

Background information: Validation of Skin Irritation Testing

In 2003, ECVAM launched a formal validation study of two cell culture test systems employing artificial human skin (EPISKIN, EpiDerm). The aim of the study was to replace the regulatory Draize skin irritation test, a test introduced into safety tests for drugs and chemicals 60 years ago currently performed on albino rabbits. The objectives were to assess the relevance and reproducibility within and between laboratories of these test systems with a set of 58 coded test chemicals for which high quality animal data were available. Test chemicals were selected by an independent Chemical Selection Committee. To ensure high quality of the commercially produced human skin models, the facilities of the producers of the human skin models were evaluated by independent audits.

The EpiDerm test was conducted in the following laboratories: Zentralstelle fuer die Erfassung und Bewertung von Ersatz- und Ergaenzungsmethoden zum Tierversuch (ZEBET at the German federal institute for risk assessment, coordinator) Germany, Institute for *In vitro* Sciences (IIVS) USA and BASF Germany. The EPISKIN test was conducted in the following laboratories L'Oréal (lead lab and developer of the test) France, Unilever UK and Sanofi-Synthélabo France. The main endpoint measured for both EpiDerm and EPISKIN was cell viability. However, a second endpoint, a danger signal released by cells to start inflammatory responses in the body (interleukin-1 α), was added for those chemicals which did not reduce cell viability. The results of this validation study showed that, for EPISKIN, sensitivity (correct prediction of irritants) was 91% and specificity (correct prediction of non-irritants) was 79 for EpiDerm, sensitivity was only 62% but specificity was 89%.

The study has been forwarded to the ECVAM Scientific Advisory Committee (ESAC) with a proposal that EPISKIN could be considered as a replacement for the rabbit skin irritation method and EpiDerm as a constituent of a testing strategy. An ESAC statement on the scientific validity of the EPISKIN assay as full replacement to the current animal test is pending for the forthcoming ESAC meeting on 27th of April.

The test is urgently required for cosmetic testing, since the respective animal test is banned in this area of use from 2009 onwards. The animal test was also foreseen for about 10.000 chemicals within the REACH program. In light of the expected validity statement, the test strategies developed for REACH under coordination of ECVAM over the last two years foresee already the use of the novel non-animal method.