**Reactivity of Electrophiles toward N-Term Nucleophiles –**

**A Chemoassay Battery to Identify Potential Skin Sensitizers**

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A key step in triggering allergic contact dermatitis is the sensitization of skin through dermal contact with allergens as industrial chemicals and cosmetic ingredients. Currently, skin sensitization potency is assessed by the murine local lymph node assay (LLNA), an animal test that is still the recommended method in REACH. The molecular initiating event of the adverse outcome pathway leading to skin sensitization is the covalent binding of electrophiles to nucleophilic groups of dermal proteins and peptides. In this context, the N-term forms a prominent target site that can react with aldehydes and α,β-unsaturated carbonyls. Employing model nucleophiles as surrogates for endogenous nucleophilic groups, kinetic chemoassays provide access to reactivity information in terms of second-order rate constants.1-3 In this communication, a kinetic Chemoassay battery is employed for assessing the electrophilic reactivity of selected aldehydes and α,β-unsaturated carbonyls toward the N-term through the second-order rate constant *k*NH2. The results are compared with literature data for the compounds´ LLNA potency in order to discriminate between non-sensitizing and potentially sensitizing candidates.

1 Böhme A, Thaens D, Paschke A, Schüürmann G 2009. Kinetic glutathione chemoassay to quantify thiol reactivity of organic electrophiles-application to α,β-unsaturated ketones, acrylates, and propiolates. *Chem. Res. Tox.* 22: 742–750.

2 Böhme A, Thaens D, Schramm F, Paschke A, Schüürmann G 2010. Thiol reactivity and its impact on the ciliate toxicity of α,β-unsaturated aldehydes, ketones, and esters. *Chem. Res. Toxicol.* 23: 1905–1912.

3 Thaens D, Heinzelmann D, Böhme A, Paschke A, Schüürmann G 2012. Chemoassay screening of DNA-reactive mutagenicity with 4-(4-nitrobenzyl)pyridine - Application to epoxides, oxetanes, and sulfur heterocycles. *Chem. Res. Toxicol.* 25: 2092–2102.