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EpiDerm | Data Sheet

Features

- 3D NHEK-Based, Highly Differentiated Model
- Completely Serum-Free Media System
- Human Skin-Like Structure
- Highly Reproducible
- Easy to Handle Cell Culture Inserts
- *In Vivo*-Like Lipid Profile
- All *In Vivo* Ceramides Present
- Broad-Narrow-Broad Lamellar Spacing
- Metabolically Active
- Comparable Barrier Properties to *In Vivo*
- Quantifiable, Objective Endpoints
- Cost Effective Alternative to Animal and Clinical Testing

Validated/Regulatory Applications

- OECD TG 439 *In Vitro* Skin Irritation Test
- OECD TG 431 *In Vitro* Skin Corrosion Test
- OECD TG 498 *In Vitro* Phototoxicity Test
- ISO 10993-23:2021 *In Vitro* Skin Irritation Test for Medical Device Extracts

Additional Applications

- Genotoxicity
- Skin Absorption
- Dermal Drug Delivery
- Safety / Toxicity
- Formulation optimization

The EpiDerm Model

Mattek's EpiDerm model is a three-dimensional tissue that consists of normal, human-derived epidermal keratinocytes (NHEK). These NHEK have been cultured at the air-liquid interface to form a multilayered, highly differentiated tissue with mitotic and metabolic features comparable to human epidermis. Histological cross-sections exhibit *in vivo*-like morphological features including the stratum basale, stratum spinosum, stratum granulosum and corneocytes of the stratum corneum. Epidermis-specific differentiation markers such as profilaggrin, involucrin, cytokeratin 1, and cytokeratin 10 are appropriately localized. Ultrastructural characteristics consistent with *in vivo* epidermis include intercellular lamellar lipid layers in the stratum corneum, keratohyalin granules, tonofilament bundles, and desmosomes.

The EpiDerm model is a well-established, highly reproducible platform for those seeking alternatives to animal testing. It is validated under the Organisation for Economic Co-operation and Development (OECD) guidelines for skin irritation testing, skin corrosion testing, and phototoxicity testing. It is also widely used for formulation research and toxicity assessment of cosmetics, household products, pharmaceuticals, and petrochemicals. EpiDerm provides a more cost- effective and efficient alternative to both animal and clinical tests.

Additional Information

• Weekly delivery
• Shipment from the US or Europe
• Multiple culture inserts formats
• Various media formulations*

* Available anti-fungal free, antibiotic free, hydrocortisone free and phenol red free

EpiDerm Histology

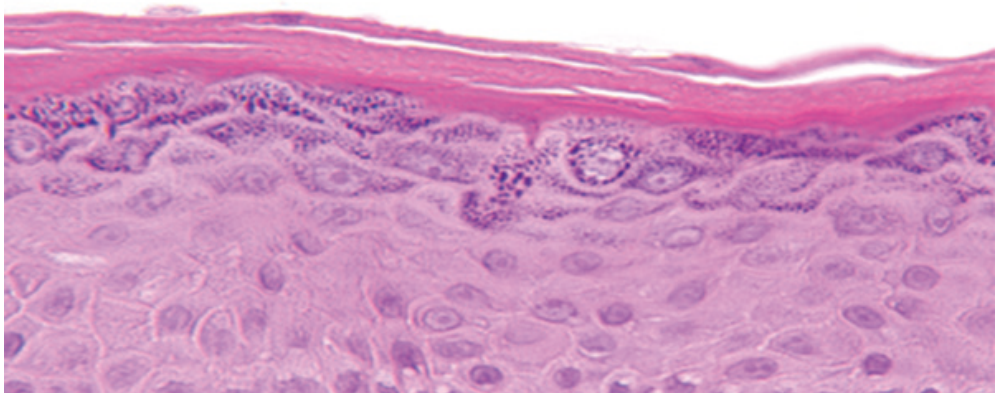

Figure 1. Histological cross-section of EpiDerm tissue model (H&E stained) shows highly differentiated tissue with organized basal, spinous, granular, and cornified cellular layers.

Safety/Toxicity

EpiDerm in regulatory toxicology

For a model to be accepted for use in a regulated assay, specifically for OECD acceptance, the model must provide reproducibility, reliability, and accuracy for predicting specific endpoints. EpiDerm, which has been produced since the 1990s, has demonstrated these characteristics with consistent QC values over the course of 19 years (Table 1). The consistent production of the EpiDerm model has resulted in acceptance of the 3D tissue in three different OECD guidelines (Table 2) to allow researchers to assess irritation, phototoxicity, or corrosion potential of various compounds (Figure 2).

Summary of yearly average from quality control (QC) testing of EpiDerm (EPI-200) tissue from 1996 to 2015.
ET-50 values are obtained after the exposure of RHE tissue to 100 microliters of 1.0% Triton X-100. The AC acceptance range of 4.7-8.7 hr was established in 1996.

Calendar Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
ET-50 (min)	6.73	6.91	7.47	6.63	6.50	6.59	6.85	6.20	6.27	6.01	5.92	6.80	6.34	5.91	6.26	6.71	5.81	6.04	6.75	7.42
Avg CV* (%)	9.31	9.73	9.38	5.80	6.14	9.62	9.82	11.4	13.0	14.7	14.9	12.2	13.6	13.7	14.77	13.47	12.32	11.70	9.40	12.44

* Intermediate point was added to the assay in 2004 in order to increase precision of the ET-50 assay. This caused the average CV to increase slightly.

Table 1. Average ET-50 values from 1996-2015

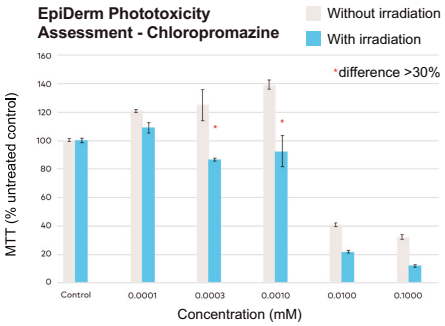

Figure 2. EpiDerm can be used to assess phototoxicity following OECD TG 498. To determine phototoxicity, EpiDerm tissues are topically exposed to a potential phototoxin (chlorpromazine). Tissues are then irradiated with a non-toxic dose of UV (data demonstrates 10J exposure, 45min) and then tissue viability is determined using the MTT assay. A compound is considered phototoxic if exposure to UV decreases tissue viability by >30% compared to tissue not exposed to UV.

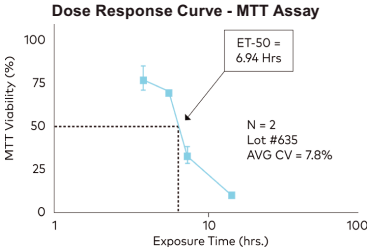

Figure 3. The exposure time necessary to decrease tissue viability to 50% (ET-50) for different product formulations is determined using the MTT assay (sample graph demonstrating effects of 1% Triton X-100). ET-50's are used to rank order irritation of the formulations to identify the least irritating one.

Drug Delivery/Permeation

The ultrastructural similarity between EpiDerm and *in vivo* skin makes EpiDerm an ideal model to assess drug-delivery and skin permeation changes. EpiDerm can be used with Mattek Permeation Devices or Permegear Franz Cells and allows for determination of average flux and permeability coefficients following apical application of compounds.

Non-regulatory toxicology and genotoxicity

In addition to acceptance in regulatory toxicology, EpiDerm's consistent model production and similarity to human skin ensures the model can be used for evaluation of toxicity of compounds in a non-regulated setting (Table 2). These tests are typically conducted using the MTT ET-50 assay which allows for rank ordering of compounds by irritancy responses based on the time-to-toxicity results (Figure 3). Furthermore, the *in vivo* relevance of the EpiDerm model has shown relevance in assessment of genotoxic potential of various compounds.

Method	**Standard Use/Tested Materials**	**Regulated**
Skin Irritation OECD 439	• Non-irritant vs irritant determination • Final Formulation	Yes
Skin Irritation for Medical Devices ISO 10993-23	• Non-irritant vs irritant determination • Medical device extracts	Yes
Skin Corrosion OECD 431	• OECD GHS determination of corrosive vs non-corrosive • UN GHS Sub-categorization 1A, 1B, 1C • Formulation chemicals	Yes
Photoxicity OECD 498	• Determination of phototoxins from non-phototoxins • Formulation chemicals	Yes
MTT ET-50	• Rank order formulations • Common in R&D studies	No

Table 2. Overview of Toxicity Tests using EpiDerm

MATTEK
Now Part of Sartorius

Mattek North America Headquarters
200 Homer Ave
Ashland, MA 01721
US: + 1 (508) 881-6771

For further information, visit
www.mattek.com or email
support@mattek.com