SELECTION OF REFERENCE CHEMICALS TO VALIDATE *IN VITRO* CYTOTOXICITY ASSAYS FOR ESTIMATING *IN VIVO* STARTING DOSES FOR ACUTE ORAL TOXICITY

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The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and NICEATM convened an international workshop in October 2000 to evaluate the validation status of *in vitro* methods for predicting acute systemic toxicity (see http://iccvam.niehs.nih.gov). As an interim step to developing and ultimately using *in vitro* cytotoxicity methods to accurately predict rodent oral LD50s for regulatory purposes, workshop participants recommended the use of *in vitro* methods to predict the *in vivo* LD50 starting dose in situations where other credible information was unavailable. It was conjectured that such an approach would reduce the number of animals required for acute toxicity testing. In a joint effort with the U.S. EPA, and in collaboration with the European Centre for the Validation of Alternative Methods (ECVAM), NICEATM is organizing a multi-laboratory study to validate the utility of two *in vitro* cytotoxicity tests for identifying the starting dose for *in vivo* acute toxicity tests. A major aspect of the study design was the selection of an appropriate number of test chemicals that represented 1) a wide range of toxicity, 2) the types of chemicals regulated by the various U.S. regulatory agencies, and 3) those with human toxicity data and/or human exposure potential. Based on these criteria, a preliminary list of approximately 100 chemicals was compiled by mining several publicly available data sets. A priority list of 60 chemicals representing the 6 acute toxicity hazard classifications in the Globally Harmonized Scheme was created based on compatibility with the test systems, availability and quality of existing rodent oral LD50 data, human exposure data, commercial availability, ease of shipping, and availability of information on mechanism of action. [1]Supported by NIEHS contract N01-ES-85424 with ILS, Inc.