

Alternative and Integrated Approaches to Skin Sensitization:  
Recent Progress and the Way Forward

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Recent significant progress has been made in reducing and refining the use of animals for assessing skin sensitization potential of chemicals. Progress is also being made in developing methods and strategies that may eventually provide for partial or full replacement of animal use. The validation and international regulatory acceptance of the murine local lymph node assay (LLNA) now allows it to be used in place of standard guinea pig based assays in most testing situations and fully eliminates the potential pain and distress that could previously occur with this testing. New approaches such as use of a LLNA limit dose test will further reduce the numbers of animals needed for this procedure. New models and approaches are also being developed that may eventually allow for decisions about skin sensitization potential of a substance to be made without animals. These include advances in structure-activity relationship models, assessment of protein and peptide bonding potential, and the evaluation of responses in mechanism based cellular systems. Integration of the responses from a battery of test models such as these is also expected to provide improved predictions of sensitization potential. Adding knowledge about physical and chemical attributes of substances associated with sensitivity or non-sensitivity may further strengthen such predictions. Evaluation of these integrated approaches will require adequate validation of each individual model as well as the entire test battery with the same set of reference substances for which there is high quality data from the accepted reference test method. High quality data from human studies for the same reference substances are also desirable,

where this can be ethically accomplished. Regulatory acceptance of a proposed integrated testing approach will require demonstration that the approach will provide for equivalent or improved prediction of sensitization potential. Further development, validation, and integrated use of mechanism-based sensitization testing models can be expected to further reduce animal use while providing for continued protection of human health.