DoE 3: Exposure Modelling

ISES Europe Training Series

Natalie von Goetz, Wouter Fransman

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Overview of All Training Videos

DoE 1) Basic Concepts and Principles in Exposure Science

DoE 2) Fundamentals of Environmental Chemistry and (Eco)Toxicology

DoE 3) Exposure Modelling

DoE 4) Exposure Monitoring

DoE 5) Exposure Assessment and Risk Characterisation

DoE 6) Risk Management and Sustainability Assessment

DoE 7) Relevant Legislative Frameworks

DoE 8) Risk Communication and Stakeholder Engagement

DoE 9) Statistics and Epidemiology

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Domain of Expertise (DoE) 3:
Exposure Modelling

Module 1	Introduction, context&regulation, concepts for exposure modelling
Module 2	Human exposure modelling: General concepts and worker
Module 3	Human exposure modelling for the general population
Module 4	Environmental exposure modelling
Module 5	Validation&evaluation, advantages&limitations, conclusions

DoE 3: Exposure Modelling

Module 2

Human exposure modelling: General concepts and worker

Dr. Wouter Fransman

Presenter: Dr. Wouter Fransman

Meet Today's Presenter: **Dr. Wouter Fransman**

Current Role:

Principal investigator | Netherlands Organisation for Applied Scientific Research (TNO)

- **Previous Roles:**

  Institute for Risk Assessment Sciences (IRAS; Utrecht University)

  Institute of Occupational Medicine (IOM)

- **Education:**
  - PhD Occupational Health (Utrecht University)
  - MSc Environmental Sciences (Wageningen University)
  - MSc Safety Assessment (Delft University of Technology)
- **Special Expertise:** Statistical modelling, Exposure assessment, Risk assessment, Epidemiology

Context and Disclaimers

About This Lecture

This lecture provides an **introductory framework**, with some topics simplified for ease of understanding.

Disclaimer

- The content presented herein does not necessarily reflect the opinions, views, or positions of the presenters' employer or any affiliated organizations.
- References to specific organizations, tools, or entities are for illustrative purposes only and do not imply endorsement or critique.
- While every effort has been made to ensure the accuracy of the information presented, errors or omissions may occur.

Learning Objectives

1. What are exposure models? How do they relate to exposure measurements?
2. Purposes of exposure models in different research areas (environment, occupational, consumer)
3. Provide knowledge of scientific and technological principles of exposure modelling
4. How do they fit in with wider exposure assessment approaches?
5. Types of exposure models available, introducing a tiered approach to modelling
6. Exposure models for various routes of exposure (inhalation, dermal, ingestion)
7. General advantages and limitations of exposure models
8. General things to consider when using exposure models
9. Where to find more information?

Content

1. **From Source to Dose**
2. Occupational Exposure Modelling
3. Tiered Exposure Modelling
4. Dermal Exposure Modelling
5. Aggregate Exposure Modelling
6. Summary

From Source to Dose

Source

External Exposure

Entrance barrier

- Mouth
- Mouth/Nose
- (Skin surface)

Intake

Internal Exposure/Internal Dose

Internal fate

Absorption barrier

- G.I. tract
- Lung
- Skin

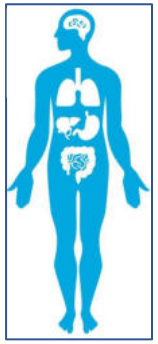
G.I. tract: gastro-intestinal tract

Uptake

Target tissue

Biologically effective dose

Effect



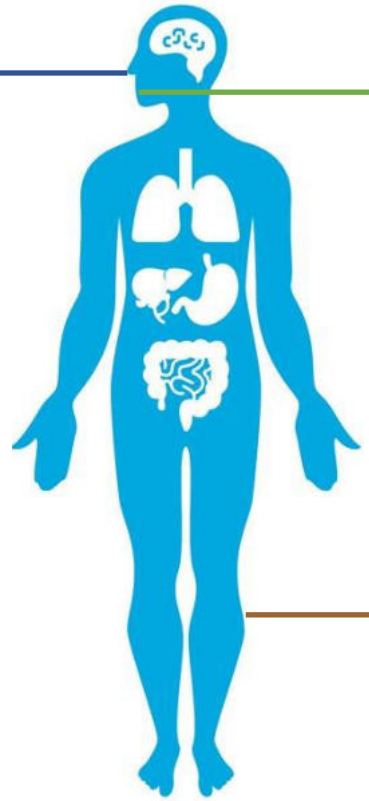
All figures designed by Freepik

Source: adapted from U.S. EPA, 1997

Intake Routes

Inhalation

- Air (Aerosols, vapor, gas)
- Dust



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Ingestion

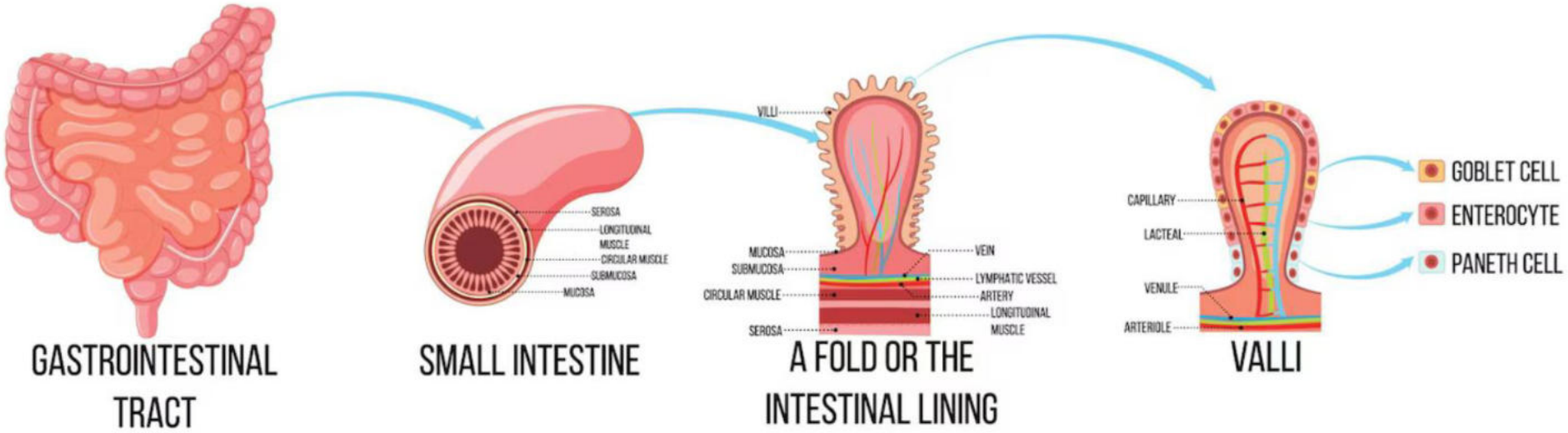
- Food
- Drugs
- Dust
- Cosmetics
- Personal care products

Dermal uptake

- Protection wear like gloves
- Cosmetics
- Personal care products
- Textiles

Oral Uptake (Ingestion)

The gastro-intestinal tract



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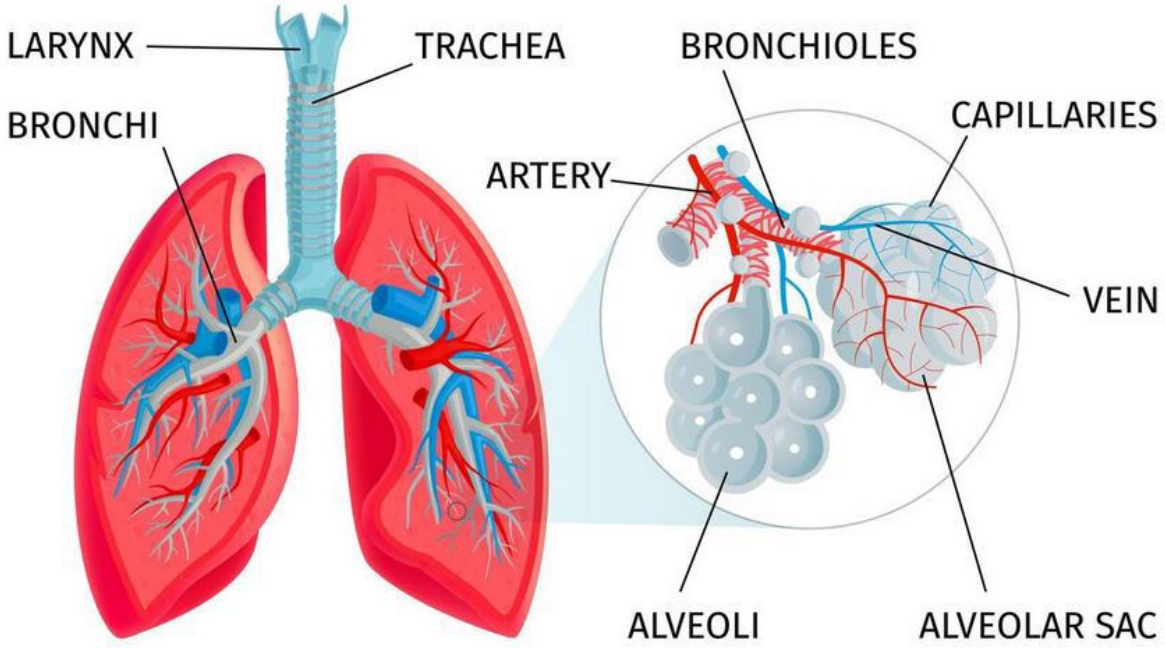
- intestine of adult persons: ≈ 8 m long
- surface (villi): ≈ 400-500 m²
- lined with mucosa (mucous membrane)
- intestinal wall: 1-4 mm

Inhalation – The Respiratory Tract



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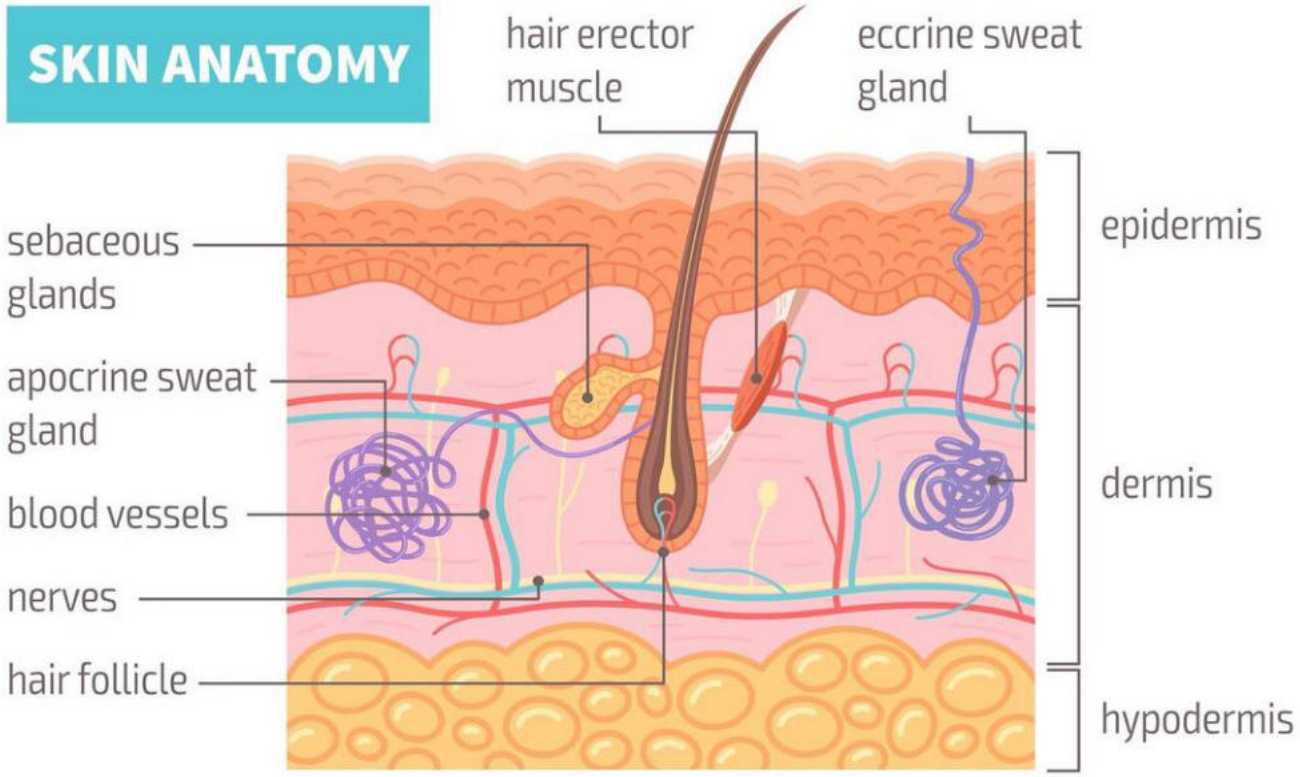
- 300 Mio Alveoli
- total surface: 100 m^2
- air-blood barrier of 0.1-1.5 µm: epithelium of the alveoli, basal membrane and endothelium of the capillaries
- Perfusion: 6 L/min
- Different particle size fractions deposit in different parts of the respiratory tract

Dermal Uptake – The Skin



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- 12-15% of an adult's bodyweight
- total surface: 1-2 m^2
- thickness of 0.5-2 mm (epidermis, dermis and subcutanous layer)
- perfusion: 0.5 L/min

Uptake Rates/Fractions

- Mostly assumed for **ingestion** and **inhalation** of organic chemicals: uptake fraction of 1
- For most organic chemicals **dermal uptake** is <<1

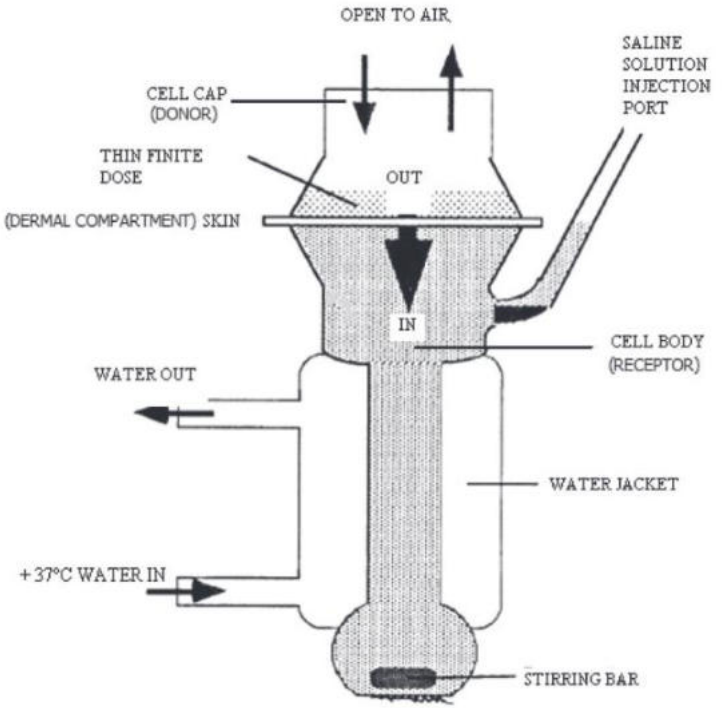
>>> assumptions for dermal uptake are critical for exposure assessment

Experimental assessment of dermal uptake

- in vivo (mice, rats, humans-stripping)
- in vitro: diffusion cell

membranes: 1. human dermis and epidermis
2. pig skin (ear)

Receptor fluid: should be physiologically conductive, e.g. NaCl-solutions with proteins

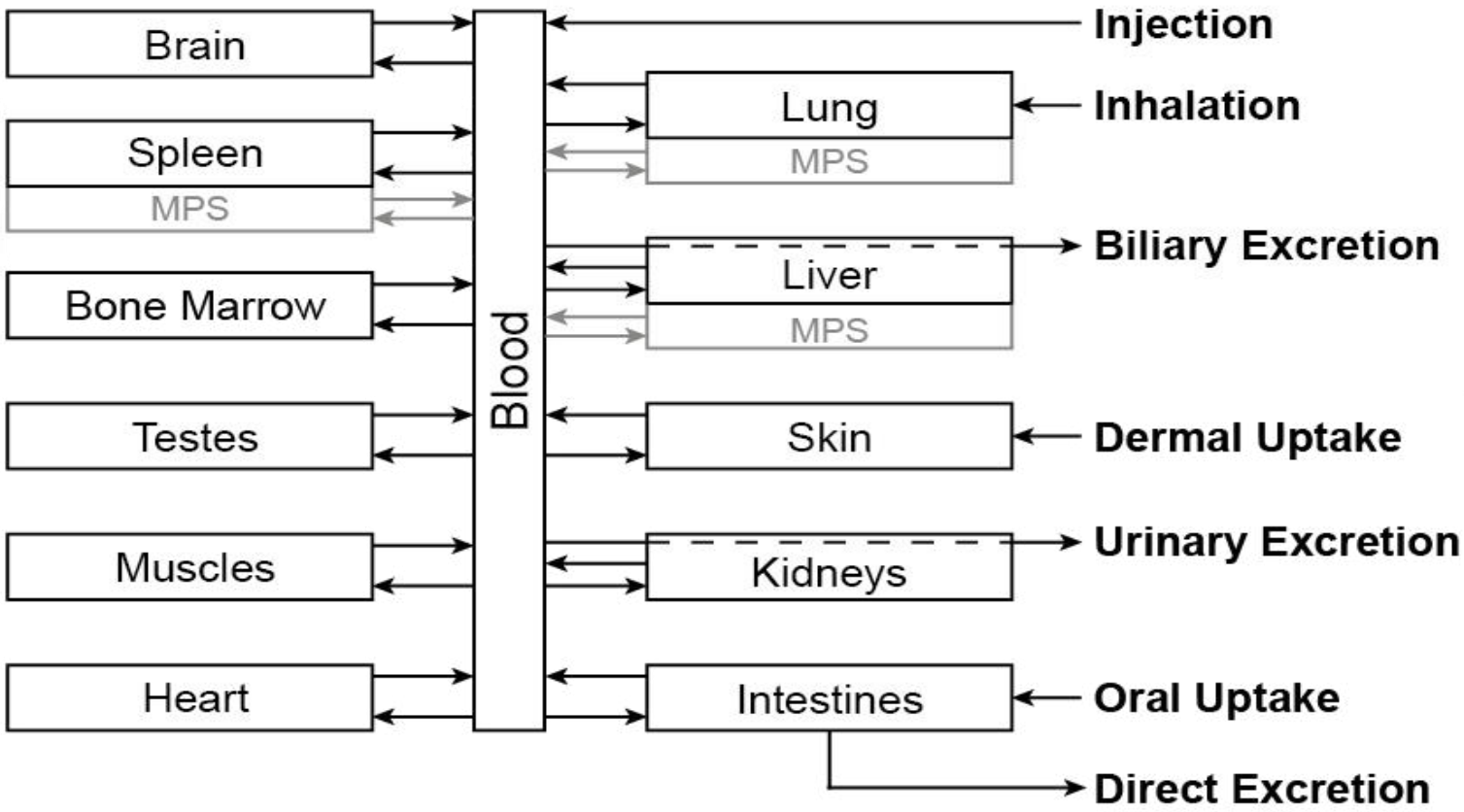


Diffusion cell (Franz cell)

Guillard et al., 2011 Toxicol Mech Methods https://doi.org/10.3109/15376516.2011.610386

Toxicokinetics

Partitioning inside the human body:
Physiologically-based pharmacokinetic (PBPK) model



Bachler et al., 2013 Int J Nanomedicine https://doi.org/10.2147/IJN.S46624

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Worker & Consumer Exposure Modelling

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	Worker (Occupational)	Consumer
Receptor	Human Being	
Effect Assessment	Toxicology, Epidemiology	
Bounding conditions	Largely known conditions	Highly variable
Dominant methods	↓ Measurement Modelling	↓ Modelling
Legislation	Well-established: REACh, OEL	Food legislation, for all products new under REACh

Exposure Models Workers

'Essentially, all models are wrong, but some are useful' (George Box 1987)

Source – receptor approach

Model
Based on source-receptor approach

→

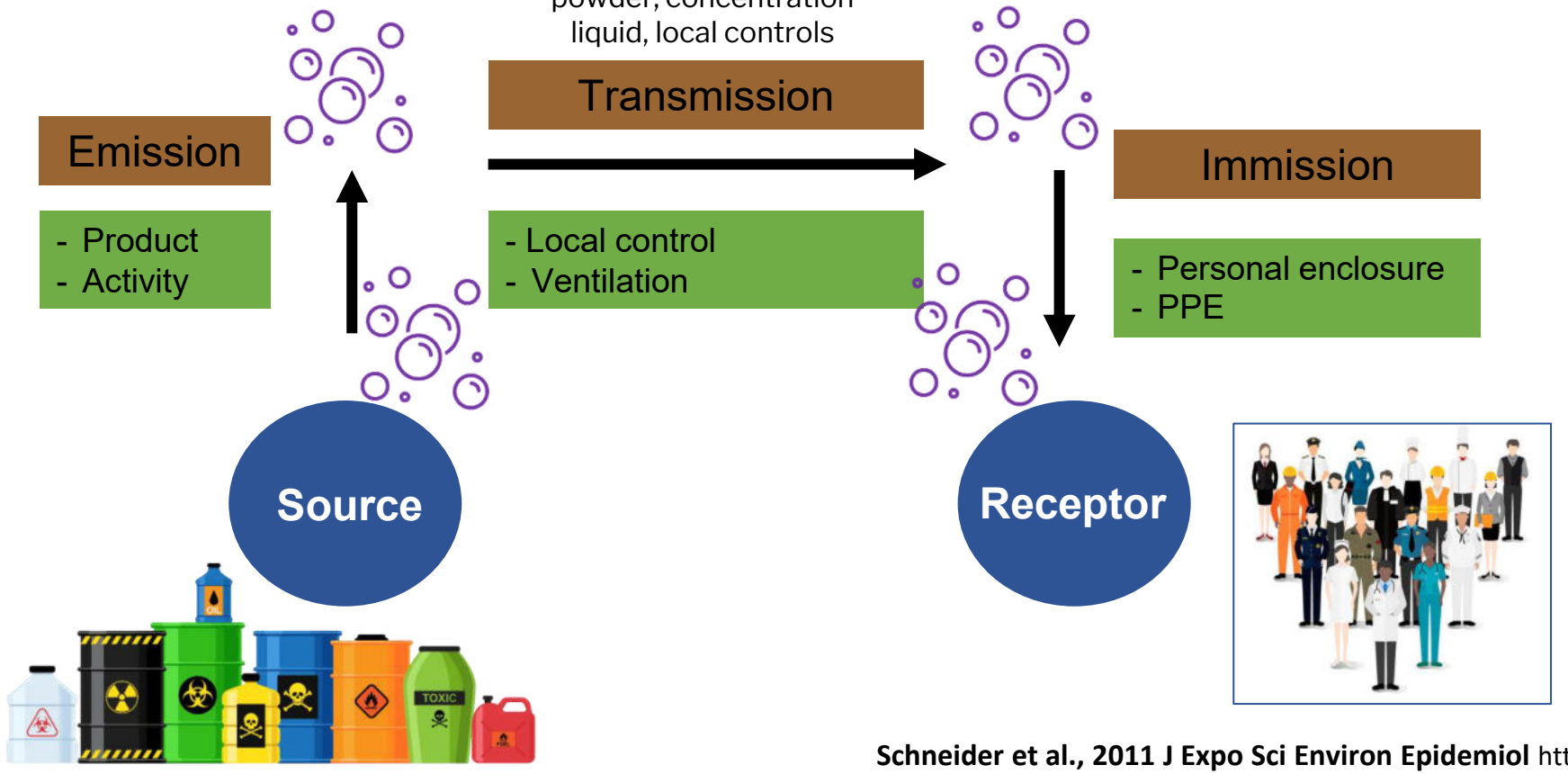
Input parameters
e.g.: activity, dustiness powder, concentration liquid, local controls

→

Assign Multipliers

→

Exposure



Designed by Freepik

Schneider et al., 2011 J Expo Sci Environ Epidemiol https://doi.org/10.1038/jes.2011.4

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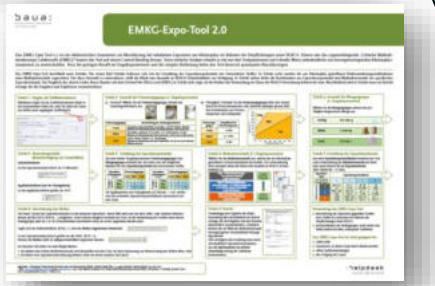
Tiered Exposure Modelling

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport
ConsExpo
consumer | exposure



Exposure band \ Hazard band	A	B	C	D	E
1	3	3	3	2	1
2	3	3	2	2	1
3	3	2	2	1	1

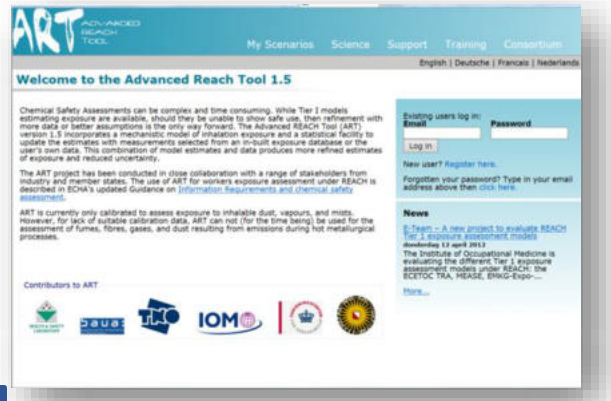
Reduced complexity

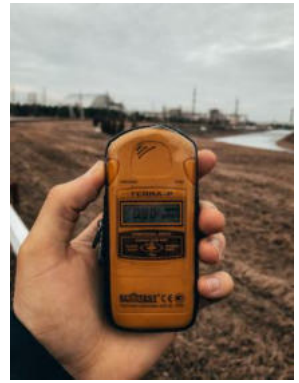
Tier 1

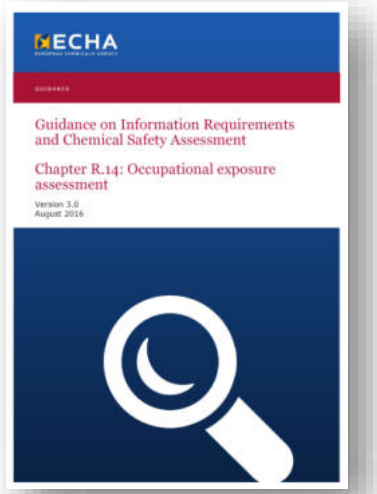
Generic higher tier

Specific approach

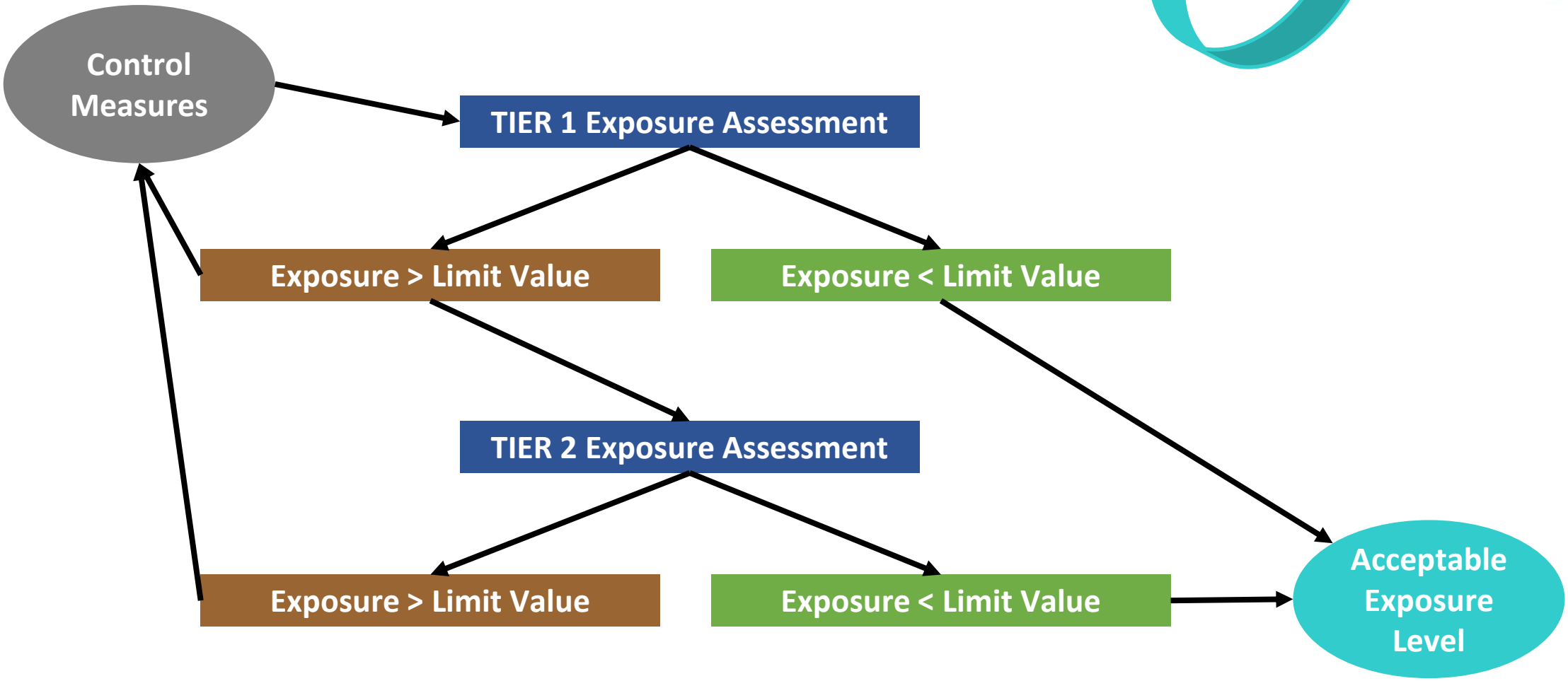
Increased precision







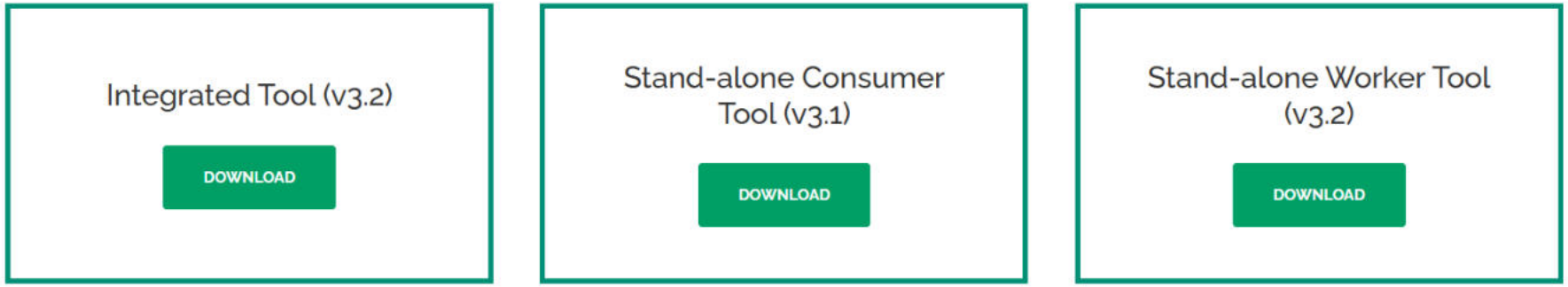
Tiered Approach



ECETOC TRA

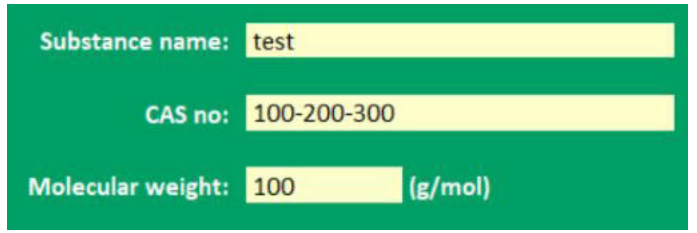
ECETOC's **Targeted Risk Assessment (TRA)** tool (MS Excel)

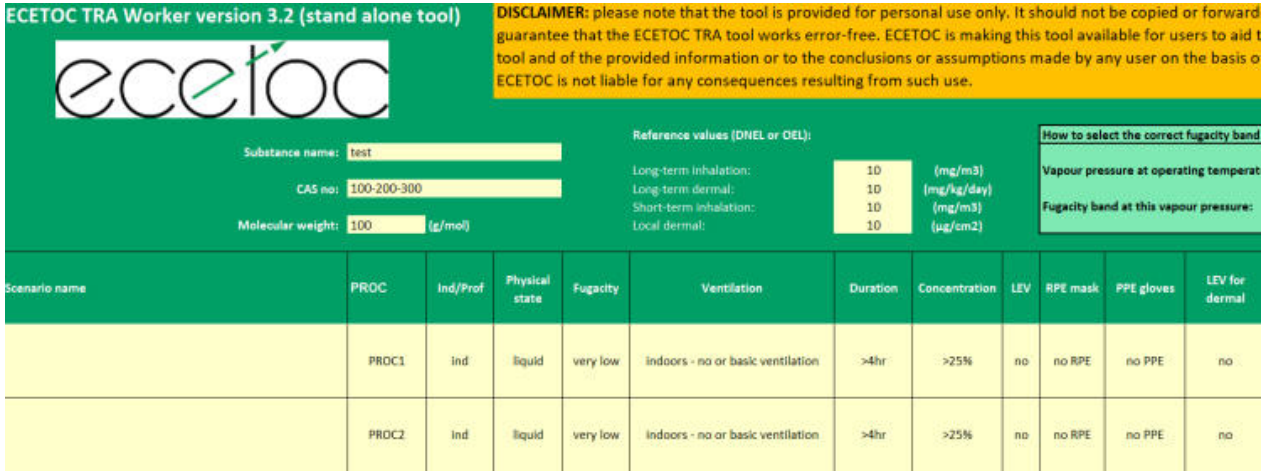
- Calculates the risk of exposure from chemicals for workers, consumers and the environment.
- Has been identified by REACH as a preferred approach for evaluating consumer and worker health risks
- Downloadable from: https://www.ecetoc.org/tools/tra-main/tra-download/ in three different versions:
  - The Integrated tool, which allows users to estimate exposure/risk for workers, consumers and environment
  - The Standalone Consumer tool, which allows users to estimate exposure/risk for consumers
  - The Standalone Worker tool, which allows users to estimate exposure/risk for workers



ECETOC TRA v3.2

- Identification of substance and physico-chemical data entry
- Reference values (DNEL or OEL) entry
- Worker Assessment-data entry
  - Process Category (PROC)
  - Industrial/professional
  - Physical state
  - Fugacity
  - Ventilation
  - Exposure duration modification and short-term prediction
  - Concentration
  - Local exhaust ventilation (LEV)
  - Respiratory protective equipment
  - Personal protective equipment (PPE) for the skin
  - LEV for dermal

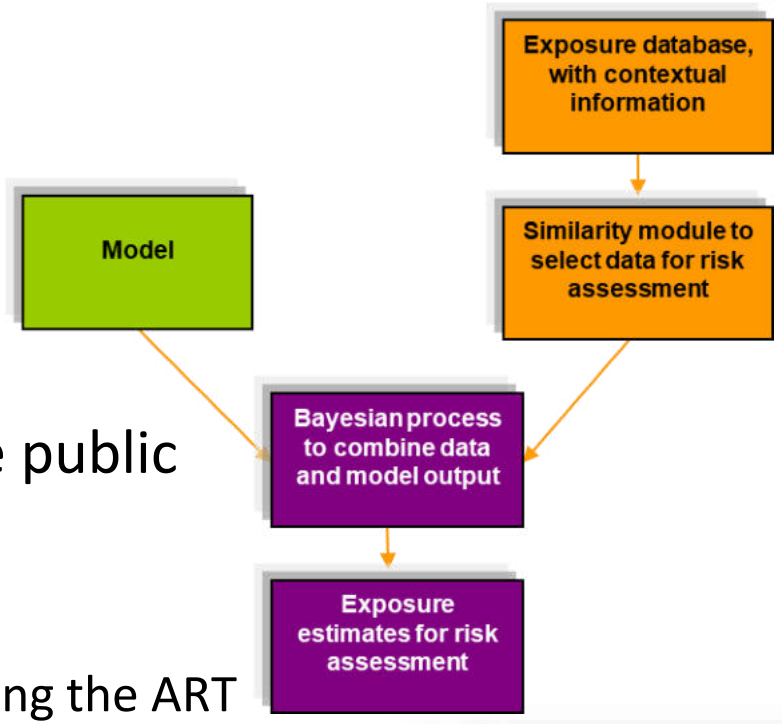


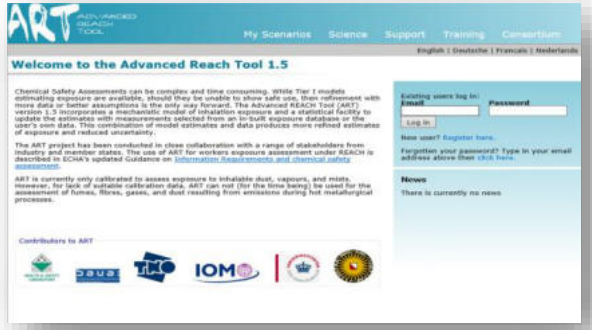


The Advanced Reach Tool (ART)

- The web application is available on www.advancedreachtool.com

- The ART framework exists of:
  - The ART algorithms which are published in the public domain.
  - A web application version 1.5 including:
    - the IT tool to estimate inhalation exposures following the ART algorithms
    - The database including data from the developers and funders





The Advanced Reach Tool (ART)

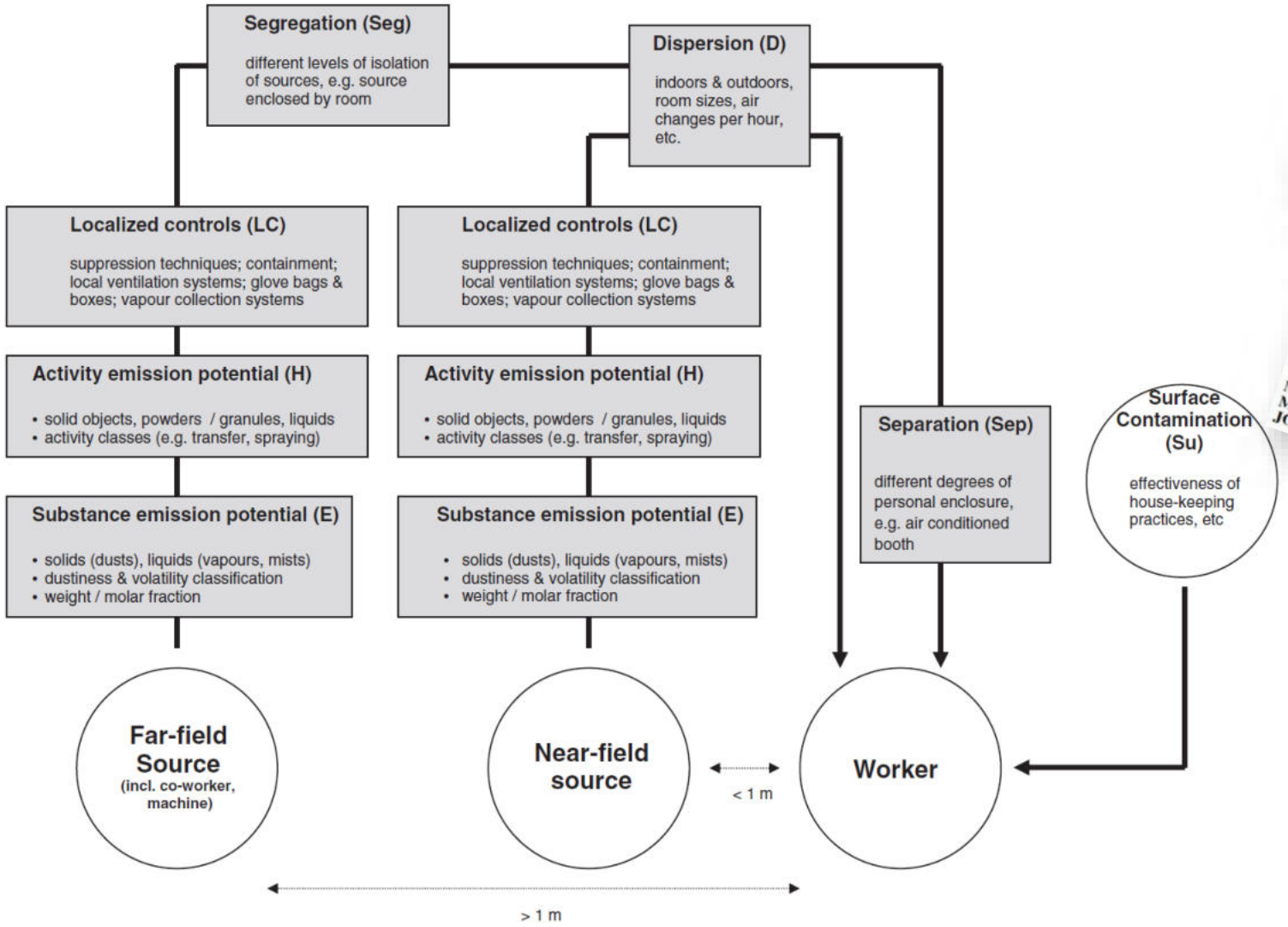
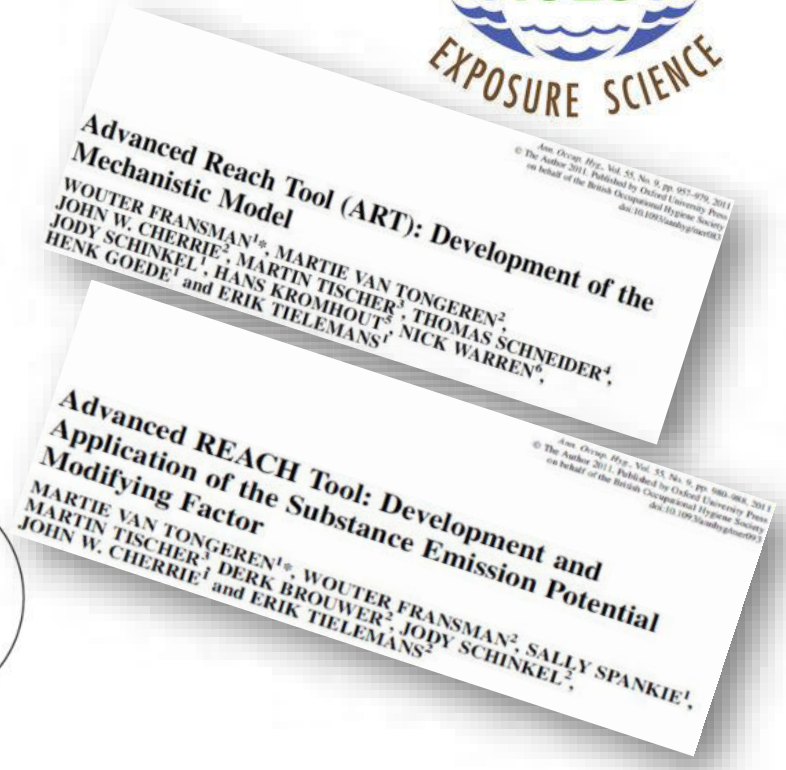
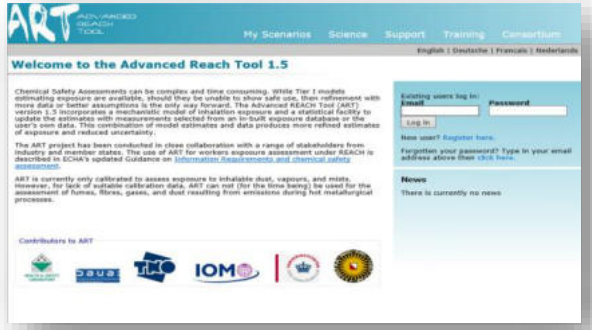


Fig. 1. Flow diagram of the ART mechanistic model.





Assign multipliers & Calculate Model Scores

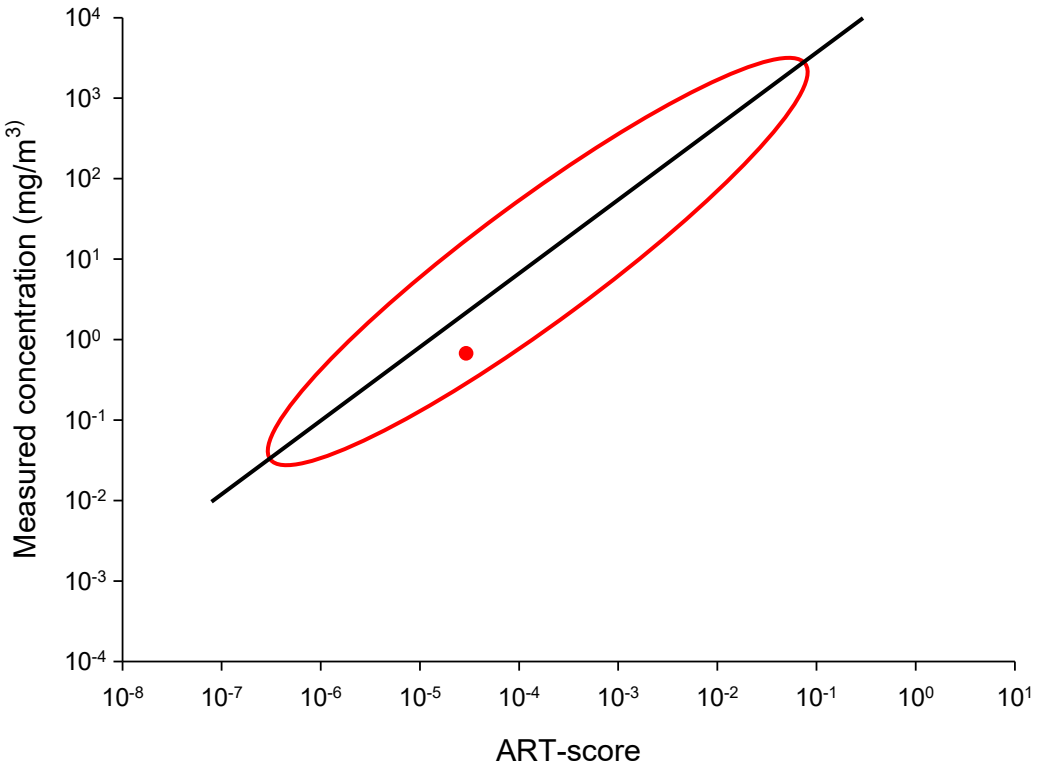
NF and FF source	NF	Description	Score
Substance Emission Potential (E)	E	Extremely fine powder	1
Activity Emission Potential (H)	H	Transfer 0.1-1kg Careful Open process	0.09
Localised Controls (LC)	LC	Fume cupboard	0.01
General Ventilation (D)	D	10 air changes per hour 300 m^3 room	0.8
Surface factor (Su)	Su	Demonstratable & effective housekeeping	0.001

- $C_{nf} = (E_{nf} * H_{nf} * LC_{nf}) * D_{nf}$
  $= (1 * 0.09 * 0.01) * 0.8 = 0.00072$
- $Su = Su\text{-}factor*(E * H * LC * D)$
  $=0.001\ (1 * 0.09 * 0.01 * 1.1) = 7.2 * 10^{-6}$
- Task Score = time fraction$*(C_{nf} + Su)$
  $= 1 * (0.00072 + 7.2 * 10^{-6})$
  $= 0.000727$

Risk/Control Banding (Tier 1)

Exposure band \ Hazard band	A	B	C	D	E
1	3	3	3	2	1
2	3	3	2	2	1
3	3	2	2	1	1
4	2	1	1	1	1

Calibration of Exposure Model (Tier 2)



$$Ln(Y_{ijk}) = X_{ijk} = \beta \cdot Ln(ART)$$

$$Ln(Y_{ijk}) = X_{ijk} = \beta \cdot Ln(ART) + \delta_i + \varepsilon_{ij}$$

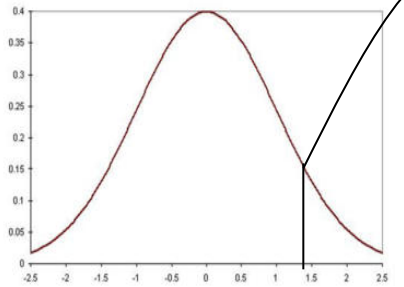
- Investigate the relation between ART-score and measured concentration
- Quantification in units (mg/m^3)
- Quantify the level of uncertainty of the mechanistic model.
- Calibration for the different exposure forms
  - Abrasive dust, dust, vapours, mist

Model – Output (Tier 2)

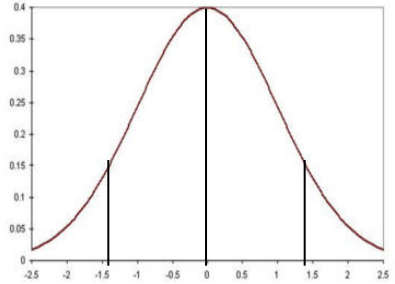
Explicit treatment of variability and uncertainty

- *Percentile of distribution*
- *Uncertainty of estimate*

Variability



90^{th} , 75^{th} , 50^{th} percentile



Uncertainty

Inter-quartile, 80 %, 90 %, 95 % CI

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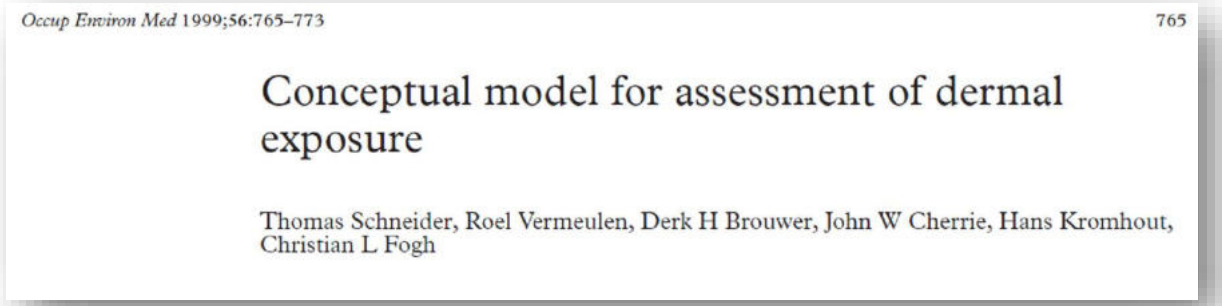
Conceptual Model Dermal Exposure

- Dermal exposure network (1996-1999)
  - Set up to bring together experts in the field of (dermal) exposure assessment
  - Goal: Develop a general model
    - standard for definitions in dermal exposure
    - framework that systematically describes transport of a contaminant mass from exposure source to surface of the skin
    - structure for evaluating dermal exposure both qualitatively and quantitatively
- Resulted in a conceptual model for dermal exposure
  - Contaminant mass transport processes
  - Interactions between compartments
  - Dermal exposure pathways



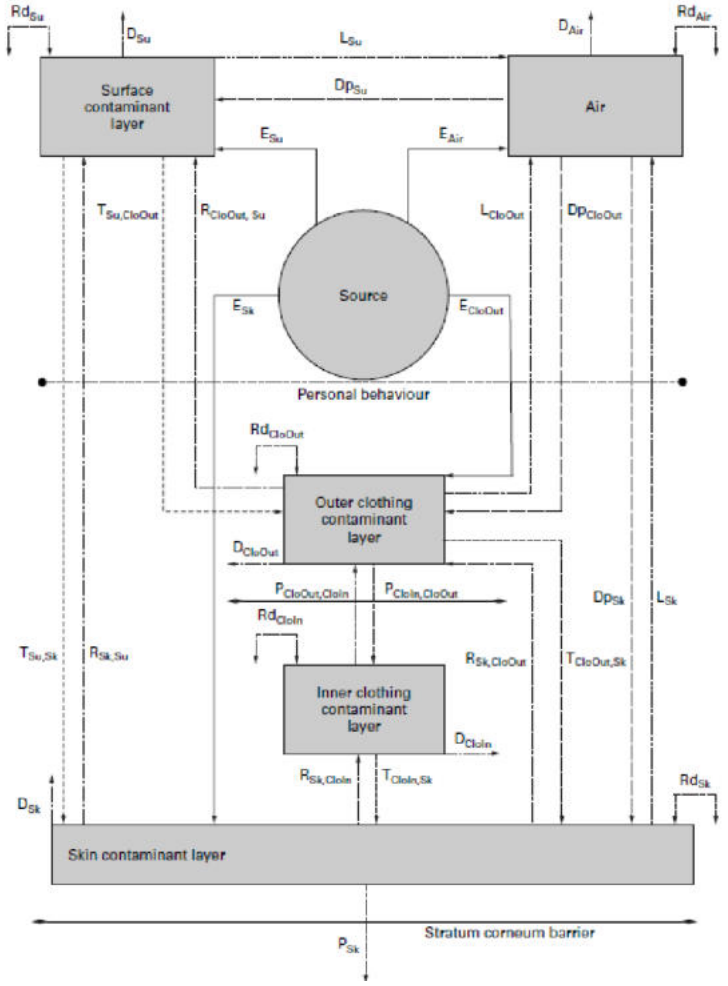
Occup Environ Med 1999;56:765–773 765

Conceptual model for assessment of dermal exposure

Thomas Schneider, Roel Vermeulen, Derk H Brouwer, John W Cherrie, Hans Kromhout, Christian L Fogh

Conceptual Model Dermal Exposure

- 6 compartments
  - Source (S): process or activity from which a mass is introduced into any of the compartments
  - Air: Vapours and dispersed particles
  - Surface contaminant layer (Su)
  - Outer clothing contaminant layer (CloOut)
  - Inner clothing contaminant layer (CloIn)
  - Skin contaminant layer (Sk): layer of contaminants, sweat, skin oil and barrier cream (if applied)
- 2 barriers
  - Clothing
  - Skin
- 8 transport routes
  - mass transport from the source to compartments and sinks
  - Below dotted line personal behaviour begin to influence transport processes (e.g. movement)
  - Units: mass/time or mass/event

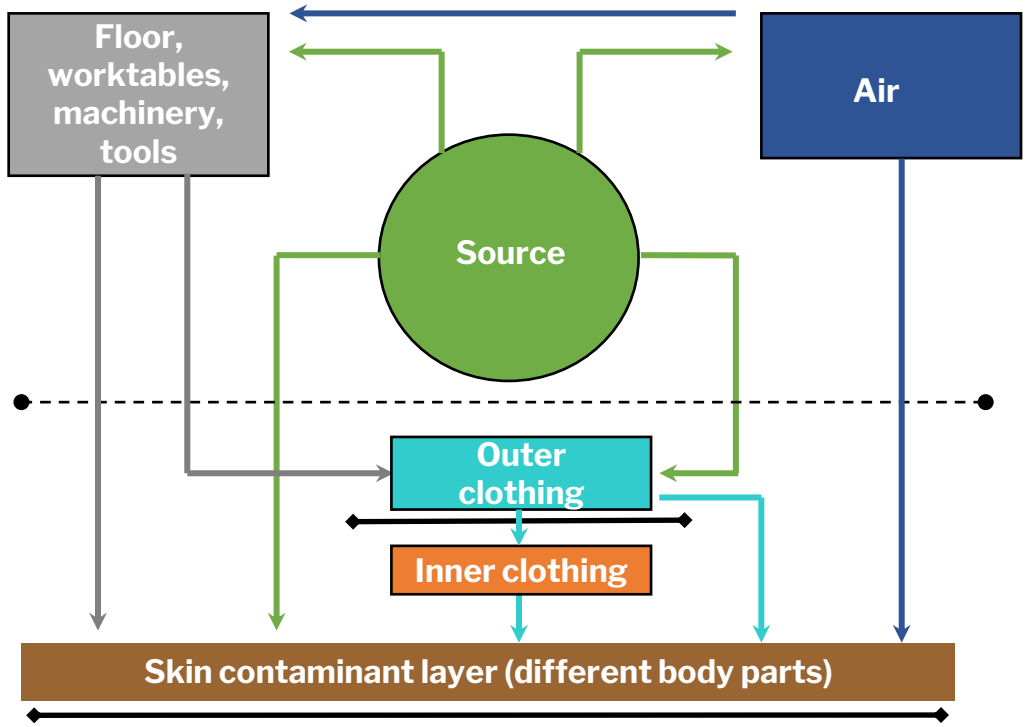


Schneider et al., 2000 Ann Occup Hyg https://doi.org/10.1016/S0003-4878(00)00048-X

Conceptual Model Dermal Exposure

Simplified

- Simplified model shows the most important routes between compartments from the source and towards the skin
- 3 main routes of exposure:
  - Emission
  - Deposition
  - Transfer
- Covers both potential and actual exposure
  - Potential: exposure on the so called outer layer (e.g. (protective) clothing)
  - Actual: exposure that actually reaches the skin
- Deals with exposure on outer layer compartment (skin/clothing) external exposure
  - **Does not take into account uptake !**



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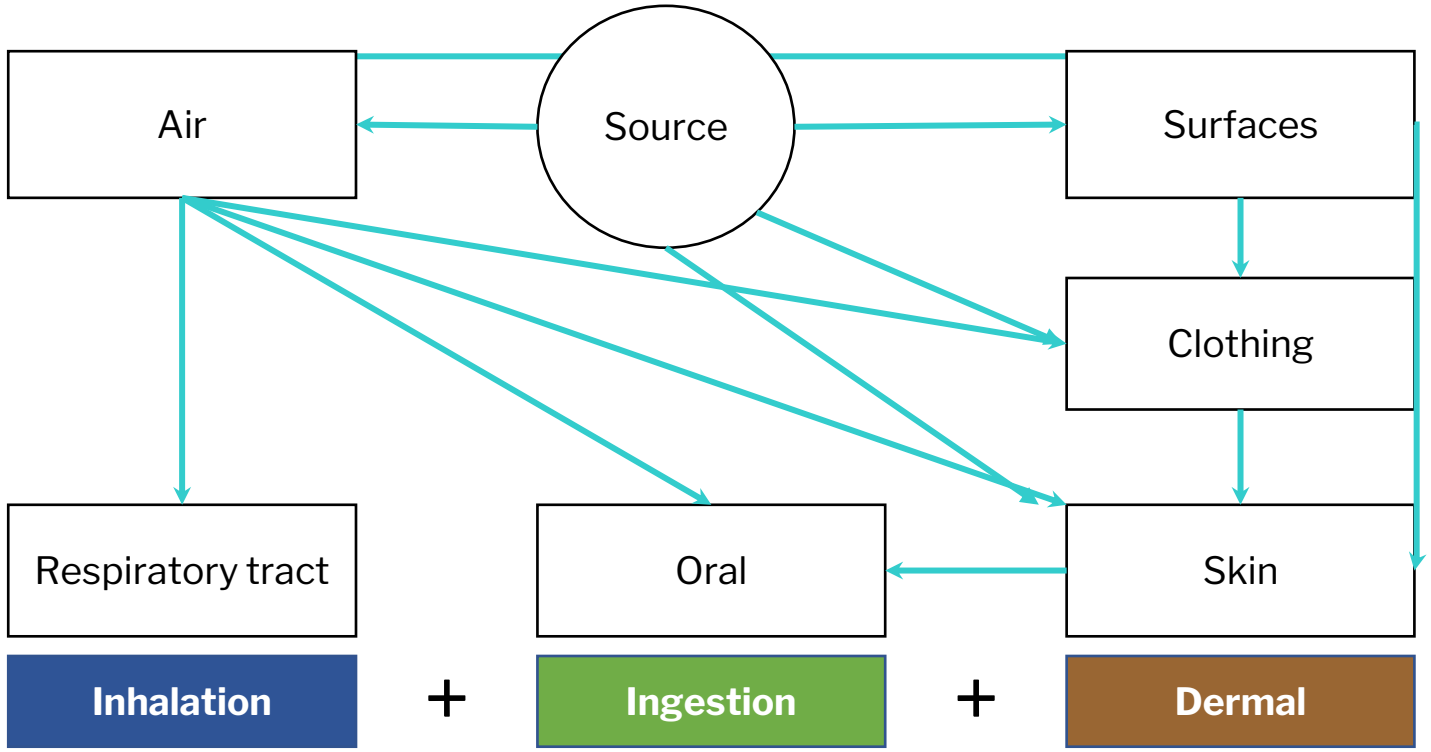
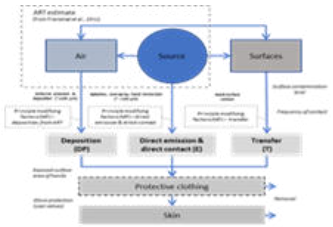
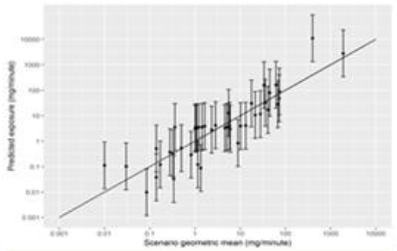
Exposure Routes

Also taking into account other exposure routes



Inhalation + Dermal Exposure Modelling





ART mechanistic model

ART software platform

(Dermal) mechanistic model

Statistical calibration model

Measurement data

dART model

Dermal Advanced REACH Tool (dART)—Development of a Dermal Exposure Model for Low-Volatile Liquids

Henk A Goede, Kevin McNally, Jean-Philippe Gorce, Hans Marquart, Nick D Warren, Wouter Fransman, Martin Tischer, Jody Schinkel

Annals of Work Exposures and Health, Volume 63, Issue 6, July 2019, Pages 624–636, https://doi.org/10.1093/annweh/wxy106

Published: 09 March 2019 **Article history**

Calibration of the Dermal Advanced REACH Tool (dART) Mechanistic Model

Kevin McNally, Jean-Philippe Gorce, Henk A Goede, Jody Schinkel, Nick Warren

Annals of Work Exposures and Health, Volume 63, Issue 6, July 2019, Pages 637–650, https://doi.org/10.1093/annweh/wxz027

Published: 16 May 2019 **Article history**

Oral (Inadvertent) Worker Exposure

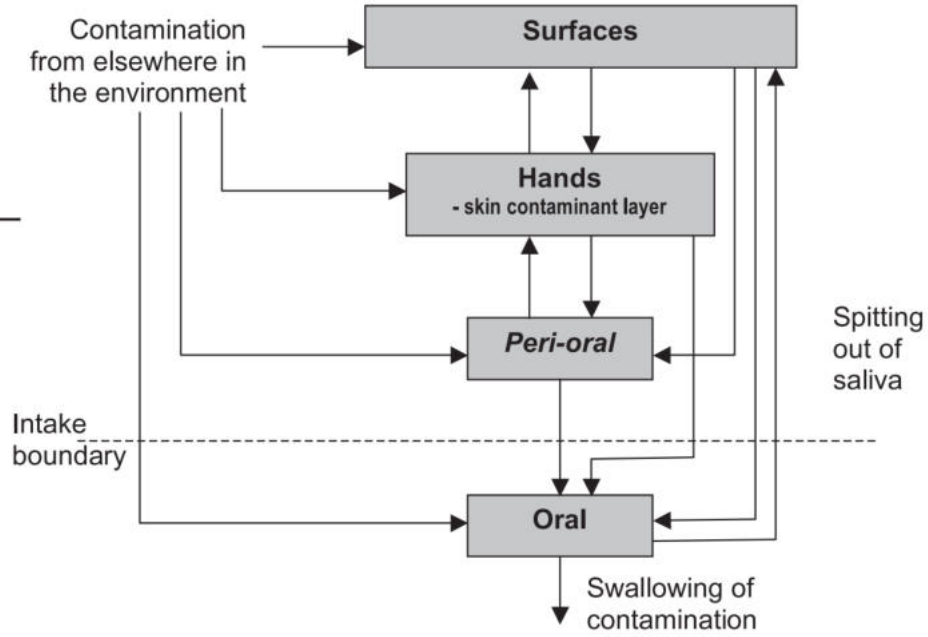
Table 1. Distribution of ingestion exposure to the six different groups of workplace contaminant for the UK working population

Contaminant group	Total number of exposed workers (×1000)	Proportion of total exposed (%)	Proportion of total UK working population (%)
Pesticides	320	7.2	1.1
Metals	1500	33	5.2
Pharmaceuticals	890	20	3.1
Radionuclides	32	0.7	0.1
Pathogens	980	22	3.4
High molecular weight	750	17	2.6
Total	4500	100	15.6

HSE Health and Safety Executive

Inadvertent ingestion exposure in the workplace

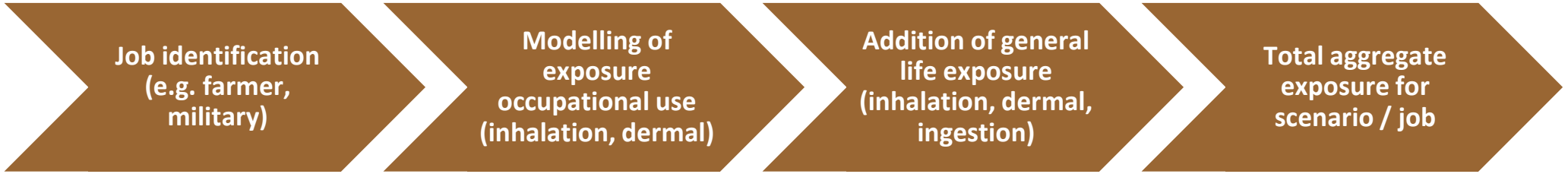
Prepared by the **Institute for Occupational Medicine** for the Health and Safety Executive 2007



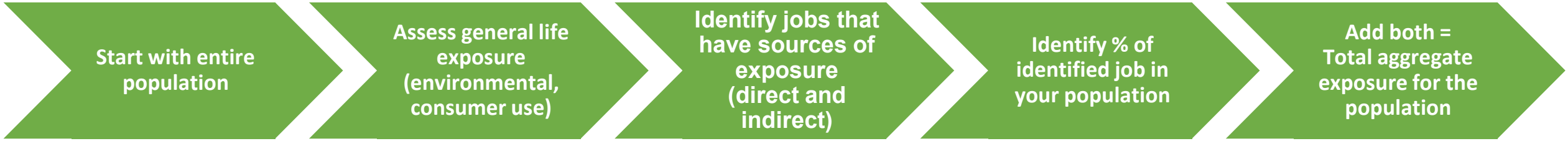
Cherrie et al., 2006 Ann Occup Hyg https://doi.org/10.1093/annhyg/mel035

Aggregate Exposure Modelling Approaches

- **At scenario / job level**



- **At population level**



Content

1. From Source to Dose
2. Occupational Exposure Modelling
3. Tiered Exposure Modelling
4. Dermal Exposure Modelling
5. Aggregate Exposure Modelling
6. **Summary**

Summary

- All routes of exposure need to be considered
- Calculation of aggregate exposure necessary, often spans several different legislations
- Tiered approach is followed and depends on factors like level of concern, data availability, model availability, etc.
- Validation of models important, but often difficult

Consequent Modules

Module 3:

- Explores human biomonitoring (HBM) in greater detail

Module 4:

- Human exposure modelling for the general population

Module 5:

- Validation & evaluation, advantages & limitations, conclusions

Future training videos:

- Additional details may be covered by ISES Europe in specialized training videos.

Thank You!

We appreciate your participation and attention

We encourage you to explore other ISES Europe training videos for deeper insights and broader understanding

Access all videos via: **https://ises-europe.org/**

Further Reading

ISES-Europe Exposure Model Inventory

ISES-Europe

https://ises-europe.org/exposure-platform/data-and-information-sharing

Guidance on Information Requirements and Chemical Safety Assessment – Chapter R.14: Occupational exposure Assessment (Version 3.0)

European Chemical Agency (ECHA)

https://echa.europa.eu/documents/10162/17224/information_requirements_r14_en.pdf

Guidance on Information Requirements and Chemical Safety Assessment – Chapter R.15: Consumer exposure Assessment (Version 3.0)

European Chemical Agency (ECHA)

https://www.echa.europa.eu/documents/10162/17224/information_requirements_r15_en.pdf