Use of human acute toxicity data for the evaluation of *in vitro* assays in the ACuteTox project

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The ACuteTox project is designed to develop an *in vitro* testing strategy for prediction of acute human systemic toxicity. In similarity with the Multicenter Evaluation of *In Vitro* Cytotoxicity (MEIC) programme (1989-1998), the main goal of this new international project is to replace the acute animal toxicity tests by *in vitro* and *in silico* assays.

For this purpose about 100 chemicals will be tested in several *in vitro* model systems, with special emphasis to target-organ toxicity (neurotoxicity, hepatotoxicity and nephrotoxicity), biotransformation and biokinetics. To validate the obtained *in vitro* data and the test strategies, it will be necessary to compare these data with human lethal and sub-lethal blood concentrations and with animal toxicity data (LD50 values for rat and mice). A new database, AcuBase, containing human, animal and *in vitro* data, will be generated in the framework of the ACuteTox project.

The Work Package 1 of the ACuteTox project is collecting acute human toxicity data in accordance with previously established criteria in MEIC programme (1). The main sources of data are clinical cases and forensic medicine data obtained from scientific journals, MEIC monographs, toxicology handbooks, and from the Swedish Poison Information Centre. For all chemicals studied, the data concerning toxicokinetics (absorption, distribution and elimination), target organs, metabolism and toxicological mechanisms are also collected.

For evaluation of the *in vitro* data, the average sub-lethal and lethal blood concentrations from acute single-dose poisoning will be calculated from the time-related lethal concentration curves. Analysis of the variability and reproducibility of the *in vivo* data will be performed, as well as comparison of human and animal *in vivo* data.

Reference

1. Ekwall B., Clemedson C., Crafoord B. et al. (1998) MEIC Evaluation of Acute Systemic Toxicity. Rodent and human toxicity data for the 50 reference chemicals. *ATLA* **26,** 571-616.