## Integration of effect biomarkers in human biomonitoring

C. Ladeira<sup>1,2,3\*</sup>

<sup>1</sup> H&TRC- Health & Technology Research Center, ESTeSL-Escola Superior de Tecnologia da Saúde, Instituto Politécnico de Lisboa, 1990-096 Lisbon, Portugal <sup>2</sup> NOVA National School of Public Health, Public Health Research Centre, Universidade NOVA de Lisboa, Lisbon, Portugal <sup>3</sup> Comprehensive Health Research Center (CHRC), Lisbon, Portugal \* carina.ladeira@estesl.ipl.pt

Human biomonitoring is an important tool for assessing exposure to chemicals and their health risks. Once human internal exposure to a chemical is shown, the complementary use of effect biomarkers can help bridge health consequences by providing data on pre-clinical manifestations of disease with a probability to be prevented. Effect biomarkers that measure genetic damage are potent tools to address the carcinogenic and/or mutagenic potential of chemical exposures, increasing confidence in regulatory risk assessment decision-making processes. The micronucleus (MN) test is recognized as one of the most successful and reliable assays to assess genotoxic events, which are associated with exposures that may cause cancer. There is fair evidence of significant increase in MN frequency in patients with cancer and other chronic diseases compared with controls, substantiating its predictive value. Promising approaches, such as combined effect biomarkers open the possibility to evaluate the combined effects of complex chemical mixtures in human samples, and efforts are needed to integrate these approaches in risk assessment. Although effect biomarkers are gaining ground in human biomonitoring, new challenges are still arising. To move towards the next generation of human risk assessment is crucial to establish bridges between standard approaches of effect biomarkers and new approach methods (NAMs) and tools for increase the mechanistically-based biological plausibility in human studies, such as the adverse outcome pathways (AOPs) framework. Human epidemiological studies with biomarkers of effect play an invaluable role in identifying health effects with chemical exposures and may provide a tool for improving risk assessment and may be especially useful in the case of risk assessment of chemical mixtures.

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