DERMAL EXPOSURE MODELLING

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EXPOSURE ASSEMENT/MODELLING

- 1920-1950 exposure instruments were developed to measure dust and vapour concentrations in the air
- 1960s personal air sampling
- Not possible to measure all situations
  - Modelling as an alternative

- 90s Estimation and Assessment of Substance Exposure (EASE)
- End 90s COSHH essentials

- From 2000 – nowadays a variety of models has been developed.

- Although dermal work-related diseases has been linked to occupational (lead) exposure since 1920s, it looks like dermal exposure assessment has never been in the same league as inhalation exposure assessment

EFFECTS OF DERMAL EXPOSURE

- Local effects (mechanical, irritating, allergic)
- Systemic effects (concentration gradient / diffusion, absorption)
- Infection diseases (due to degradation of the barrier properties of the skin)
- For most of the low-volatile substances, dermal exposure is the primary route of exposure
- Because of the focus on inhalation exposure, many highly volatile substances has been replaced by low-volatile substances

DERMAL EXPOSURE MODELLING / ASSESSMENT

- Dermal exposure assessment is taking into account in the agriculture sector
  - As dermal exposure is the most important route for the neurotoxic low-volatile pesticides

- Ther’re many models for Plant Protection Product (PPP).
  - Mostly very specific for a set of activities
  - Mostly emperical models.
  - Many exposure measurement data available
  - Standard procedures for measuring dermal exposure developed
  - Dermal exposure assessment needed for registration

  - The BROWSE model is a recently developed (first) deterministic model

DERMAL EXPOSURE / GENERIC MODELS

- ECETOC TRA
  - Tier 1 exposure model with a dermal module
  - Based on the EASE concept
  - Cumulative 8-hrs skin loading (ug/cm2/day / mg/kg/day)

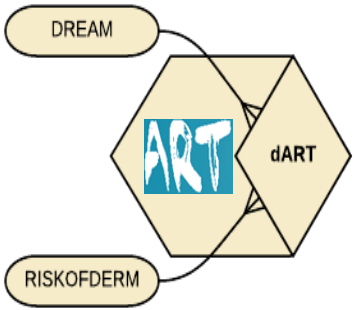
- RISKOFDERM (ROD)
  - Deterministic model based on conceptual model → exposure determinants
  - Models developed per Dermal Exposure Operation (DEO) unit (similar exposure routes)
  - Estimate is data-driven
  - Not generally accepted by industry (because of underlying data)
  - RISKOFDERM-Toolkit basis for dermal control-banding module of STM (comparable with COSH-Essentials)

DERMAL EXPOSURE / GENERIC MODELS

- BEAT (Bayesian Exposure Assessment Toolkit)
  - Focus on biocides, accepted within Europe
  - Bayesian integration of expert knowledge and exposure measurement data
  - Complex Bayesian framework and seen as ‘Black box’

- DREAM (DeRmal Exposure Assessment Method)
  - Based on conceptual model → exposure determinants, algorithms
  - Observational model with use of questionnaires → semi-quantitative estimates

- dermal Advanced REACH Tool (dART) (expected online end of summer 2016)
  - Based on conceptual model → exposure determinants, algorithms
  - Calibration with exposure measurement data
  - Limited applicability domain



PERFORMANCE OF DERMAL EXPOSURE MODELS

- Honestly, we don't really know……
- Exposure models are in general validated to a limited extend and results are difficult to compare
- Evaluation of Tier 1 Exposure Assessment Models under REACH (ETEAM) Project
  - Sponsored by BAUA
  - Evaluation of inhalation and dermal models
- Results: 4.2.5.4 Dermal exposure
- "The quantity of dermal exposure data available was judged to be insufficient to allow for a reasonably comprehensive evaluation of the dermal exposure estimates from the tools. In addition, dermal measurements were obtained using different methods, leading to different results for which no consistent conversion factors exist (Gorman Ng et al., 2014). Hence, no results for dermal exposure are presented in this report".

- At the moment we are validating the dermal module of ECETOC TRA (sponsored by CEFIC)

COMPLEXITY OF DERMAL EXPOSURE MODELING

- Why is it so dificult?

- Complex exposure proces (many exposure data is needed (in the field and experimental))
- Different sampling methods
- What is the most relevant metric to express dermal exposure? (see next presentations)
- Effect of protective gloves and/or clothing (type of material, status/maintenance of material)
- Frequency of contacts (event-based)
- Not uniform contamination of surfaces (because of spillages)
- Transfer from surface to skin (effect of; viscosity, type of surface, type of contact,…)
- Cleaning / decontamination of skin during measurements
- Resuspension or evaporation from the skin
- Maximum loading of the skin
- ……

DERMAL EXPOSURE MODELLING

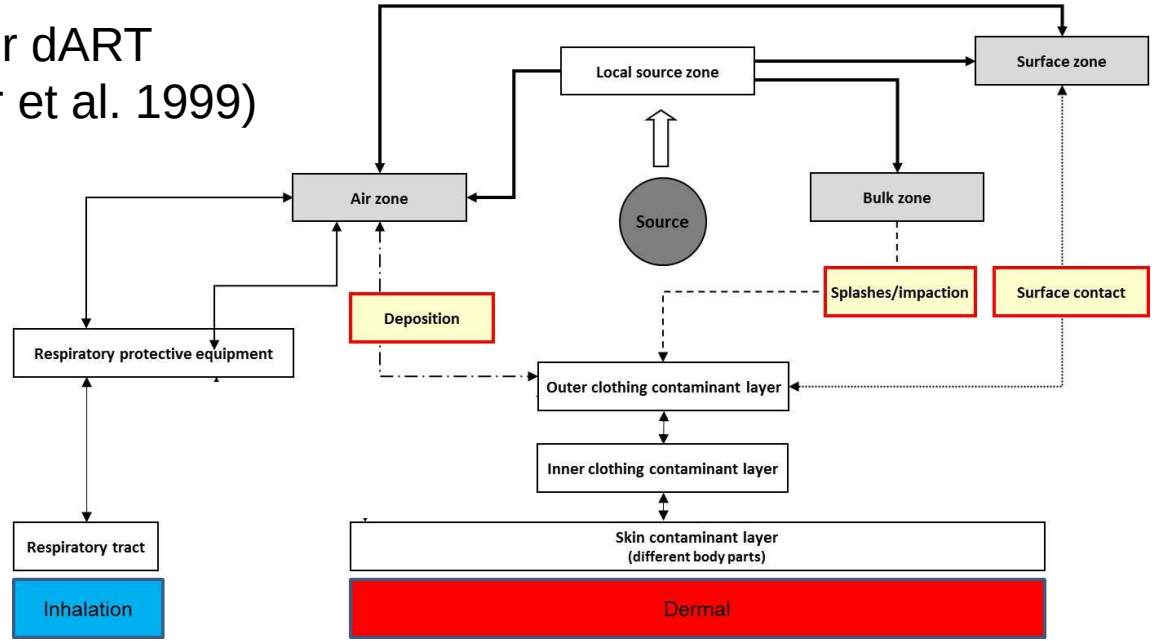
- Will dermal exposure modelling be possible?
- YES!
- How?
  - Start with a conceptual framework of dermal exposure
  - Link all the initiatives allready done
    - Measuring, modelling, experimental work
    - Experimental work on various transfer processes
  - SYSDEA to come up with standard sampling methods
  - Identify knowledge gaps
  - Identify data gaps

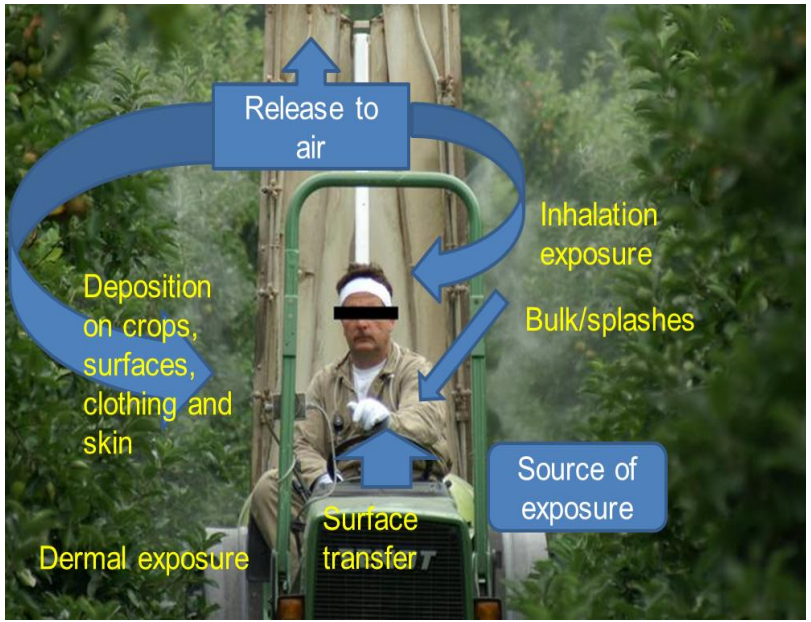
The Relationship Between Inadvertent Ingestion and Dermal Exposure Pathways: A New Integrated Conceptual Model and a Database of Dermal and Oral Transfer Efficiencies

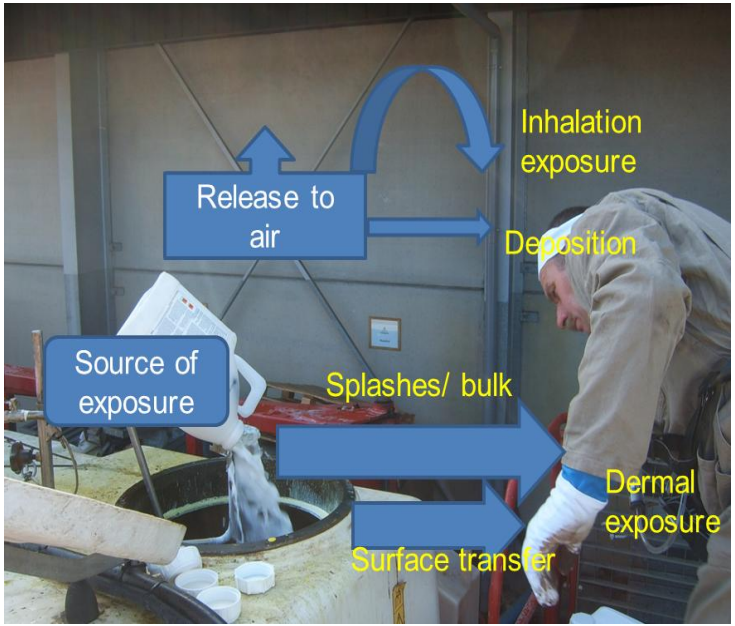
MELANIE GORMAN NG[1,2]*, SEAN SEMPLE[1,2], JOHN W. CHERRIE[1,2], YVETTE CHRISTOPHER[3], CHRISTINE NORTHAGE[4], ERIK TIELEMANS[5], VIOLAINE VEROUGHSTRAETE[6] AND MARTIE VAN TONGEREN[1,2]

DERMAL EXPOSURE MODELING / COMPLEX EXPOSURE

Conceptual model for dART
(based on Schneider et al. 1999)




Release to air
Inhalation exposure
Deposition on crops, surfaces, clothing and skin
Bulk/splashes
Source of exposure
Surface transfer
Dermal exposure


Inhalation exposure
Release to air
Deposition
Source of exposure
Splashes/ bulk
Dermal exposure
Surface transfer

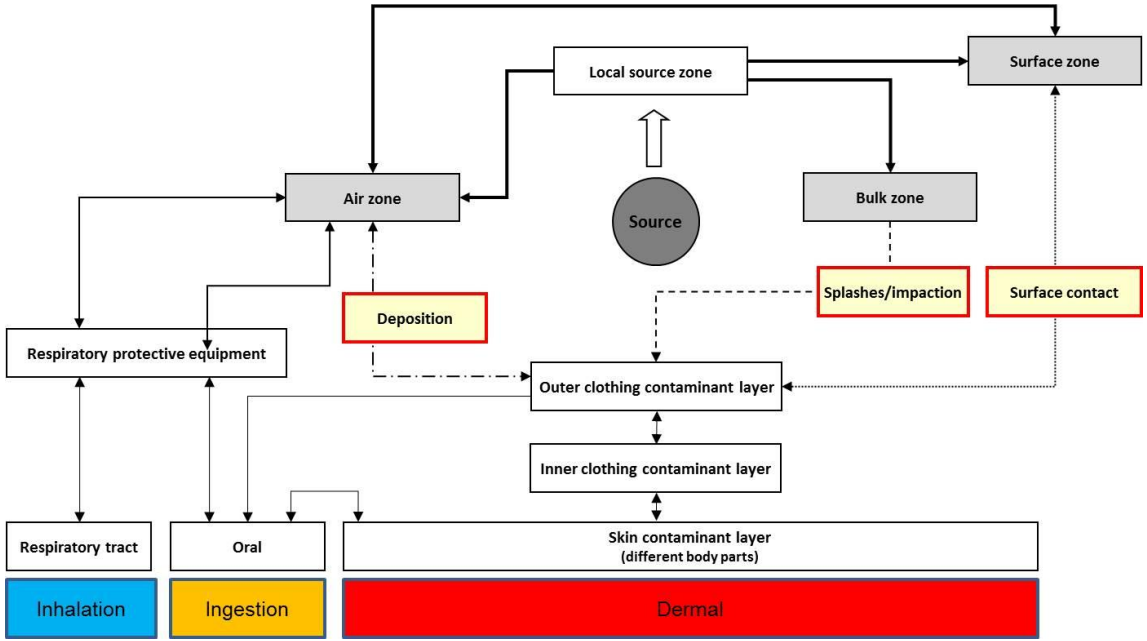
GENERAL FRAMEWORK

- Based on conceptual and mechanistic model
- Inhalation and dermal exposure
- Exposure determinants and relations based on literature / experiments
- Effect of gloves
- Transfer coefficients (could be) included
- …..

Limitations

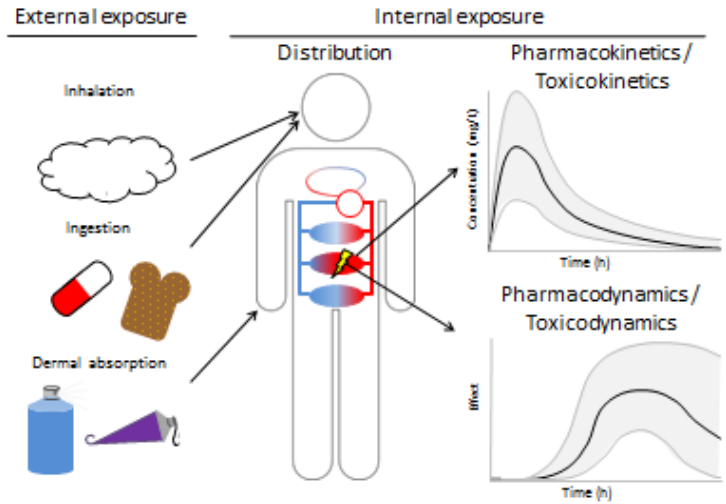
- Exposure measurement data is needed to calibrate/underpin the model
  - Uniform collection of data
    - Sampling methods (SYSDEA)
    - Contextual information (mechanistic model)
  - DNELs for dermal exposure

NEXT STEPS: AGGREGATED POTENTIAL EXPOSURE



NEXT STEPS: INTENRAL EXPOSURE

External – Internal exposure modeling



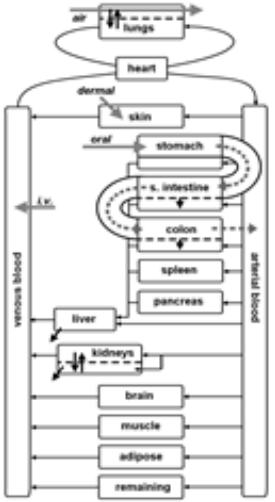
External – Internal exposure modeling

Aim:
To predict blood/target site concentrations of chemicals based on their physicochemical properties and external exposure estimates.

Method:
Interactive PBPK model with different routes of exposure

Species
Humans, ages 0 – 100 of all possible sizes.
Rats

Case studies
- Benzene
- Chlorpyrifos



CONCLUSIONS

- Although highly relevant, in practise dermal exposure assessment/modelling is still the little brother of inhalation exposure

- With all the work already done, it's possible to make sophisticated models for:
  - potential dermal exposure (dART)
  - aggregated exposure (BROWSE)
  - internal exposure (benzene, chlorpyrofos)

- However more experimental and field data is needed!!
  - SYSDEA: standardised exposure measurement methods
  - DNELs for dermal exposure: push by legislation:

THANK YOU FOR YOUR ATTENTION

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