



Percutaneous Absorption Services



Leading the Field of *In Vitro* Toxicology

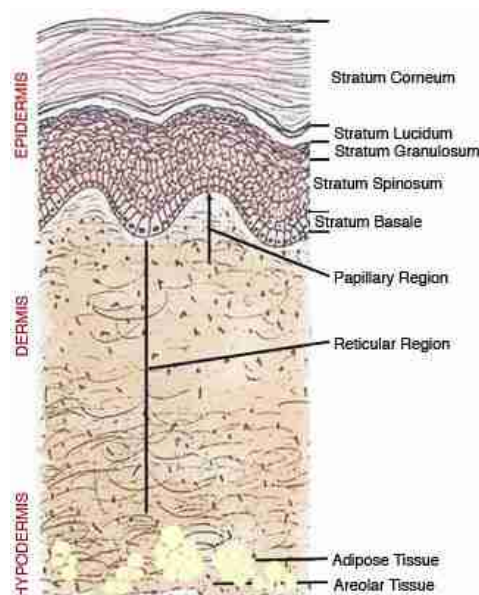
One of the primary roles of the skin is to form a barrier to protect humans from substances contacted in the environment. Permeation of a substance through the skin depends upon a number of factors, including: area of contact; duration of exposure; lipophilicity (fat solubility), molecular weight, concentration of the test substance, integrity of the stratum corneum, and thickness of the epidermis. The qualities of the outermost layer of the skin, the stratum corneum, typically determines the rate of dermal penetration.

Percutaneous absorption describes the transport of a test article from the apical (outer) surface of the skin into the systemic circulation. Percutaneous absorption is considered to occur by passive diffusion; however, biotransformation of the test substance within the skin (metabolism) prior to systemic absorption can occur.

Industrial and toxicology laboratories are actively seeking alternative methods for the determination of percutaneous absorption that not only reduce/replace the use of animals but also more reliably predict actual response in human skin. Cosmetic, household product, pharmaceutical and petrochemical companies have initiated *in vitro* toxicity testing to evaluate their raw materials and final product formulations.

CeeTox offers an *in vitro* screen for testing the percutaneous absorption of chemicals and cosmetics/personal care products. A growing body of data indicates that the model CeeTox uses effectively provides a non-animal means to assess permeation and penetration of test articles of varying physicochemical properties.

The *in vitro* test measures the permeability of a test substance through a multi-layered, reconstructed human epidermis model. The 3-D model is a normal



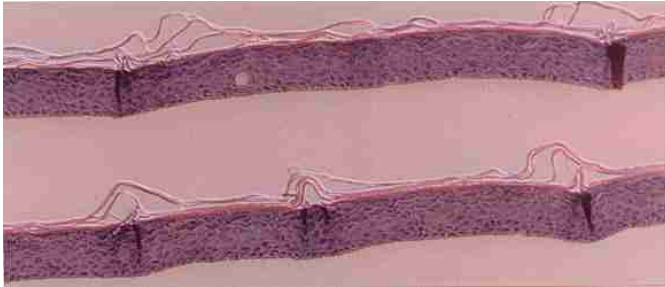
Source: <http://www.lionden.com/SkinLayers.jpg>
Used with permission.

(non-transformed), human cell-derived, metabolically active, 3-dimensional organotypic *in vitro* skin model. It closely mimics human epidermis, both structurally and biochemically. The percutaneous absorption protocol allows researchers to quantitatively measure the permeability characteristics of their experimental materials. The assay can determine relative flux rates, transdermal permeability, cytotoxicity, and metabolic stability of different compounds or different formulations of the same compound after topical application.

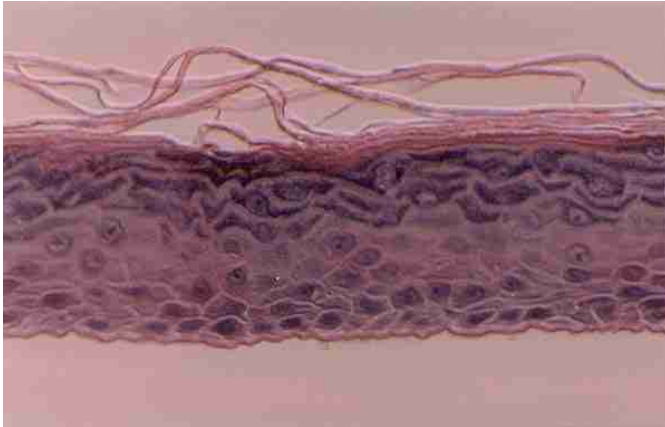
The model exhibits *in vivo*-like morphological and growth characteristics which are uniform and highly reproducible. It consists of organized basal, spinous, granular, and cornified layers analogous to those found *in vivo*. It is mitotically and metabolically active. Markers of mature epidermis-specific differentiation such as, the K1/K10 cytokeratin pair, involucrin, and type I epidermal transglutaminase have been localized in the model.

Types of materials that have been tested using the 3-D epidermal system include cosmetics and their constituents, household products, and pharmaceuticals.

Skin Model



Low Magnification 100x



High Magnification 400x

Source: www.mattek.com/pages/products/epiderm

Donor solutions, aliquots of all time points taken, tissue rinsates, and tissue extracts are analyzed for parent test compound and metabolites using appropriate chromatographic (HPLC, LC/MS) or radiometric (liquid scintillation counting) methodology.

Reporting may take three basic forms. Our standard report includes data charts and graphs detailing results of the assays run. A detailed report is optionally available as well. This report includes:

- Executive Summary
- Objective
- Experimental Design
- Results
- Tables and Figures
- Materials and Methods
- Appendix (if necessary)

Finally, a report complying with GLP requirements is available for those studies performed according to GLP regulations.

Percutaneous Absorption Screen	
Purpose of Assay	Dermal penetration testing, also known as percutaneous penetration, measures the absorption or penetration of a substance "through the skin barrier and into the skin" (OECD, 2004).
Cell Model	Skin Model
Assays Performed	Solubility Analysis Active Pharmaceutical Ingredient (API) Analysis MTT
Controls	Vehicle, positive, negative and no compound controls
Number of Concentrations	1
Number of Replicates	3
Number of Time Points	16 for API (0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 21, 21.5, 22, 23, 24, 25 hours), 1 for MTT (24 hours)
Standard Turn Around Time	3 weeks from sample and tissue receipt

References:

Dermal penetration (2008, May 12) from <http://www.alttox.org/ttrc/toxicity-tests/dermal-penetration/>

ECVAM. (2002). Biokinetics. *Altern. Lab. Anim.* 30, Suppl. 1, 56-57.

MatTek Corporation, Percutaneous absorption from http://www.mattek.com/pages/products/epiderm/percutaneous_absorption

OECD. (2004). Guidance Document for the Conduct of Skin Absorption Studies. OECD Series on Testing and Assessment. No. 28. OECD. Paris, France.

