



## **DEVELOPMENT OF AN EPIDERM II IN VITRO SKIN IRRITATION TEST (SIT) FOR THE GLOBALLY HARMONIZED SYSTEM (GHS) OF CLASSIFICATION AND LABELING OF CHEMICALS**

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**Purpose:** Recent legislation and a ban on animal testing for cosmetics have heightened the need for validated in vitro skin irritation tests (SIT)s. The EpiDerm model has been validated for in vitro skin corrosion testing worldwide, and for in vitro SIT in the EU in studies sponsored by the European Center for the Validation of Alternative Methods (ECVAM). The EU SIT system distinguishes 2 classifications - skin irritants (R38) and non-irritants (no label). However, a UN treaty endorsed by the US, EU, China, Japan, Australia and others has outlined a GHS of Classification and Labeling of Chemicals. The GHS classifies skin irritancy of chemicals into three categories: non-irritant, slight irritant or irritant. Therefore, additional efforts are underway to validate an EpiDerm SIT for GHS.

**Methods:** 15 test chemicals with known in vivo Draize skin irritation scores were applied to EpiDerm to identify in vitro skin irritation biomarkers and establish a preliminary EpiDerm-GHS-SIT prediction model. Biomarker endpoints evaluated include EpiDerm viability (MTT assay) and inflammatory mediator release by ELISA and/or Multiplex (Bio-Rad BioPlex) assays.

**Results:** The MTT viability response was the most predictive and least variable biomarker, providing 80% concordance with the in vivo Draize classification (i.e. 80% sensitivity and specificity for assigning GHS classifications). Among the mediators investigated, significant levels of IL-1a, IL-1ra, IL-8, IL-18, GROa and PGE2 were produced by EpiDerm tissues. These biomarkers did not improve the classification. This preliminary prediction model will be further tested and refined to form the basis for formal multi-laboratory EpiDerm- GHS-SIT validation studies.

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