



Regulatory Requirements for In Vitro Systems to Meet Performance Standards During Validation and Over Time

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A recent US National Research Council report (June, 2007) envisions humane alternative toxicological tests that are faster, less expensive, and more accurate than their animal counterparts. In fact, in vitro tissue models have been or are in the process of being validated as alternatives to animal testing for safety evaluation of cosmetics, pharmaceuticals, and consumer products. Currently available organotypic human models include dermal (EpiDerm, EpiDerm-FT), ocular (EpiOcular), ectocervical (EpiVaginal) and airway (EpiAirway). As these models become formally validated, regulatory agencies and other users need to be assured that the models will provide consistent, high quality data over time, not just during the validation process (K. Gupta et al., *Regul Toxicol Pharmacol.* 2005 Dec; 43(3):219-24). Recommended guidelines include "full characterization of cells or tissues, sampling of each lot ... for performance, and regular use of controls and benchmark chemicals to provide assurance of consistency of assay performance" (A. Rispin et al. *Regul Toxicol Pharmacol.* 2006 Jul; 45(2):97-103). The current poster summarizes the long-term reproducibility and performance of in vitro epidermal (EpiDerm) and ocular (EpiOcular) models against benchmark chemical treatment. Quality control testing of weekly batches of EpiDerm and EpiOcular was performed using the MTT assay. The exposure time needed to reduce the viability to 50% (ET-50) for Triton X-100 was determined. For EpiOcular, the yearly average ET-50 values have ranged from 22.0 minutes to 27.3 minutes. The coefficients of variation (CV) for the negative control tissues (exposed to ultrapure H₂O) have averaged under 6% for every year since 1997. In addition, the yearly average CV for all tissues has never exceeded 6.7%. For EpiDerm, the yearly average ET-50 values have ranged from 5.9 hrs to 7.5 hrs. The coefficients of variation (CV) for the negative control tissue (exposed to ultrapure H₂O) have averaged under 7.5% for every year since 1996. These results over the past 14 years of commercial production address regulatory concerns regarding performance standards over time.

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