

Lecture: skin models as alternatives to animal testing

Follow-up validation of the modified EpiDerm Skin Irritation Test (SIT): results of a multi-centre study of twenty reference test substances

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In April 2007, ECVAM endorsed two alternative *in vitro* 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, the EpiDerm SIT was endorsed for use in a tiered testing strategy, where irritating results are accepted and non-irritating results may require further testing by another method (e.g. QSAR).

Based on results published by Faller and Bracher (*Skin Pharmacol. Appl. Skin Physiol.* 2002, 15, suppl. 1, 74–91), and analysis of the results of the ECVAM validation study, there was evidence that differences in the barrier properties between the two 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, when testing chemicals from the pre-validation and validation studies, a significant increase in sensitivity (84%) was obtained, while maintaining an acceptable specificity of the method.

In autumn 2007, an international multi-centre validation study employing ZEBET (D), BASF (D), IIVS (USA) and ZET(A) was performed to evaluate reproducibility of the modified EpiDerm method. 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 modified method and validation data were submitted to ECVAM for scientific review in April 2008. It is foreseen to be completed in October 2008.

Keywords: human 3D skin model, in vitro skin irritation testing, validation