International Validation of In Vitro Test Protocol (EpiDerm- SIT) to Replace the In Vivo Rabbit Test for Hazard Identification of Chemicals

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In April 2007, ECVAM endorsed 2 alternative test methods (EPISKIN and EpiDerm Skin Irritation Tests (SIT)) as replacements of the in vivo rabbit skin irritation test. While EPISKIN was recognized as a stand alone method, EpiDerm SIT was endorsed for use in a tiered testing strategy (OECD TG 404), where irritating results are accepted and non-irritating results may require further testing by another method.

Based on published data and analysis of results of the ECVAM validation study, there was evidence that differences in the barrier properties between the 2 models were responsible for the lower sensitivity of EpiDerm SIT when using an identical protocol as used for EPISKIN. Therefore, modifications of the exposure conditions were introduced to the EpiDerm SIT protocol: a)exposure time was increased from 15 min to 60 min; b)the temperature during the exposure was increased to 37°C. With these modifications, significant increase in sensitivity was obtained, while maintaining an acceptable specificity of the method.

In autumn 2007, an international validation study was performed to evaluate reproducibility and confirm the predictive ability of the modified EpiDerm SIT method. Results of the study are presented here. Overall, sensitivity and specificity of 80% were obtained, which is comparable to results for the EPISKIN SIT for the same set of chemicals (sensitivity of 70%, specificity 80%). The inter-laboratory reproducibility of the modified EpiDerm SIT and its concordance with the in vivo rabbit data was also very good. The method was endorsed by ECVAM in November 2008 as full replacement method and has gained regulatory acceptance in the EU as one of three methods described as B.46 of Annex III of the REACH regulation.