



Development of an EpiDerm™ In Vitro Skin Irritation Test (SIT) for the Globally Harmonized System (GHS) of Classification and Labeling of Chemicals

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Determination of skin irritation potential is an international regulatory requirement to ensure safe handling, packaging, labeling and transport of chemicals and evaluation of cosmetics and household products. Recent legislation and a ban on animal testing for cosmetics have heightened the need for validated in vitro SITs. 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 (corresponding to in vivo Draize skin irritation scores < 1.5), slight irritant (Draize score 1.5 – 2.3) or irritant (Draize score > 2.3). The EpiDerm model has been validated for in vitro skin corrosion testing worldwide, and in vitro SIT in the EU in studies sponsored by the European Center for the Validation of Alternative Methods (ECVAM). However, the EU SIT system distinguishes only 2 classifications – skin irritant (R38) and non-irritant (no label), and thus will not satisfy the worldwide GHS SIT system. Therefore, additional efforts are underway to validate an EpiDerm SIT for GHS. In results reported here, 15 test chemicals with known in vivo Draize skin irritation scores, chosen to avoid borderline classifications, 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. Among the mediators investigated, significant levels of IL-1a, IL-1ra, IL-8, IL-18, GROa and PGE2 were produced by EpiDerm tissues. 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). 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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