NEWSLETTERNEWSLETTERNEWSL

OCT 2006

ACuteTox
– Research Project For Alternativ Testing

CONTACT: ERICA TOFT, EXPERTRÅDET AB, RÅDAN 3, SE-191 40, SOLLENTUNA, TEL. +46 8 627 99 80, Erica.Toft@expertradet.se

The first year of the development of a in vitro testing strategy for prediction of human acute systemic toxicity

Project rationale

There are more than 30,000 chemicals on the Western European market, but only 5,000 have been characterised in terms of toxicity. The 7th amendment to the European Union's Cosmetics Directive and the European Union's soon-to-be-implemented REACH (Registration, Evaluation and Authorisation of Chemicals) proposal will dramatically increase the need for toxicity testing in the near future. It has been estimated that in excess of 4 million laboratory animals would be needed if these toxicity tests were carried out using conventional test methods.

Project objectives

The ACuteTox (Optimisation and Prevalidation of an *In Vitro* Test Strategy for Predicting Human Acute Toxicity) project is a five-year research project commenced in January 2005, aiming at developing tests of acute toxicity of chemicals without use of laboratory animals. The project, with 35 partners from 13 European countries, has an overall budget of €16 million of which €9 million are contributed by the European Union's Sixth Framework Programme for Research and Technological Development (FP6).
The ACuteTox project will develop *in vitro* (in an artificial environment outside the living organism) tests to eliminate the need for *in vivo* (within a living organism) tests, i.e. animal tests. The central hypothesis of the project is that acute toxicity tests can be carried out on cell cultures instead of on animals. The ACuteTox project will enable almost complete elimination of *in vivo* testing of *acute* toxicity, while simultaneously reducing the cost and increasing the validity of the tests when compared to conventional *in vivo* testing.

Members from 13 European countries participate in the project.

Results Year 1

The ACuteTox project progresses very well and according to plan. The accomplishments during the first project year are summarised in the subsequent paragraphs.

EU contract no.
LSHB-CT-2004-512051

Generation of databases with *in vivo* and *in vitro* data

A central element of the project is to develop comprehensive databases of *in vivo* and *in vitro* acute toxicity data. *In vivo* data are compiled from both animal tests and human poisoning accidents, while the *in vitro* data stem from several previous research projects (wherein ACuteTox partners participate) and tests carried out within the present project. The database, which ultimately will incorporate toxicity data for 100-140 chemicals, is developing according to plan and will be completed in 2006.

Selection and refinement of *in vitro* tests

Previous research projects have shown that combinations of *in vitro* tests are capable of determining the acute toxicity quite well; a 70% *in vitro/in vivo* correlation has been demonstrated. However, ACuteTox will pay particular attention to those cases where the *in vitro/in vivo* correlation is unsatisfactory in order to further improve the ability to predict acute toxicity. The approach is to add new *in vitro* tests (for biokinetics and organ specific toxicity) to a basal set of cytotoxicity assays. These new tests will function either as correctors or alerts that indicate when an In vitro approach may be insufficient. Computer modelling and experimental studies are combined to investigate if the inclusion of different biokinetic factors could improve unsatisfactory correlation. Moreover, specific toxicity of the nervous system, kidney and liver are being experimentally characterised using organ-specific cell cultures with the aim to find the most appropriate test assays for organ specific toxicity to be included in the final testing strategy. This substantial and critical work is ongoing and is progressing well, with several chemicals already assessed.

Development and implementation of *in vitro* test strategy

The ultimate challenge of the ACuteTox project is to integrate the knowledge amassed into an expert system capable of providing a reliable value for a chemical's acute *in vivo* toxicity and then to ensure that the *in vitro* test strategy developed shall achieve regulatory approval and become widely implemented in industry. These critical steps are scheduled to commence in the second half of the project.

Further information

For more detailed information about the ACuteTox project, please visit the project website *www.acutetox.org* or contact Erica Toft (*Erica.Toft@expertradet.se*), telephone: +46 8 627 99 80).

EU contract no.
LSHB-CT-2004-512051