PRELIMINARY (PHASE I) RESULTS OF A VALIDATION STUDY TO EVALUATE THE RELIABILITY AND RELEVANCE OF TWO IN VITRO CYTOTOXICITY ASSAYS FOR PREDICTING RODENT AND HUMAN ACUTE SYSTEMIC TOXICITY

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In order to assess the reliability and relevance of two in vitro basal cytotoxicity assays for predicting acute systemic toxicity in rodents and humans, NICEATM and ECVAM designed and started a joint validation study in July 2002. The 3T3 neutral red uptake (NRU) assay and the normal human keratinocyte (NHK) NRU assay are being tested in three laboratories to assess the toxicity of seventy-two coded chemicals representative of all five Globally Harmonised System (GHS) hazard classification categories as well as the unclassified category. The Registry of Cytotoxicity (RC) Prediction Model will be applied to the new set of data to evaluate its predictive ability for rodent LD_{50} values whereas human acute lethal blood concentrations collected from the literature and from the Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) in vivo database (MEMO) will be used to establish and evaluate the relationship between in vitro results and in vivo human acute toxicity. The three-phase design of the study allows the establishment of (1) a historical positive control database with sodium lauryl sulfate (SLS) in each laboratory (Phase Ia); (2) a two-stage protocol performance and optimisation phase with three coded chemicals (Phase Ib) and with nine coded chemicals (Phase II); and (3) a formal validation study with sixty coded chemicals (Phase III). Results obtained in Phase Ia and Phase Ib will be presented and the intra- and inter-laboratory reproducibility of the data will be discussed. Supported by NIEHS contract N01-ES-85424, EPA IAG DW-75-93893601-0, and European Commission contract N° 19416-2002-04 F2ED ISP GB.