

CEFIC Long-range Research Initiative Request for Proposals (RfP)

LRI Request for proposal (project code LRI-B13)

Title:

Development of an in silico model of dermal absorption

Background

The dermal absorption of a chemical is influenced by a variety of factors, such as its physicochemical properties (including molecular size, lipophilicity, and aqueous solubility), its interaction with the formulation in which it is applied to the skin, and the where and for how long and to what extent the exposure on the skin is likely to be. Traditionally, estimation of exposure is achieved by focusing on a single-chemical based assessment in simple formulation matrices, such as water. Recent international workshops like the IHCP ^[1]-ECETOC Workshop on “Exposure and Risk Assessment of Chemical Mixtures in Consumer Products^[2]” and the US EPA “Exposure-Based Chemical Prioritization” workshop^[3] have highlighted the paucity of suitable data that enable more accurate estimations to be made of the true nature of dermal exposures. Reflecting upon current data availability current dermal penetration models:

- Do not address the effect of formulation on resultant skin or systemic dose
- Do not reliably predict the systemic bioavailability as well as internal skin dose for local toxicity (e.g. sensitisation) for diverse chemical classes
- Lack data to evaluate performance with respect to the above issues across a range of chemistries

A mechanistic in silico model that addresses these deficiencies would greatly enhance our ability to predict dermal absorption of chemicals with a wide range of physicochemical properties and that would also account for formulation effects. It is anticipated that the incorporation of improved understanding of these various processes within an in silico model would provide industry and regulatory bodies with an effective and reliable tool to be used in the quantitative risk assessment of dermally applied materials.

[1] Institute for Health and Consumer Protection

[2] JRC, Ispra, Italy: 29-30th January 2009

[3] April 6-7, 2010 in Research Triangle Park, North Carolina

Objectives

The objective of this project is to develop a mechanistic model for dermal absorption, which would be capable of explaining complex real world data and also be easily accessible to industrial and government regulatory risk assessors. In particular, the project would be expected to:

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- Project dermal absorption of chemicals with a wide-range of physicochemical properties, including neutral lipophilic and hydrophilic chemicals, ionisable organics, and permanently charged chemicals.
- Assess the sensitivity of varying formulation matrices with respect to varying properties of the chemical of interest.
- Provide projections of the mass of chemical that penetrates the skin from a given exposure, and a measure of the associated uncertainty of the projection.
- Mechanistic insight regarding processes that influence dermal absorption, and which can be validated against independent observations.

Scope

It is anticipated that this project will be structured and staged in a manner that ensures that the work products are regularly delivered and reviewed. It is also expected that any proposals are verified against a representative range of case examples (to be selected by the researchers in consultation with LRI), covering commonly encountered consumer products and formulation matrices. It is expected that the findings will be developed into a series of peer reviewed publications, following a process that involves stakeholder discussion and presentation at suitable scientific conferences. This project would be expected to complement and leverage on-going LRI and other activities in the area. The successful research group would liaise with and take account of the findings and outcomes of such other work. Exploring possibility to use this as a tool in a regulatory context (e.g. REACH) is encouraged.

LRI Funding

€ 500 K

Timing

3 years

Partnering/Co-funding

Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package

DEADLINE FOR SUBMISSIONS: August 31, 2012

Please see www.cefic-lri.org for the project proposal form and further guidance for grant applications.