

NICEATM REQUESTS INFORMATION ON TECHNOLOGIES USED FOR INHALATION TESTING

| Information on device and /or technology | |
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| Product | Precision-cut lung slices |
| Size | Tissue sections in size of 200 µm x 8 mm in diameter |
| Application | Alternative for acute inhalation toxicity: Tissue based <i>ex vivo</i> testing of substances and mixtures using submers cultures in a robust and efficient way for routine applications |
| Compatibility/ kind of tissue culture system | Commercial 24-well multiwell plate |
| Amount of samples | Within one donor several substances, concentrations with appropriate controls |
| Exposure type | Submers |
| Endpoint Measurements | Cytotoxicity, inflammation, bronchoconstriction, and genotoxicity |
| Information on data from non animal tests for identifying acute inhalation hazard potential | |
| Scientific background | Within a BMBF-funded project rat precision-cut lung slices (PCLS) were standardized and prevalidated. The project was conducted in three independent laboratories. In all participating laboratories, PCLS were prepared freshly and exposed 20 industrial chemicals. Toxicity was assessed by released lactate dehydrogenase (LDH assay) and by mitochondrial activity (WST-1 assay). In addition, protein content and pro-inflammatory cytokine IL-1 α were measured by BCA assay and ELISA, respectively. For all endpoints a sigmoid concentration-response model was fitted to the data and IC50 values were calculated. For each endpoint test acceptance criteria were established. More than 900 concentration-response curves were fitted and analysed. The results show that (i) the test protocol is transferable for practical use, (ii) the WST-1 endpoint is most reliable, and (iii) comparison with <i>in vivo</i> data (GHS classes and LC50 data from <i>in vivo</i> inhalation) provides prediction models that can be used for assessment of acute toxicity of substances. Results have been presented as posters and talks on congresses and will be published soon. |
| Information on corresponding <i>in vivo</i> data for substances test | |
| | Correlation of <i>ex vivo</i> IC50 with <i>in vivo</i> inhalation LC50 and oral LD50 values has been included in the above described project. Correlation of <i>ex vivo</i> IC50 with <i>in vivo</i> GHS classification has also been done. |
| Outlook | |
| | Currently we are working on development of acute inhalation toxicity testing using PCLS with P.R.I.T. exposure technology. |