ECRAN Regional Workshop
on Compliance with REACH/CLP Regulations
TAIEX/ECRAN 60319

Introduction on hazard and risk assessment under REACH

Martin Murín, MSc.

Ekotoxikologické centrum Bratislava s.r.o.

Tomášikova 10/F
821 03 Bratislava
Tel/Fax.: +421 45943712 / 45945223
E-mail: ekotox@ekotox.sk
www.ekotox.eu

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

HAZARD & RISK ASSESSMENT - roles

- **Legislative background**
  - Industrial Chemicals
  - Pesticides
  - Biocides
  - Pharmaceuticals
  - …contaminated areas (“specific risk assessment”)
  - Point sources – environment, human health…

- **Assessment of a Priority Chemicals – SVHC**
- **Hazard vs Risk**
- **RISK ASSESSMENT – RISK MANAGEMENT**

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

LIKELIHOOD (probability) **How likely is the event to occur at some time in the** *(Linear Scale time specific matrix)*	**CONSEQUENCES** **What is the Severity of injuries /potential damages / financial impacts (if the risk event actually occurs)?** *(Logarithmic Scale, property industry specific matrix)*				
	Insignificant	Minor	Moderate	Major	Catastrophic
	No Injuries First Aid No Envir Damage << $1,000 Damage	Some First Aid required Low Envir Damage << $10,000 Damage	External Medical Medium Envir Damage <<$100,000 Damage	Extensive injuries High Envir Damage <<$1,000,000 Damage	Death or Major Injuries Toxic Envir Damage >>$1,000,000 Damage
Almost certain - expected in normal circumstances (100%)	MODERATE RISK	HIGH RISK	HIGH RISK	CRITICAL RISK	CRITICAL RISK
Likely – probably occur in most circumstances (10%)	MODERATE RISK	MODERATE RISK	HIGH RISK	HIGH RISK	CRITICAL RISK
Possible – might occur at some time. (1%)	LOW RISK	MODERATE RISK	HIGH RISK	HIGH RISK	CRITICAL RISK
Unlikely – could occur at some future time (0.1%)	LOW RISK	MODERATE RISK	MODERATE RISK	HIGH RISK	HIGH RISK
Rare - Only in exceptional circumstances 0.01%)	LOW RISK	LOW RISK	MODERATE RISK	MODERATE RISK	HIGH RISK

Summary Table of Available Tools for Risk Assessment

Categories		Links to Available Materials	Explanation
Hazard Assessment	**Gathering existing information**	OECD Existing Chemicals database	OECD-wide agreed hazard assessments elaborated in the OECD Co-operative Chemicals Assessment Programme
		eChemPortal	Global Portal to Information on Chemical Substances
		Manual for the Assessment of Chemicals (Chapter 2)	A set of guidance documents for (initial) risk assessment developed for the OECD Co-operative Chemicals Assessment Programme. See chapter 2 for gathering data
	Evaluating existing information	Manual for the Assessment of Chemicals (Chapter 3)	See chapter 3.1 for determining the quality of existing data
	Generating new data	Test guidelines	Test methods for assessing (hazard) properties of chemicals
		The OECD (Q)SAR Project	Guidance and tools for filling data gaps by non-testing methods.
	Assessing the hazards	Manual for the Assessment of Chemicals (Chapter4) & (Chapter 5)	Chapter 4 provides guidance assessing the hazards of chemical substances to man and the environment Chapter 5 provides guidance on elaborating a hazard assessment report.
		Series on Testing and Assessment	Guidance documents and reports related to assessment of several inherent effects

This Project

Environment and Climate Regional Accession Network ECRAN

What is risk assessment?

EPA uses risk assessment to characterize the nature and magnitude of health risks to humans (e.g., residents, workers, recreational visitors) and ecological receptors (e.g., birds, fish, wildlife) from chemical contaminants and other stressors, that may be present in the environment. Risk managers use this information to help them decide how to protect humans and the environment from stressors or contaminants. Note that "risk managers" can be:

- federal or state officials whose job it is to protect the environment,
- business leaders who work at companies that can impact the environment, or
- private citizens who are making decisions regarding risk.

At EPA, environmental risk assessments typically fall into one of two areas:

- Human Health
- Ecological

Risk assessment is, to the highest extent possible, a scientific process. In general terms, risk depends on the following factors:

- How much of a chemical is present in an environmental medium (e.g., soil, water, air),
- How much contact (exposure) a person or ecological receptor has with the contaminated environmental medium, and
- The inherent toxicity of the chemical.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Risk Assessment

European Union

GENERIC RISK ASSESSMENT

- **Human Health RA**
  - scenarios for workers and consumers
- **Environmental RA**
  - exposure through environ. compartments
  - ecosystems & human beings

USA

SITE SPECIFIC RISK ASSESS.

- **Human Health RA**
  - all exposure routes incl. environ. compartments
- **Ecological RA**
  - ecosystems, endangered species
  - all stressors

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Risk Assessment

Environment and Climate Regional Accession Network ECRAN

- **Effect Assessment**

Data: toxicological and ecotoxicological data incl. environmental fate

ADI/TDI (UN); ***RfD (US EPA);***

DNEL / DMEL / PNEC, occupational exposure limits (***OEL***)

- **Exposure Assessment**

European Agency for Safety and Health at Work

Data: measured concentrations, monitoring, models

Exposure levels / PEC

- **Risk Characterisation**

Data: toxicity / ecotoxicity, emissions into environment and exposure based on standardised conditions

GOAL: control and management of chemicals

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

EU legislation - Risk Assessment

- **Guidance Document in Support of Commission Directive 93/67/EEC on Risk Assessment for <u>New</u> Notified Substances and Commision Regulation (EC) No. 1488/94 on Risk Assessment for <u>Existing</u> Substances**

  European Commision, CR-48-96-001-EN-C

  REACH Regulation – Guidance documents

  http://echa.europa.eu/guidance-documents/guidance-on-reach

*** RA for Human Health** ***Environmental Risk Assessment**

*** Use of (Q)SARs / models** ***Use Categories**

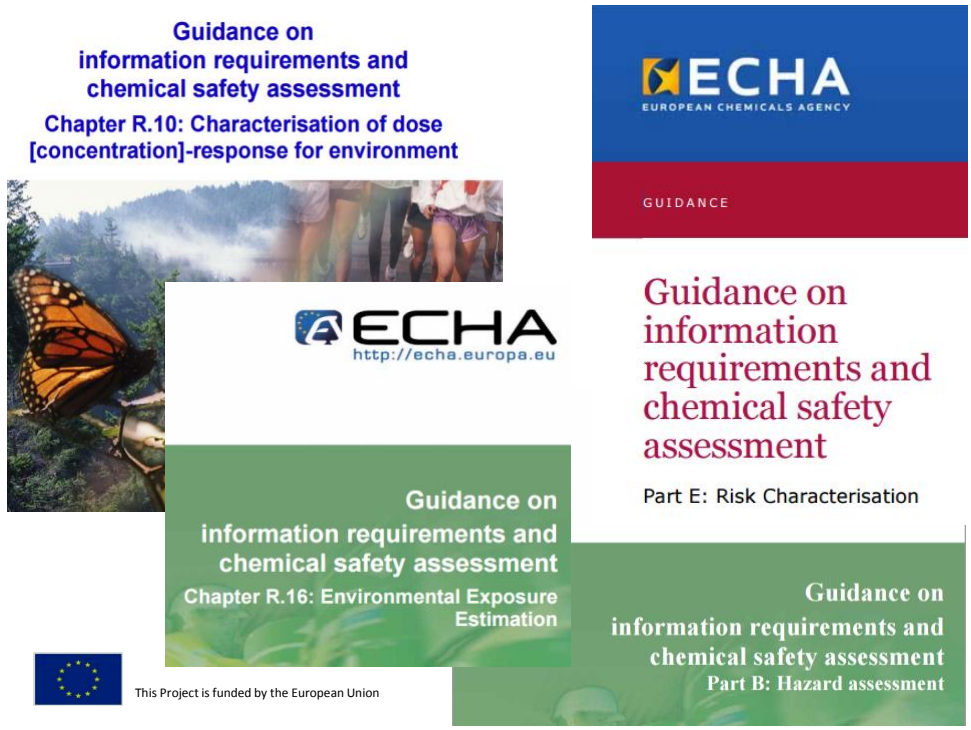
*** RA Report Format** ***Emmision Scenario Documents**

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

This Project is funded by the European Union

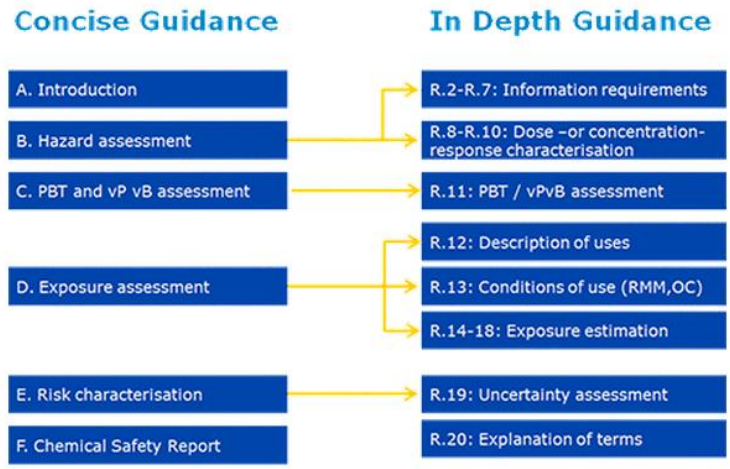
Project implemented by Human Dynamics Consortium



This Project is funded by the European Union

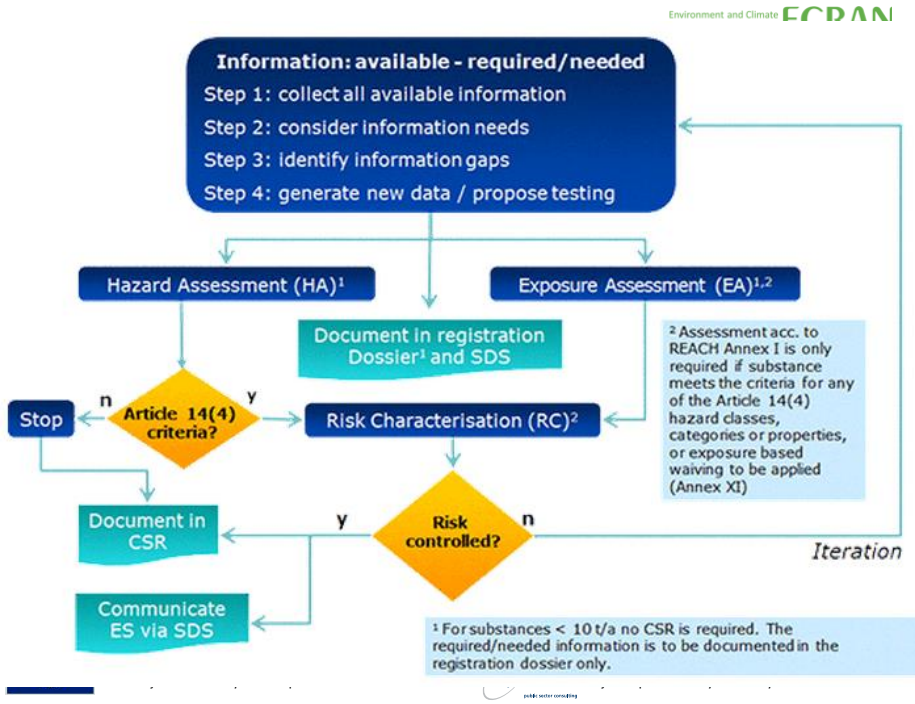
Environment and Climate Regional Accession Network ECRAN

EU Risk Assessment Guidance



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium



Environment and Climate Regional Accession Network ECRAN

Effects Assessment

- **Hazard Identification**
  - **classification / other hazard**
- **Dose (concentration) - response (effect) assessment**
  - **Derived No Effect Level (DNEL)**
  - **Derived Minimal Effect Level (DMEL)**
  - **Predicted No-Effect Concentration (PNEC)**

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Adverse effects of a toxicant

- Adverse effects
  - any change from an organism's normal state
  - dependent upon the concentration of active compound at the target site for a sufficient time.
- Toxicant (Poison)
  - Man-made (synthetic) substance that presents a risk of death, disease, injury, or birth defects in living organisms through absorption, ingestion, inhalation, or by altering the organism's environment.
  - In comparison, a **toxin** is produced in nature by a living animal or plant.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

What is a Poison?

All substances are poisons;

there is none that is not a poison.

The right dose

differentiates a poison and a remedy.

Paracelsus (1493-1541)

This Project is funded by the European Union

Project implemented

Environment and Climate Regional Accession Network ECRAN

Dose

The amount of chemical entering the body

This is usually given as

mg of chemical/kg of body weight = mg/kg

The dose is dependent upon

* The environmental concentration
* The properties of the toxicant
* The frequency of exposure
* The length of exposure
* The exposure pathway

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

What is a Response?

The degree and spectra of responses depend upon the dose

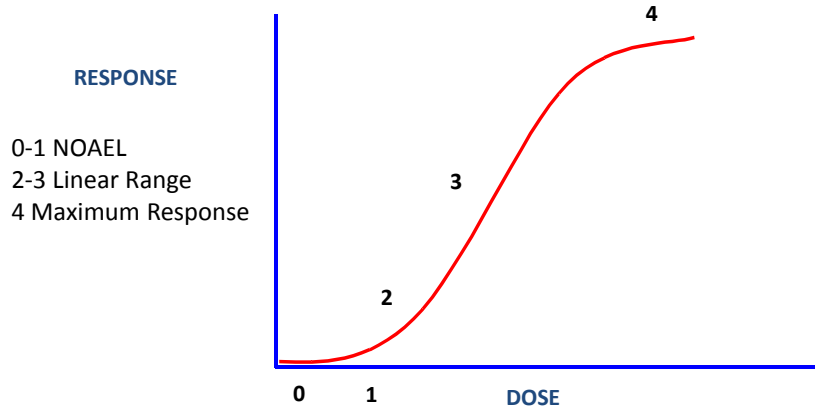
- Change from normal state
  - could be on the molecular, cellular, organ, or organism level--the symptoms
- Local vs. Systemic
- Reversible vs. Irreversible
- Immediate vs. Delayed

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Dose-Response Relationship:

As the dose of a toxicant increases, so does the response.



DOSE DETERMINES THE BIOLOGICAL RESPONSE

This Project is funded by the European Union
Project implemented by Human Dynamics Consortium

LD_{50}

- Quantal responses can be treated as gradient when data from a population is used.
- The cumulative proportion of the population responding to a certain dose is plotted per dose--10-30 fold variation w/in a population
- If Mortality is the response, the dose that is lethal to 50% of the population LD_{50} can be generated from the curve
- Different toxicants can be compared--lowest dose is most potent

This Project is funded by the European Union
Project implemented by Human Dynamics Consortium

LD_{50} Comparison

Environment and Climate Regional Accession Network ECRAN

Chemical	LD_{50} (mg/kg)
Ethyl Alcohol	10,000
Sodium Chloride	4,000
Ferrous Sulfate	1,500
Morphine Sulfate	900
Strychnine Sulfate	150
Nicotine	1
Black Widow	0.55
Curare	0.50
Rattle Snake	0.24
Dioxin (TCDD)	0.001
Botulinum toxin	0.0001

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure: Pathways

- Routes and Sites of Exposure
  - Ingestion (Gastrointestinal Tract)
  - Inhalation (Lungs)
  - Dermal/Topical (Skin)
  - Injection
    - intravenous, intramuscular, intraperitoneal
- Typical Effectiveness of Route of Exposure
  iv > inhale > ip > im > ingest > topical

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure: Duration

Acute	< 24hr	usually 1 exposure
Subacute	1 month	repeated doses
Subchronic	1-3mo	repeated doses
Chronic	> 3mo	repeated doses

Over time, the amount of chemical in the body can build up, it can redistribute, or it can overwhelm repair and removal mechanisms

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Absorption, Distribution, Metabolism, and Excretion

- Once a living organism has been exposed to a toxicant, the compound must get into the body and to its target site in an active form in order to cause an adverse effect.
- The body has defenses:
  - Membrane barriers
    - passive and facilitated diffusion, active transport
  - Biotransformation enzymes, antioxidants
  - Elimination mechanisms

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Chemicals bevaviour

- Physico-chemical parameters that determine which compartment a chemical will go:

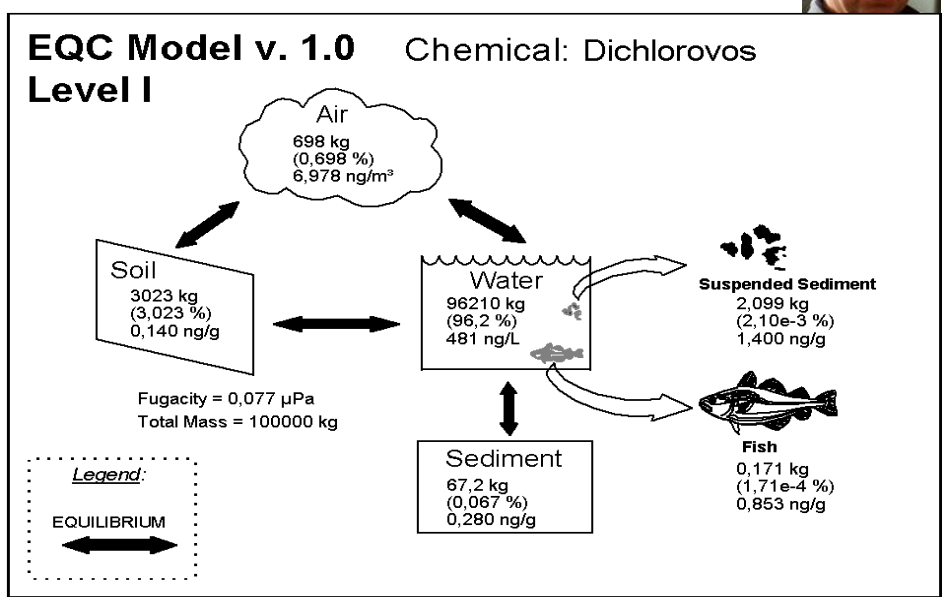
- Aboitic compartment
  - **Air: - Henry constant (H), The pressure of a gas above a solution is proportional to the concentration of the gas in the solution**
  - **water: - water solubility (S)**
  - **Soil/sediment:- soil sorption coefficient (Koc)**

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

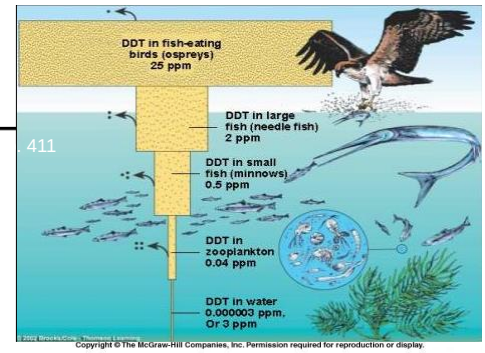
Fate in the environmental compartments - models

- Donald Mackay

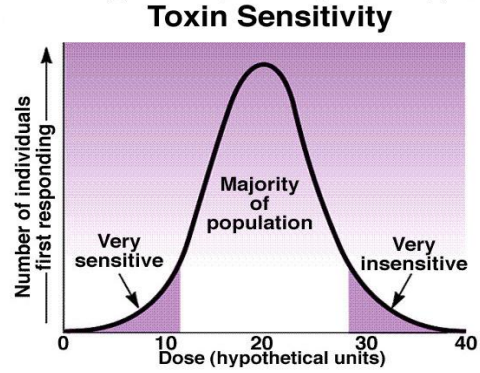


Toxicology

- Toxicity
- Dosage
- Bioaccumulation
- Biomagnification
- Synergism
- Response
- Acute effect
- Chronic effect



This Project is funded by the European Union



Environment and Climate Regional Accession Network ECRAN

TOXICOLOGY: Assessing Chemical Hazards

Toxicity: measure of how harmful a substance is in causing injury, illness, or death to living organisms.

FACTORS AFFECTING TOXICITY:

1) Dose: the amount of substance ingested, inhaled or absorbed...

This Project is funded by the European Union

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

Toxicology and Ecotoxicology are similar but not identical.

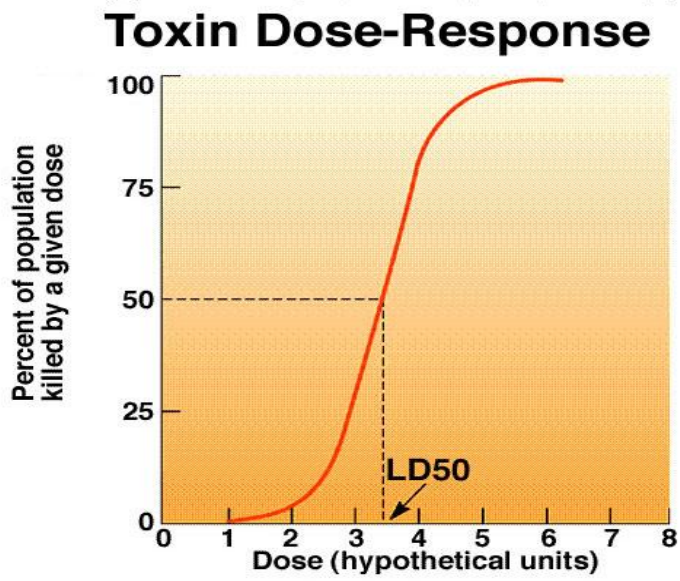
Toxicology	***Ecotoxicology***
Absorption	Release into the environment
Distribution	Fate and Disposition
Metabolism	Metabolism
Elimination	No counterpart!

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

CHEMICALS: Major Types of Toxicity



Environment and Climate Regional Accession Network ECRAN

Dose-Response Curves

- Dose-response
- Nonthreshold
- Threshold

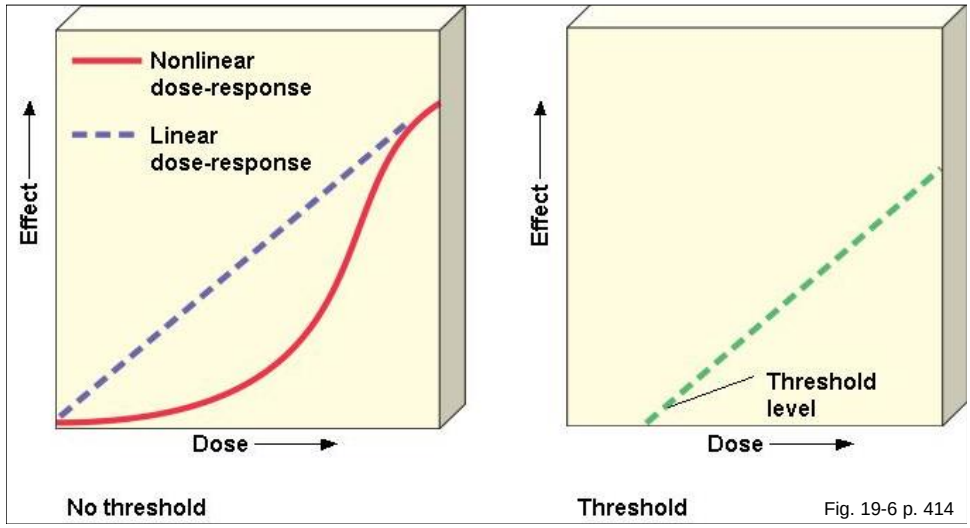
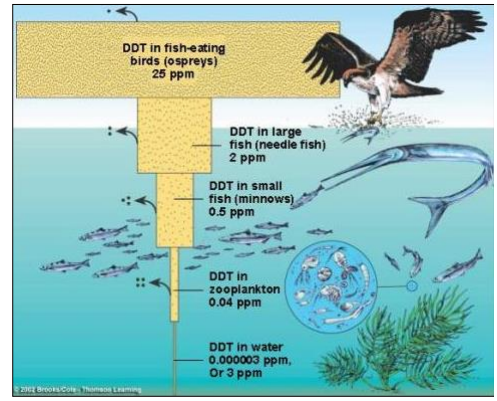


Fig. 19-6 p. 414

Factors Affecting Harm Caused By A Substance

1) Solubility (water soluble move through environment easily)
2) Fat Soluble (can accumulate in body tissue and cells)
3) Persistence (how long before it breaks down)

- Bioaccumulation
- Biomagnifications



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Effects Assessment - steps

- **Hazard identification**: The aim of the hazard identification is to identify the effects of concern. The aim is also to review the classification of the;
- **Dose (concentration) - response (effect) assessment:** At this step the predicted no effect concentration (PNEC), shall, where possible, be determined.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

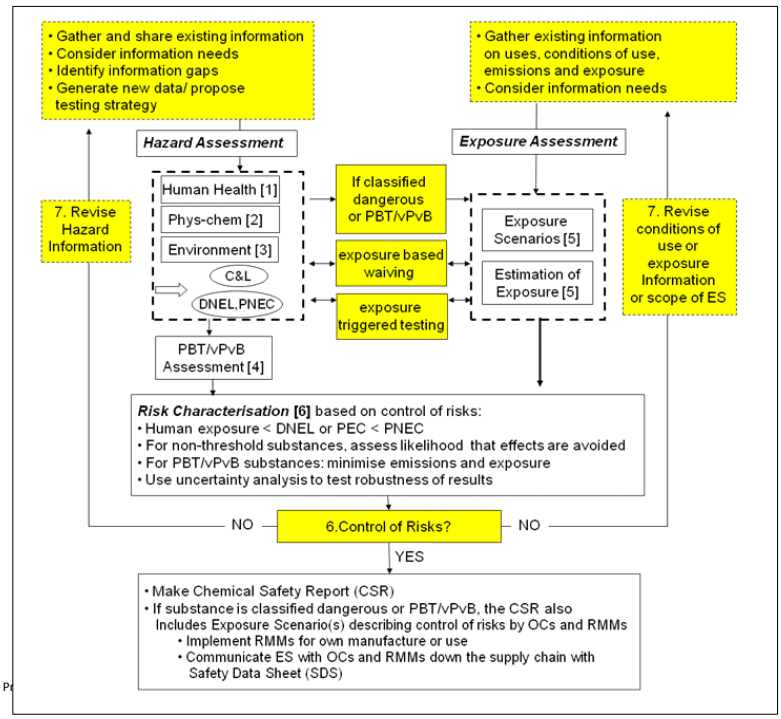
No GLP Studies?

NO GLP data may be used for the risk assessment, if valid conclusions can be drawn from them.

This means that the data, and the test methods used to generate them, must be evaluated in order to determine whether they are of sufficient quality for use in risk assessment. Such an evaluation will require the use of expert judgement, but the determination of data as being valid or not valid must be both justified and transparent.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium



Environment and Climate Regional Accession Network ECRAN

Hazard/Risk Communication

Extended Safety Data Sheet – Exposure Scenario

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

1. ES 1: Formulation. Various products

1.1. Title section

Environment	
CS 1: *Formulation of mixtures*	ERC 2
Worker	
CS 2: *Raw material transfer and/or dispensing with dedicated equipment*	PROC 8b
CS 3: Mixing, milling, dispersing, completion. Batch. Closed systems	PROC 3
CS 4: Mixing, milling, dispersing, completion. Batch. Open systems	PROC 5
CS 5: *Transfer and/or dispensing with non-dedicated equipment*	PROC 8a
CS 6: *Transfer and/or dispensing with dedicated equipment*	PROC 8b
CS 7: *Filling small containers in dedicated lines*	PROC 9
CS 8: Equipment cleaning and maintenance	PROC 8a

Comment [ECHA1]: Formulation takes place in a range of industrial settings, from environments where good control standards apply to those where control are limited or non-existant. This exposure scenario assumes that industrial control standards apply

Comment [ECHA2]: A field "ES name" that provides a short description of the scope of the ES can be included here. This will be considered for implementation in the next version of Chesar.

Comment [ECHA3]: The approach to describing open and closed processes is under consideration. In this example, it is stated in the CS title whether the process is open or closed

1.2. Conditions of use affecting exposure

1.2.1. Control of environmental exposure: *Formulation of mixtures* (ERC 2)

Amount used, frequency and duration of use (or from service life)
Daily amount per site <= 0.5 tonnes/day
Annual amount per site <= 100.0 tonnes/year
Technical and organisational conditions and measures
Collect water from process and/or cleaning operation as waste
Conditions and measures related to treatment of waste (including article waste)
Hazardous waste incineration

Comment [ECHA4]: Some conditions of use (e.g. indoor use, basic general ventilation, process temperature) are valid for all workers' contributing scenarios. These "common conditions of use" could be reported in one place. This will be considered for implementation in the next version of Chesar.

Comment [ECHA5]: The numbering of the contributing scenario (CS1, CS2, ... as it is in the Title section) could be included here. This will be considered for implementation in the next version of Chesar.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

1.2.2. Control of worker exposure: *Raw material transfer and/or dispensing with dedicated equipment* (PROC 8b)

Product (article) characteristics
Covers percentage substance in the product up to 100 %.
Amount used (or contained in articles), frequency and duration of use/exposure
Avoid carrying out activities involving exposure for more than 1 hour. *The duration specified here is within the context of an eight hour work day*
Technical and organisational conditions and measures
Provide a basic standard of general ventilation (1 to 3 air changes per hour).
Conditions and measures related to personal protection, hygiene and health evaluation
Wear suitable gloves tested to EN374. For further specification, refer to section 8 of the SDS.
Use suitable eye protection.
Other conditions affecting workers exposure
Indoor use
Assumes process temperature up to 40.0 °C

Comment [ECHA6]: Although this statement does not constrain the use of the substance, it is included because making explicit the upper boundaries for concentration and duration increases clarity for the recipients.

ESCom standard phrases for concentration of 100% and duration of 8 hours include the statement "unless otherwise stated". This statement was removed as it is preferable that any other different limits that apply are given.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

1.3.2. Worker exposure: *Raw material transfer and/or dispensing with dedicated equipment* (PROC 8b)

Route of exposure and type of effects	Exposure estimate	RCR
Inhalation, systemic, long-term	12.5 mg/m³ (TRA Worker 3.0)	0.506
Dermal, systemic, long-term	2.742 mg/kg bw/day (TRA Worker 3.0)	0.392
Combined routes, systemic, long-term		0.898

1.3.3. Worker exposure: Mixing, milling, dispersing, completion. Batch. Closed systems (PROC 3)

Route of exposure and type of effects	Exposure estimate	RCR
Inhalation, systemic, long-term	3.75 mg/m³ (TRA Worker 3.0)	0.152
Dermal, systemic, long-term	0.69 mg/kg bw/day (TRA Worker 3.0)	0.099
Combined routes, systemic, long-term		0.25

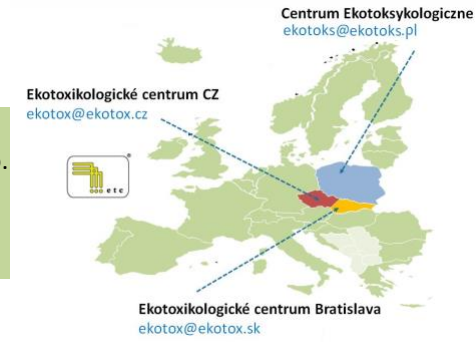
1.3.4. Worker exposure: Mixing, milling, dispersing, completion. Batch. Open systems (PROC 5)

Route of exposure and type of effects	Exposure estimate	RCR
Inhalation, systemic, long-term	6.25 mg/m³ (TRA Worker 3.0)	0.253
Dermal, systemic, long-term	2.742 mg/kg bw/day (TRA Worker 3.0)	0.392
Combined routes, systemic, long-term		0.645

Environment and Climate Regional Accession Network ECRAN

Questions? Comments?

Martin Murín, MSc.
Ekotoxikologické centrum Bratislava s.r.o.
Ekotoxikologické centrum CZ s.r.o.
Centrum Ekotoksykologiczne Sp. z o.o.
www.ekotox.eu



This Project is funded by the European Union