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Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin



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Upstream applications from a risk perspective Specific issues from RAC

Urs Schlüter

Given for this Presentation

- Substance listed on Annex XIV for a **human health** effect
- **RAC reference DNEL** or **dose-response-relationship** is used for risk assessment in the AfA
(echa.europa.eu/applying-for-authorisation/evaluating-applications)
- **Relevant information** is described and documented in an open and transparent matter, e.g.:
 - Process description is sufficient
 - Not too many tasks covered in one exposure scenario
- **Alternatives** are evaluated and **not available or not suitable** for one of the reasons
 - Technical & economical not feasible before the sunset date
 - Overall risk reduction not expected

Exposure Assessment – Process Description

- **It is critical that RAC can understand the processes – descriptions, diagrams, photographs, videos, all help**
- **Be thorough, describe the exposure situation qualitatively and quantitatively**
 - Who is exposed to what, where, for how long and how often, which route of exposure, during which task ...
 - Assess the relevance for the different exposed group
 - Present data, historical and current monitoring data (air monitoring, biomonitoring, environmental monitoring ...)
- **Evaluate the literature and its relevance for the AfA**
 - Annex XIV substances were evaluated in the past
 - Use evaluations that are relevant and representative
 - Discard and document reliably if information is not relevant

Exposure Assessment – Exposed Groups

- **Number of exposed individuals per group is a central input parameter**
- **Exposure assessment is different for different groups**
 - Relevance of exposure routes changes with exposed groups
 - Options and reliability are different for the different routes
- **Groups of exposed individuals**

Collectives	Routes of exposure
Directly exposed workers	Inhalation, dermal, (oral)
Indirectly exposed workers	Inhalation
Consumer (if relevant)	Dermal, oral
Man via the environment	Oral via contaminated food and water
	Inhalation via contaminated air
	Different for local / regional exposed collectives

Representative Measurements – Comparable Workplaces

Table R.14-2: Indicative number of measurements needed to determine confidently that the true RCR is below 1

		<u>R</u>isk <u>C</u>haracterization <u>R</u>atio (RCR)		
		RCR: < 1 – 0,5	RCR: < 0,5 – 0,1	RCR: < 0,1
Variation and uncertainty in the data	Low GSD < 2	~ 20 – 30	12 – 20	6 – 12
	moderate GSD 2 – 3,5	~ 30 – 50	~ 20 – 30	~ 12 – 20
	high GSD > 3,5	> 50	~ 30 – 50	~ 20 – 30

Variation/uncertainty can be caused by true variation in exposure (as indicated by a measure of variation) and by lack of knowledge about how representative data are for the situation to be assessed. GSD = geometric standard derivation

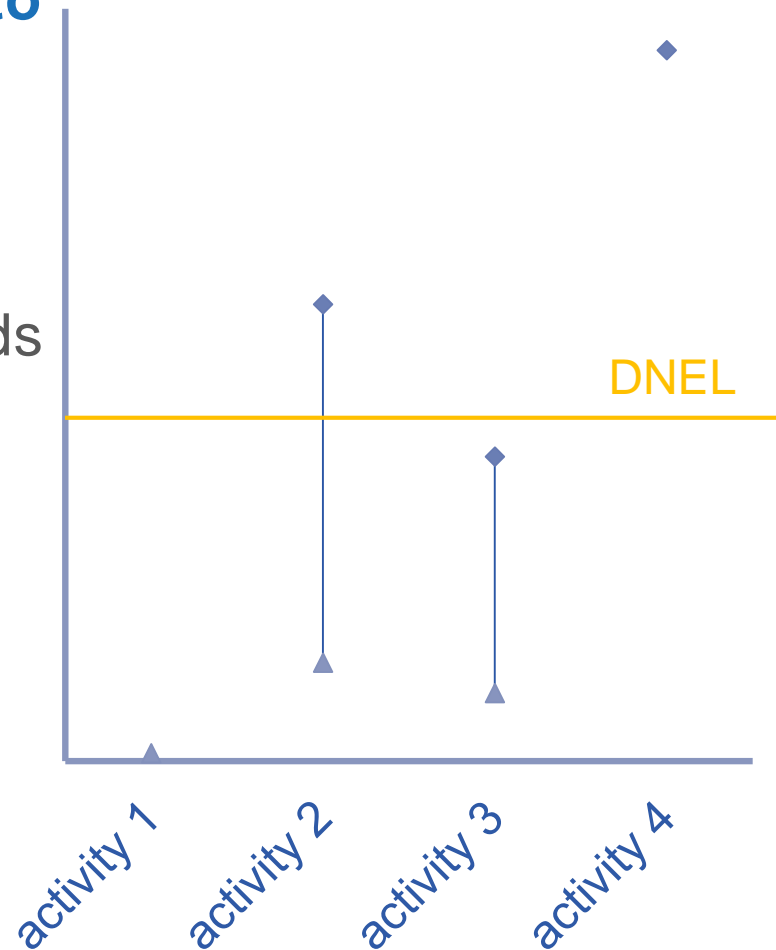
Representative Measurements – Collectives of Workplaces

How many data points are required to assess large / EU-wide collectives?

- No guidance available
- Regional & technological differences
- Differences in national OSH standards

One bad example

- Literature data only, not specific for the AfA
- Limited geographical coverage
- Maximum of 500 workers monitored, 22.000 companies would benefit
- Deficient OC and RMM description



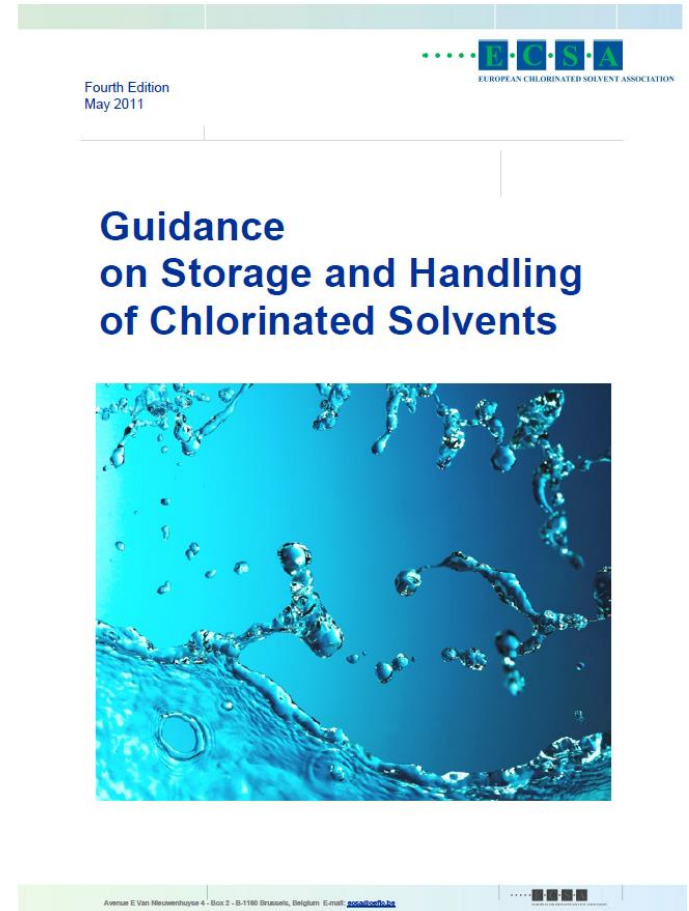
Representative Measurements – Collectives of Workplaces

One better example

- OCs and RMMs described by EU-wide guidance AND additional information
- Measurements specific for the AfA and in line with the guidance (still a low number of measurements)
- Regional differences and affected companies (IND vs. SME) deficiently described
- Supported by high quality modelling

Explanation of representativeness needs improvement

Even good exposure assessments can result in high risks



Quality & Documentation of Measurements & Modelling

Measurements

- Measurements performed according to acknowledged standards
- Contextual Information

Modelling

- Identification of the model user
- Contextual information about the modelled workplace
 - input parameters for the model
 - appropriate details about the workplace determinates
- Used model or algorithm
- Statistical characteristics of the result (if available)

Risk Assessment – Reference DNEL

$$\text{RCR} = \frac{\text{Exposure Value}}{\text{RAC Reference DNEL}}$$

- **Results in an individual value of an estimated excess of risk**
- **For directly exposed workers this means an 8 hour shift exposure with 40 years of exposure**
 - 75th percentile is generally not a reasonable worst case of an exposure distribution.
 - ECHA Guidance (R14) states that the 90th percentile should be used for the reasonable worst case.
 - 90th percentile is especially appropriate in cases with significant uncertainties regarding representativeness of data and high numbers of workplaces



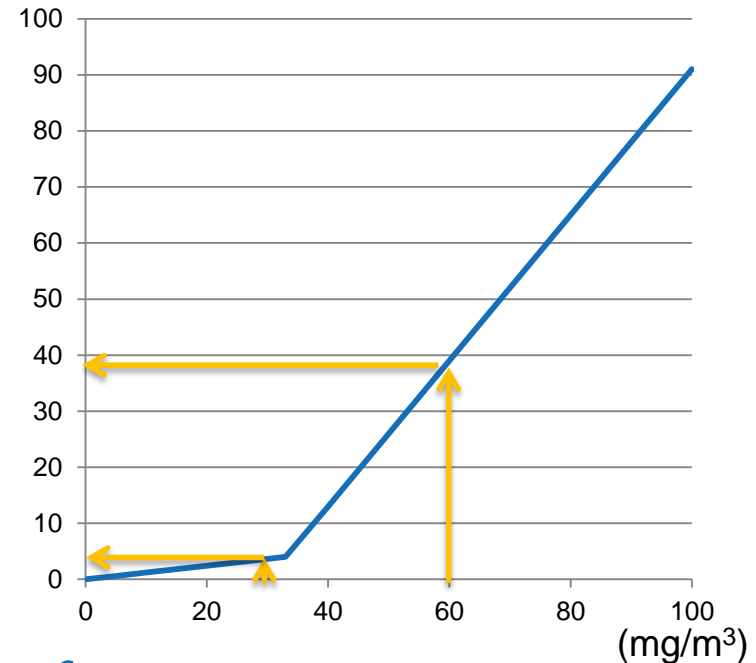
Risk Assessment – Reference Dose-Response Relationship

Inhalation exposure – Workers

8h exposure 5 days/week during 40 years, risk estimates:

- At 33 mg/m³ and above:
Excess risk = $1.3 \times 10^{-4} \text{ (mg/m}^3\text{)}^{-1}$
× concentration (mg/m³) – 0.0039
- Below 33 mg/m³:
Excess risk = $1.2 \times 10^{-5} \text{ (mg/m}^3\text{)}^{-1}$
× concentration (mg/m³)

Excess kidney cancer risk – workers ($\times 10^{-4}$)



Further dose-response relationships for:

- dermal exposure – workers
- continuous inhalational exposure – general population
- dermal exposure – general population
- oral exposure – general population

Estimated Number of Cases for Workers and Population

- Input Parameter for SEA
 - quantification of exposed collectives is compulsory
- $\text{Excess Risk} \times \text{Exposed People} = \text{estimated (additional) statistical cancer cases}^*$

	Excess risk	Exposed people	Cases*
Directly exposed workers, 40y exposure			
typical daily 'production'	10^{-4}	10000 – 100000	1 – 10
Indirectly exposed workers, 40y exposure			
Manufacturer site	10^{-9}	100000 – 1000000	< 1
General population exposed via environment, 70y exposure			
Neighbourhood – combined	10^{-7}	1000000 – 10000000	Up to 2
Broader vicinity – combined	10^{-7}	EU population	~ 50 - 60

Conclusion Measurements and Models... (John Cherrie)

”Essentially, all models are wrong, but some are useful”

“However, it is equally true that all measurements are ‘wrong’ ”

Two key things to remember:

Treat models like measurement instruments

Try to maximise the utility of the information you have, i.e. combine model and measurement data



John Cherrie
(hw.ac.uk)



George E.P. Box
(wikipedia.org)