Dermal absorption and metabolism

The dermal route of entry can play an important role in the total exposure to chemicals, such as (agro)chemicals and personal care products. In vitro studies on percutaneous absorption are increasingly performed to predict the in vivo situation, and draft OECD guidelines for both in vitro and in vivo dermal absorption testing are presently under consideration. TNO follows these international activities closely and participates in the discussions on validation and implementation of newly developed techniques.

TNO offers a full range of services for the assessment of dermal absorption and metabolism. All studies can be carried out in full compliance with the OECD Principles of Good Laboratory Practice (GLP) and the EC and ICH guidelines of Good Clinical Practice (GCP).

In vitro studies
Dermal absorption of chemicals can be tested in whole skin and/or in epidermal sheets of various species, including human, rat, rabbit, pig and mouse. Skin integrity is assessed using tritiated water prior to the experiment and an appropriate reference substance is tested in parallel. Absorption rate, permeability coefficient and lag time are calculated. In addition, the system allows the determination of the amount of the test substance remaining at the skin surface and the amount penetrating the skin (but not reaching the receptor fluid). Since active ingredients are almost never applied as pure chemicals, the influence of the product formulation on percutaneous absorption is very relevant and can be tested in vitro in a relative simple and cost-effective manner. Assessment of skin metabolism (both phase I and II) and various endpoints of skin toxicity can be included in in vitro dermal absorption studies. For each individual study, the selection of the membrane type, the receptor fluid and the diffusion cell type (static or flow-through) will be tailor-made. The following diffusion cell types are available: static 6-well system, static Franz-cells and flow-through cells (Permegear and Bronaugh systems).

Animal studies
In vivo percutaneous absorption studies are performed according to the draft OECD guideline. In addition, full ADME (Absorption, Distribution, Metabolism and Excretion) studies can be carried out.
Species available for such studies are rodents, rabbits, small livestock, dog and primates.

**Human volunteer studies**

Specific expertise is available for determining the flux of dermally absorbed substances in human volunteers. These studies can be performed under controlled work related conditions of temperature and relative humidity. Experimental protocols are available for the assessment of individual kinetics and for calculating internal exposure to the parent compound and metabolites after dermal exposure.

**References**


