEI Studies Validate Benzene and Butadiene Biomarkers in Humans

Newly published results from two Health Effects Institute (HEI) multiyear, multi-disciplinary international studies contribute significantly to our knowledge of biological markers for human exposure to benzene and 1,3-butadiene, especially at lower levels. Both investigations were funded by HEI as part of its efforts to improve science for air toxics risk assessment.

Benzene and 1,3-butadiene are used in many manufacturing processes and are components of motor vehicle emissions and cigarette smoke, among other sources. The US Environmental Protection Agency designates both compounds as human carcinogens, but major questions remain about the magnitude of the health risks they pose and how they are metabolized. For benzene, the health effects of low-level exposure—especially levels close to ambient concentrations—are not clear. For 1,3-butadiene, different species respond differently and how the human response compares to those of other species is not well understood.

Dr Qingshan Qu, of New York University School of Medicine, directed a study of workers occupationally exposed to benzene in Tianjin, China. Dr Richard Albertini, University of Vermont, directed a study of workers occupationally exposed to 1,3-butadiene in a factory near Prague in the Czech Republic. Co-investigators from many scientific disciplines and diverse parts of the world contributed to both studies.

A unique feature of the Qu and Albertini studies is the range of biomarkers that were evaluated. Both evaluated levels of several metabolites in urine (that exist for hours), adducts of the metabolites to proteins in blood (reaction products that attach to the proteins and exist for days to weeks or months), and genetic and chromosomal changes in blood cells (longer-term effects). Qu and colleagues also evaluated changes in numbers of circulating blood cells. The two studies also monitored occupational exposures over a wide range, to estimate exposures over different time periods (in particular, over a workday, 3–4 weeks, or years), and to correlate these different estimates of exposure with levels of different biomarkers.

Qu and colleagues found that exposure to benzene, even at low levels, was associated with changes in numbers of white blood cells. Levels of the metabolites *S*-phenyl-mercapturic acid and *trans,trans*-muconic acid were found to be the most useful urinary biomarkers of benzene exposure. Levels of two albumin adducts of benzene metabolites, benzene oxide and benzoquinone, were found to be useful biomarkers. Some assays identified more chromosomal aberrations in the occupationally exposed workers than in the control workers.

Of the many biomarkers of butadiene exposure that were analyzed by Albertini and colleagues, two urinary metabolites of 1,3-butadiene—known as M1 and M2—and two hemoglobin adducts—trihydroxybutylvaline and hydroxybutenylvaline—were found to be the most useful. The hemoglobin adducts exhibited the strongest correlation with measurements of 1,3-butadiene exposure, but the correlation of the urinary metabolites M1 and M2 with exposure was also quite strong.

The studies of Drs Qu and Albertini are key components of HEI's Air Toxics Program. To assist in understanding the effects of low-level exposure to benzene and 1,3-butadiene in humans, HEI has, over the past decade, funded studies that sought to identify or develop assays for biomarkers of these agents. As a result, we have improved ways to measure exposure—and ultimately refine our understanding of the magnitude of risk—especially at the low levels of exposure most people experience in their daily lives.

These new reports, including a brief *HEI Statement* summarizing the findings and HEI's independently conducted review of each study in non-technical language, are now available at www.healtheffects.org.

HEI Research Report 115, *Validation and Evaluation of Biomarkers in Workers Exposed to Benzene in China,* was conducted by Dr Qingshan Qu and colleagues at New York University School of Medicine, Tuxedo NY, USA.

HEI Research Report 116, *Biomarkers in Czech Workers Exposed to 1.3-Butadiene: A Transitional Epidemiological Study,* was conducted by Dr Richard Albertini and colleagues at the University of Vermont, Burlington VT, USA.

For more information about the Qu study, contact Dr Geoffrey Sunshine (+1-617-886-9330 ext 303; *gsunshine@healtheffects.org*); for the Albertini study, contact Dr Debra Kaden (+1-617-886-9330 ext 304; *dkaden@healtheffects.org*).