Evaluation of Potential False Negative Corrosive Chemicals in Proposed *In Vitro* Dermal Irritation Assays

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EpiDerm™ and EPISKIN™ have been proposed as replacements for the *in vivo* rabbit skin irritation test and for inclusion in an *in vitro* testing strategy to replace *in vivo* rabbit testing for regulatory hazard classification and labeling of skin corrosivity and irritation. If these methods are to be considered complete replacements for animal tests, they must provide equal or greater protection. Therefore, an *in vitro* testing strategy must be capable of identifying approximately 12% to 21% false negative corrosive substances, which are currently identified using the *in vivo* rabbit skin irritation/corrosivity test. NICEATM and ICCVAM designed a multi-phased study to assess the performance of the EpiDerm™ irritation assay when testing false negative corrosive substances to establish criteria for identifying corrosives or to identify exclusion rules for substances that cannot be accurately evaluated in an *in vitro* testing strategy. Phase 1 evaluated the effectiveness of an MTT correction step in reducing false negatives in the corrosivity assay and whether the EpiDerm™ irritation assay can distinguish dermal corrosives from irritants. Data from Phase 2 were used to inform suggestions on modifying decision criteria for the EpiDerm™ irritation protocol that would also identify corrosives. Information generated from this study, which was developed by NICEATM and ICCVAM, with input from the ECVAM Validation Study Management Team, will be critical to regulatory authorities in their consideration of *in vitro* skin irritation test methods. ILS staff supported by NIEHS contract N01-ES-35504. The views expressed above do not necessarily represent the official positions of any Federal agency.