# Evaluation of Population and Individual Variances of Urinary Phthalate Metabolites

Ralph Feltensa, Stefan Roederb, Wolfgang Ottoc, Michael Borted, Irina Lehmannb, Martin von Bergena,c,,e, Dirk K. Wissenbacha

a Department of Metabolomics, Helmholtz Centre for Environmental Research -UFZ, Leipzig, Germany b Department of Environmental Immunology, Helmholtz Centre for Environmental Research-UFZ, Leipzig, Germany c Department of Proteomics, Helmholtz Centre for Environmental Research -UFZ, Leipzig, Germany d Children’s Hospital, Municipal Hospital St. Georg Leipzig, affiliated to the University of Leipzig, Germany e Department of Biotechnology, Chemistry and Environmental Engineering Aalborg University, Aalborg, Denmark

In the context of the German Lifestyle and environmental factors and their Influence on Newborns Allergy risk (LINA) cohort study, concentrations of nine phthalic diester metabolites (monoethyl-, mono-(3-carboxypropyl)-, mono-n-butyl-, monoisobutyl-, monobenzyl-, mono-(2-ethylhexyl)-, mono-(5-hydroxy-2-ethylhexyl)-, mono-(5-oxo-2-ethylhexyl)- and mono-(5-carboxy-2-ethylpentyl)-phthalate) were quantified in urine by LC-MS/MS. As in the majority of epidemiological studies only single spot samples were available for urine analysis, the implicit assumption in this case is, that exposure data obtained from single spot samples are representative for a longer exposure period. To validate the relevance of single spot analyses we quantified the respective intra-individual variances of urine samples collected from ten volunteers once daily over a period of 30 days. Using the values for the daily variances, approximate values for the underlying population variances in the cohort samples representing the differences between the average individual metabolite levels were calculated. For most of the volunteers, daily metabolites variations were lower, than the variations observed in the epidemiological setup. The results showed that by accounting for the contribution of daily variance, the standard deviations of the log-transformed phthalate values of the cohort samples are reduced (14 % to 28 %) but still larger (3 % to 66 %) than daily standard deviation values, with the exception of MCPrP concentrations.

In contrast to persistent organic pollutants with a high bioaccumulation potential, xenobiotic compounds with a large range of exposure levels and short metabolization and excretion rates such as phthalates are problematic with regards to interday variances. In such cases, instead of trying to increase cohort size, increasing the number of samples per study participant may produce a larger benefit, since averaging individual concentration values will yield much more reliable estimates of a given person's general exposure and thereby increase the chance of discovering correlations with parameters likely to result from long-term effects such as medical outcomes.