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Innovative Environmental Services

Arno Wess
"Business Development Manager"

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1

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Some steps of my CV

03/2018 – Present	Certified Ecotoxicologist (GDCh/SETAC GLB), IBERA Certified Environmental Risk Assessor, Radiation Safety Manager, Health & Safety Officer, Business Development Manager	IES Ltd
06/2009 – 02/2018	Expert Consultant	Envigo CRS (Switzerland) Ltd. (formerly Harlan Laboratories Ltd.
05/2006 – 06/2009	Sales Manager	IBACON GmbH
11/2005 – 04/2006	G2 – Lieutenant Colonel (Military exercises)	Eurocorps, Strasbourg, France & Multinational Corps North-east, Szczecin, Poland
11/2003 – 10/2005	Sales Manager	TheraSTrat AG, Allschwil

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2

Leisure

BERGWALD PROJEKT

vhs Volkshochschule Rheinfelden e.V.

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3

General Principles / Precaution

- **Precautionary principle**
  - Bases on getting evidence of hazard level or absence
  - Determination using standardized procedures including defined Representative Organisms
    - To finally conclude on humans and the ecosystem!
  - Assessing made based on Intrinsic toxicity and properties

Alternative approach: Trust principle

Advantage of precaution is better avoidance of overlooked or underestimated hazard.

Drawbacks are higher cost & increased time for innovation

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General Principles / three “R” of animal testing

- Implementation of the animal welfare legislation (Directive 2010/63/EU on the protection of animals used for scientific purposes)
- **Reduce** the number of animals used for testing
- **Refine** the testing procedures to achieve a maximum of information “per harm”
- **Replace** animal testing whenever possible, e.g. by use of existing data, weight of evidence, in vitro methods, (Q)SAR, grouping of substances and read-across (REACH, Annex XI, 1.) or by exposure-driven omission of tests (REACH, Annex XI, 3.)

Animal welfare is the law in the regulatory laboratory

Should be compared with University research and livestock breeding …

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Substance Identity / what it means

- Start of every assessment … (not so clear as it seems)
- Physicochemical Properties
- (Stereo-)Chemical Structure (remember Thalidomide)
- Composition / Purity
- State of aggregation (basis for hazard types)
- Melting and boiling point
- Spectra etc.
- UVCB

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Substance Identity / focus of authorities

- At the beginning of chemical regulation, governmental evaluation concentrated typically on
  - Biology
  - Test organisms
  - Experimental conditions
- Then the attention switched to
  - Exposure / Analytical dose verification
- Increasingly and particularly in the industrial chemicals / REACH context, issues are raised in substance identity

A major issue

It is often downplayed, but substance identity is difficult and important for comparison & bridging principles in hazard classification and avoidance of animal and consumer harm.

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7

Hazard assessment / procedure

- Starting point: Dose descriptor (EC_{10}, NOEC, NOAEL), threshold levels
- Modification
  - Exposure extrapolation
  - Route-to-route: Dermal, oral, inhalation (particle size …)
  - Medium to medium: Water – Sediment – Soil (Equilibrium Partitioning Method, EPM)
  - Exposure duration
- Assessment Factors, AF (uncertainty factors)
  - Interspecies and intraspecies differences
  - Study duration
  - Exposure duration considering the Acute to Chronic Ratio (ACR)
  - Remaining uncertainties, e.g. data quality, suitability of replacement organisms

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Hazard assessment / result

- Safe concentrations/levels
- Predicted No-Effect Concentration (**PNEC**)
  for environmental media
- Derived No-Effect Level (**DNEL**)
  for vertebrate toxicity
- Both stating absence of effects until a certain onset level
- Derived Minimal Effect Level (**DMEL**)
  for non-threshold effects:
  The underlying assumption is that a no-effect-level cannot be established and a DMEL therefore expresses an exposure level corresponding to a low, possibly theoretical, effect, which should be seen as tolerable/irrelevant.

Safe concentrations/levels must not be exceeded

Legally binding levels are established as, e.g., Occupational Exposure Level OEL, Environmental Quality Standard (EQS), Air Quality Standard (AQS) …

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Substance replacement / ranking

- Substances suitable for the same purpose differ in their hazard level
- Substitution of a more hazardous compound by a less hazardous one seems reasonable
- Higher cost can be a consequence
- Ranking (keeping substances as use alternatives, but preferring one) may apply in cases, where e.g., a medicine is considered equivalent for a patient, but worse for the environment (Escitalopram, Sertraline in Stockholm, where sewage water treatment plant sludge is stored in abandoned mines, case dependent …)
  Individuals may not be suitable for the preferred substance due to (hereditary) predisposition
- Ranking is difficult if one hazard is lower, but another one is higher …

Ranking strategies

may assure a “greener” approach in most cases.

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Discussion / acute – chronic hazard

- Imagine a chemical preventing (PCB) burns of electronic devices, e.g., laptop computers, but bioaccumulating in humans
- Consider: Any substance becomes toxic if the dose gets high enough!

The dose makes the poison

What is it that is not a poison? All things are poison and nothing is without poison. Solely, the dose determines that a thing is not a poison.
--Paracelsus (1493–1541), the Renaissance Father of Toxicology, in his *Third Defense*

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11

Discussion / vulnerable groups

- Protection target in
  Environmental assessment is the ecosystem (also serving as a food source for humans, secondary poisoning) in
  Human toxicity it is the individual person ...
- People are different.
- Standardized methods serve the standard averages
- Single Nucleotide Polymorphisms (SNP) can cause idiosyncratic adverse reactions, e.g., to drugs and are a major cause of death.
- Other potentially vulnerable groups are, children, pregnant woman, elderly, the sick.

Risk mitigation by organizational advice

Substance use restriction is an important strategy. Allowing access to chemicals depending on profession or marketing measures (e.g., OTC versus prescription drugs) can provide solutions.

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Shortcomings of hazard assessment procedures

- **Method equivalence**
  - Use of historic data suffers from comparability with newer tests
  - Alternative methods (avoiding animal use) are even more difficult
- Ignoring (true) **Threshold toxicity and/or stereochemistry**
  - Some substances may be detoxified by (most …) people, but the pathway may have a capacity limit.
    In such cases effects may be completely absent to start suddenly at certain levels.
- Ignoring **Mixtures** / substance interactions
  - Combined exposure is common, but not assessed

Exposure assessment allows better risk evaluation

Since exposure can be strongly influenced, it is a part of regulatory strategies.

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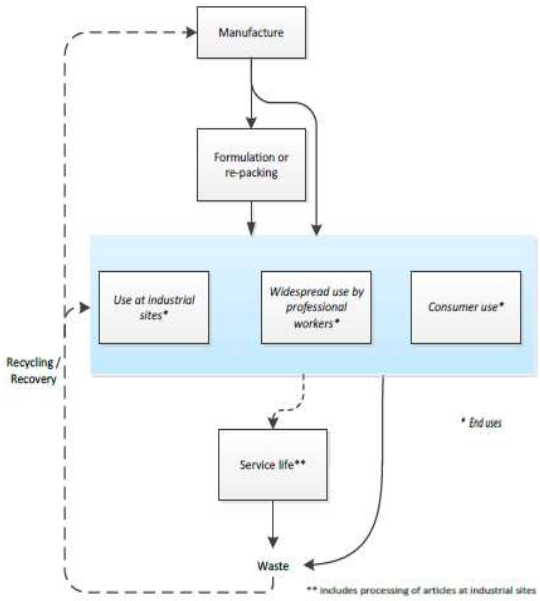
Life cycle of chemicals

Exposure depends on the life cycle stage

The four basic steps or stages in the life-cycle of a substance to which a use can be assigned are: manufacture, formulation or re-packing, end-use and (article) service life



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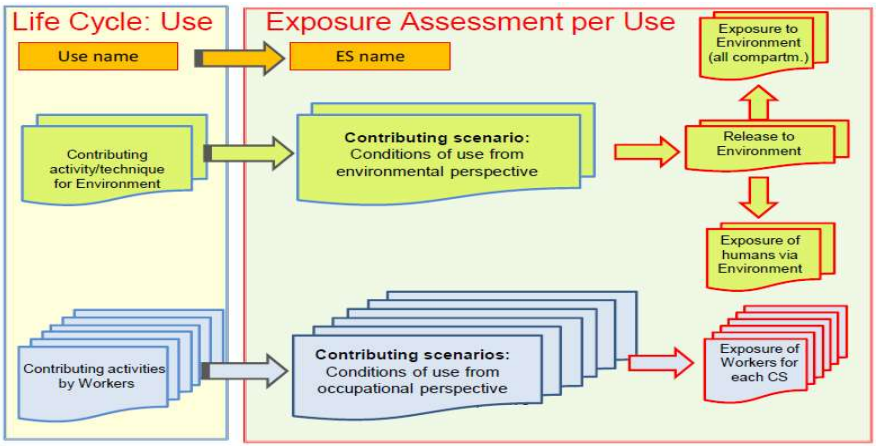
Exposure depends on life cycle & use



Exposure assessment is use dependent

Use description and characterization is highly advances in EU. Categories are defined and exposure can be estimated by the free software CHESAR, Chemical Safety Assessment and Reporting tool

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16

Steps of the exposure assessment

- **Routes**
  - Oral
  - Dermal
  - Inhalation
- **Quantification**
  - Measurement
  - Modelling
  - Secondary poisoning
- **Acute and/or Chronic**
  - Enrichment/Mobility/Persistent
- **Local and Regional scales in the environment**
  - Dilution

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Biodegradation

The potency of a chemical or a mixture of chemicals (UVCB) to undergo **decomposition,** i.e. irreversible alteration of its chemical structure by breaking down and new formation of covalent bindings.

- **Primary** biodegradation
  Change of the original structure is evidenced, potential loss of bioactivity
- **Ready** biodegradation and **inherent** biodegradation
  Ultimate Biodegradation in absence of other sources of energy and carbon within a defined time frame
- **Rapid** Biodegradation
  Ready - or Ultimate Biodegradation in simulation tests within a defined time frame
- **Ultimate** Biodegradation
  Utilisation by of the test item by microorganisms resulting in the production of carbon dioxide, methane, mineral salts and other inorganic compounds and new microbial cellular constituents (biomass)

In vitro and simulation test settings are available

While ***in vitro*** tests are always in **absence** of organic matter and media such as soil, sediment, suspended matter or any other organic carbon, **simulation** allows their **presence** in environmentally or use-related settings

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18

Check Bioavailability, consider enhancing

Ready biodegradation test can be performed in agreement with the test guidances even if the test organisms were unable to access the test substance(s).

Careful considerations are required to perform a meaningful OECD 301 test.

I consider this test might be the one with the highest percentage of test artefacts ..

On the other hand, there are many possibilities to modify the test protocol (also in agreement with the guidance) and to gain more evidence out of these studies …

19

Persistence (P), Bioaccumulation (B) and Toxicity (T)

Substances which persist in the environment can accumulate in biota. The lower the toxicological threshold levels are, the more probable is an undesired effect in ecosystems. Such effects can be local and worldwide, provided that Long Range Transport (**LRT**) occurs.

- The longer a chemical persists under environmental conditions, the more difficult is the assessment of the Environmental fate and
- the more it tends to accumulate, the more likely are damages to ecosystems and
- Every chemical has at least the polar or nonpolar "**baseline toxicity**".
- Thus, are **very Persistent ("vP")** and **very Bioaccumulative ("vB")** chemicals regarded critical without further evidence for specific toxic effects.
- In case LRT is likely or proven by Measured Environmental Concentrations (**MEC**) in remote areas (e.g. the Arctic) global action may be required and foreseen according to the Stockholm Convention on Persistent Organic Pollutants (**POP**)
  – UN level, member nations initiate

20

Initial evidence for PBT/vPvB properties

Evidence for PBT and LRT properties can be drawn from

- **Fugacity properties** expressed by partition coefficients:
  - **K_{ow} ($c_{octanol}/c_{water}$)**
  - K_{oa} ($c_{octanol}/c_{air}$)
  - K_{aw} (c_{air}/c_{water} or H' the dimensionless Henry constant)
- **Calculations particularly on the screening level**
  - QSPR (Quantitative Structure-Property Relationships, for biodegradation, vapour pressure, water solubility, Kow) and
  - QSAR (A for Activity, estimating toxicity)
- Laboratory studies and publications on abiotic stability, biodegradation, bioaccumulation (in fish, mussel or terrestrial and benthic oligochaetes), toxicokinetics (or pharmacokinetic) and in vitro metabolism studies
- **MEC** e.g. indicating LRT

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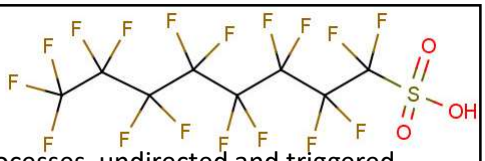
21

Enrichment mechanisms



- Equilibration due to diffusion processes, undirected and triggered by intrinsic fugacity properties:
  - Medium – organism (inner) surface
    - Via skin / gills with water (Kow defines the maximum BCF!)
    - Via intestinal mucosa with intestine contents (Kow, BAF, BSAF)
    - Via pulmonary alveoli with air (Koa, MEC, TMF, BMF)
  - Elimination processes, directed:
    - Renal elimination (Kow)
  - Conversion
    - Metabolisation (enzymatic)
    - Chemical binding to cell constituents, e.g. proteins (PFOS[1]) or lipids
    - Ionization, e.g. ion trapping as ions are not membrane-permeable, pH dependent

[1] UNEP United Nations Environment Programme (2005) Addendum to the dossier on perfluorooctane sulfonate Submission by Sweden. Persistent Organic Pollutants Review Committee First meeting Geneva, 7-11 November 2005, Agenda item 5 (e) Consideration of chemicals proposed for inclusion in Annexes A, B and C of the Convention: perfluorooctane sulfonate. Document No. UNEP/POPS/POPRC.1/CRP.1 7 November 2005

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Exposure «Enough is enough»

- Background concentrations
- Releases from
  - Natural sources
  - Due to contamination
- Degradation
  - Biotic
  - Abiotic
- Distribution
  - Between media: Water, sewage sludge, sediment, soil, air,
  - From media to organisms and within organisms
  - Fugacity, dilution

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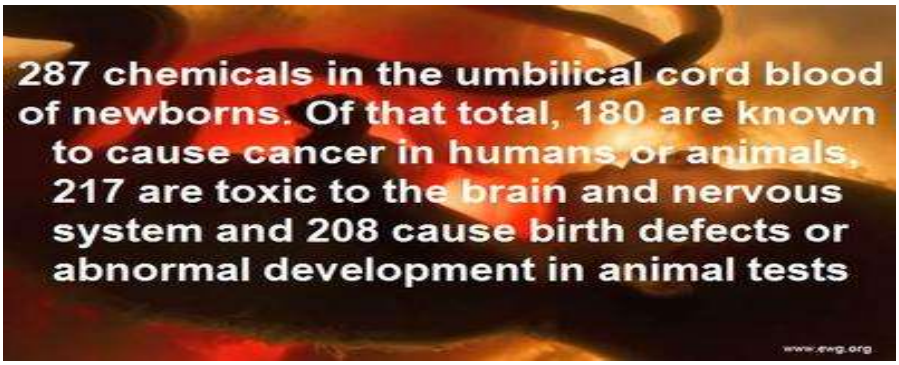
Mixed Exposures

- **«Something from nothing»**
- Additive effects (combined action) or
- Independent action
- Multiple contaminations



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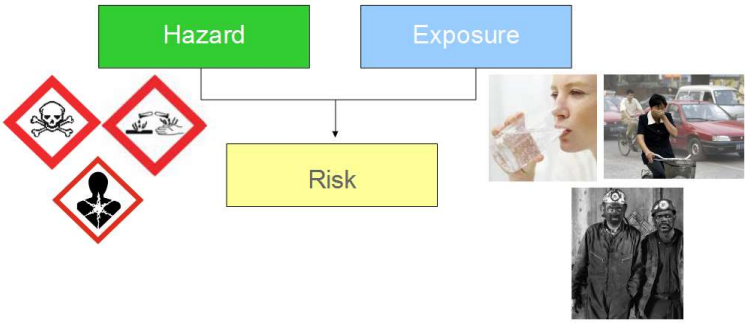
24

Risk: Defined as a quotient

- Derived safe (harmless) concentration / estimated maximum exposure
  - <1 or refinement due to
    - knowledge on effects, reducing assessment factors
      - More data up to Species Sensitivity Distribution (SSD)
      - Hazard Quotient HQ5
    - Exposure modelling / measurements
      - Risk mitigation measures
      - Exclusion from uses



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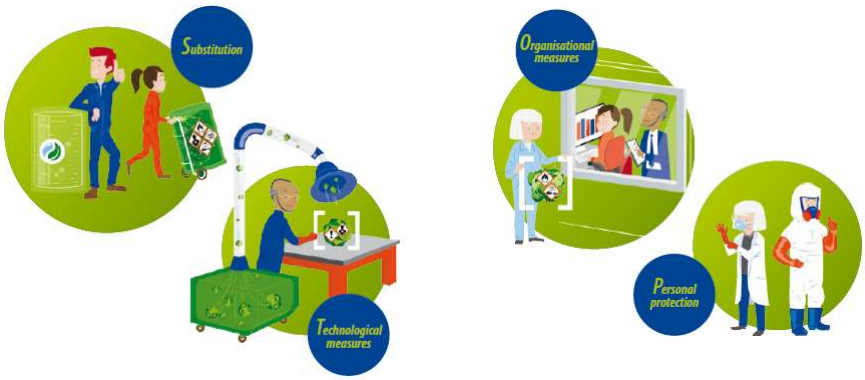
25

Risk control / STOP principle



- Substitution: Use of less toxic substance
- Technological measures: Local Exhaust Ventilation
- Organizational measures: Warning labels, MSDS
- Personnel Protection: Gloves, Glasses …

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26

26

Examples for relevance in green chemistry 1

- Glyphosate discussion based on stated facts
- Reduces
  - Carbon dioxide emissions
  - Soil compaction
- Considered likely to be a human (threshold?) carcinogenic (WHO)
- A safe level is stated (WHO) – *sensu stricto* impossible for carcinogens

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27

Examples for relevance in green chemistry 2

- Methanol fuel cell discussion based on stated facts
- Better efficiency factor than hydrogen fuel cell
- Liquid state
  - High energy density
  - No need for compression
  - Can be used in filling stations instead of gasoline or diesel
- Specific organ toxicity (to optic nerve, causes irreversible blindness) at low levels
- High vapour pressure
- Good water solubility
- Good dermal & inhalation absorption

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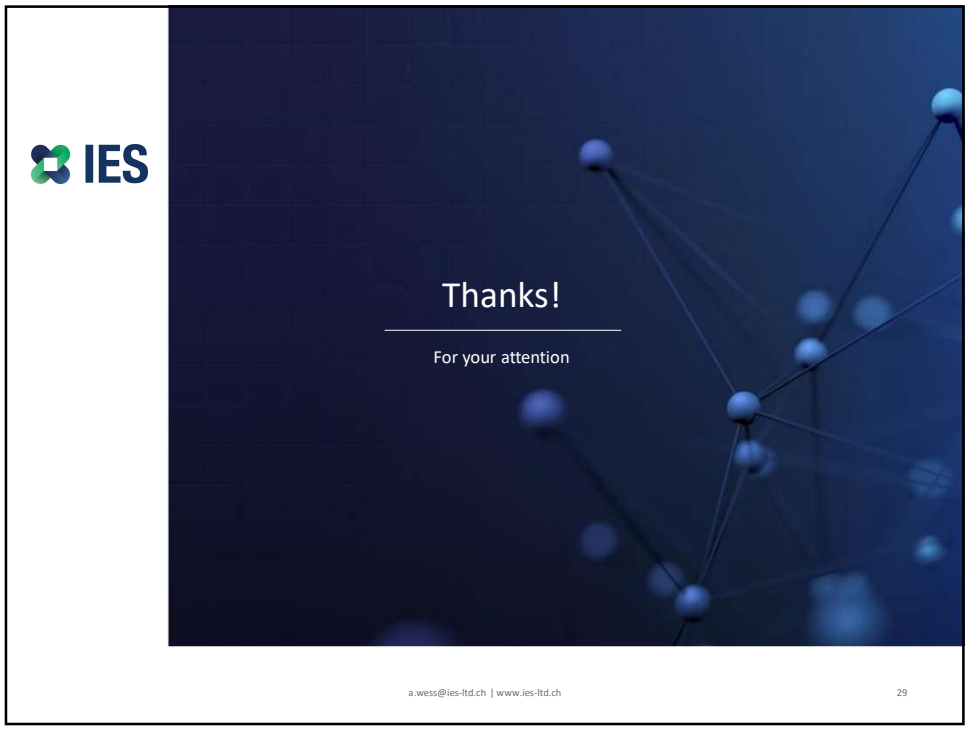
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Thanks!
For your attention
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29

29