Report of the EPAA–ECVAM Workshop on the Validation of Integrated Testing Strategies (ITS)

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Summary — The use of Integrated Testing Strategies (ITS) permits the combination of diverse types of chemical and toxicological data for the purposes of hazard identification and characterisation. In November 2008, the European Partnership for Alternative Approaches to Animal Testing (EPAA), together with the European Centre for the Validation of Alternative Methods (ECVAM), held a workshop on Overcoming Barriers to Validation of Non-animal Partial Replacement Methods/Integrated Testing Strategies, in Ispra, Italy, to discuss the extent to which current ECVAM approaches to validation can be used to evaluate partial replacement in vitro test methods (i.e. as potential ITS components) and ITS themselves. The main conclusions of these discussions were that formal validation was only considered necessary for regulatory purposes (e.g. the replacement of a test guideline), and that current ECVAM approaches to validation should be adapted to accommodate such test methods (1). With these conclusions in mind, a follow-up EPAA–ECVAM workshop was held in October 2009, to discuss the extent to which existing validation principles are applicable to the validation of ITS test methods, and to develop a draft approach for the validation of such test methods and/or overall ITS for regulatory purposes. This report summarises the workshop discussions that started with a review of the current validation methodologies and the presentation of two case studies (skin sensitisation and acute toxicity), before covering the definition of ITS and their components, including their validation and regulatory acceptance. The following main conclusions/recommendations were made: that the validation of a partial replacement test method (for application as part of a testing strategy) should be differentiated from the validation of an in vitro test method for application as a stand-alone replacement, especially with regard to its predictive capacity; that, in the former case, the predictive capacity of the whole testing strategy (rather than of the individual test methods) would be more important, especially if the individual test methods had a high biological relevance; that ITS allowing for flexible and ad hoc approaches cannot be validated, whereas the validation of clearly defined ITS would be feasible, although practically quite difficult; and that test method developers should be encouraged to develop and submit to ECVAM not only full replacement test methods, but also partial replacement methods to be placed as parts of testing strategies. The added value from the formal validation of testing strategies, and the requirements needed in view of regulatory acceptance of the data, require further informed discussion within the EPAA forum on the basis of case studies provided by industry.

Key words: integrated testing strategies, non-animal methods, validation.

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