

# Evaluation of Dermal Absorption Data based on BfR Database

**Korinna Wend, Ph.D.**

Sabine Martin, Ph.D., Lars Niemann, Ph.D.,

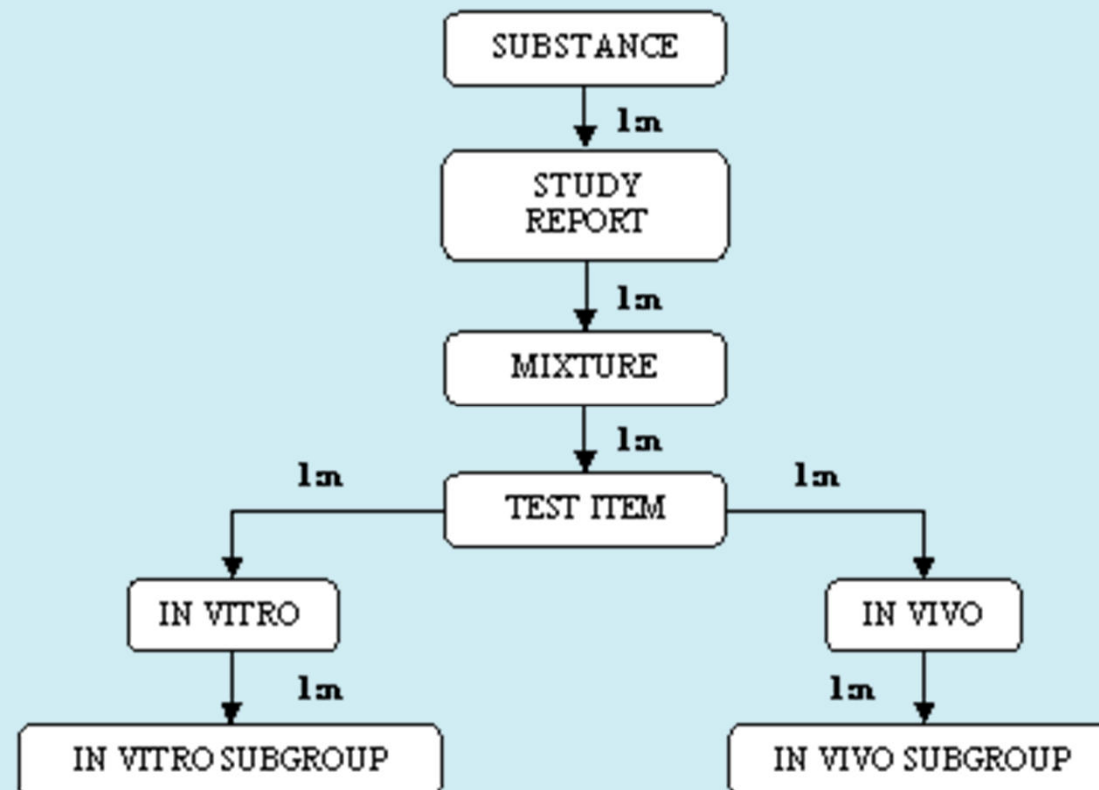
Matthias Herzler, Ph.D., Carsten Kneuer, Ph.D.

Michaela Golle, B.Sc. and Roland Solecki, Ph.D

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# BfR Data base structure

- Development of a relational data base



## BfR Data base parameter

- Physico-chemical properties
- Formulation type (e.g. SC, EC, CS, etc.)
- Study details (e.g. species, receptor fluid, skin area, tape strips etc.)
- Study design (e.g. concentration, dilution, exposure time etc.)
- Special remarks (e.g. conformity: GLP, OECD 427, OECD 428)

## BfR Database content

- No of experiments : 1553
- No of formulations : 231
- No of dermal absorption studies : 994
  - DA study type
    - *Rat in vivo* : 379
    - *Rat in vitro* : 212
    - *Human in vitro* : 387

## Criteria for BfR data base studies

### *In vitro*

- in line with OECD 428
- exposure 6-10 hrs with subsequent swabbing and termination after 24 hrs
- or
- 24-exposure with immediate termination
- amount in skin sample (dermatomed skin or isolated epidermis) separately measured and reported
- total radioactive recovery between 90 and 110 %
- may be part of a triple pack or isolated study

### *In vivo*

- in line with OECD 427
- exposure 6-10 hrs with post observation period of up to 168 hrs
- amount in skin sample separately measured and reported
- total radioactive recovery between 90 and 110 %
- submitted as part of a triple pack

## Can the EFSA defaults of 25 / 75% be confirmed?

- **Dermal absorption rates in studies on dermatomed human skin and Triple pack outcome**

	In vitro absorption above cut-off / total no. of experiments	Triple Pack available in these cases	In vitro data (human skin)	Corresponding Triple Pack outcome	Remaining concerns
Concentrates (cut-off 25%)	5 / 97	4 / 5	33.3 %	10%	No
			48.5%	3.0%	No
			79.0%	3.0%	No
			33.8%	2.0%	No
			27.6%	<b>Not available</b>	<b>Yes</b>
Dilutions (cut-off 75%)	1 / 150	0 / 1	76.3%	<b>Not available</b>	<b>Yes</b>

- **EFSA defaults 25 / 75 % confirmed by BfR data base**

## Can the EFSA defaults of 10 / 100% be supported?

- **Dermal absorption estimations on in vitro human skin studies**
  - 500 experimental data
  - 84 active substances

Name	Mol WT (g/mol)	Log P Exp	Concentration (g/l or g/kg)	Total absorption rate (Sum of means of Receptor fluid, Skin sample and Tape strips in % of radioactivity)	Deviation from 10 % default rule
Deltamethrin	505.20	4.6	25.00	6.74	No
Deltamethrin	505.20	4.6	0.118	<b>19.22</b>	<b>Yes</b>
Fluvalinate, tau	502.91	7.02	0.288	<b>18.14</b>	<b>Yes</b>

➤ **EFSA defaults 10 / 100 % not supported by BfR data base**

## Is there a higher permeability of rat skin compared to human?

- **Dermal absorption data from in vitro human studies, dermatomed skin**
  - 159 experimental data
  - 57 active substances
  - Permeability
    - Rat > Human: 91 %
    - Rat = Human: 3 %
    - Rat < Human: 6 %
- **Higher permeability of rat skin compared to human**



## Does the triple pack give lower values than hum. skin *in vitro*?

- **Dermal absorption data from in vitro studies, isolated epidermis compared to triple pack**
  - 53 experimental data
  - 19 active substances
  - DA value
    - triple pack value < in vitro human skin : 81 %
    - triple pack value > in vitro human skin : 19 %
- **Triple pack values mostly lower than in vitro human skin values**

# Outlook

- **Systematic compilation of all study reports** on dermal absorption submitted for the authorisation of pesticides
- **Derivation of proposals for further harmonisation** of the risk assessment
- Use of that data base in order to **answer questions arising within the framework of the authorisation procedure**
- **Comparison of formulations:** influence on dermal absorption
- **Development of new QSARs** regarding dermal absorption and validation/improvement of existing QSAR models

# **THANK YOU FOR YOUR ATTENTION**

Korinna Wend, Ph.D.

Federal Institute for Risk Assessment

Max-Dohrn-Str. 8-10 • 10589 Berlin

Phone: + 49 30 - 184 12 - 0 • Fax + 49 30 - 184 12 - 47 41

bfr@bfr.bund.de • www.bfr.bund.de