Environment and Climate Regional Accession Network ECRAN

Introduction Human Health Risk Assessment - General

Ike van der Putte

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Basic Toxicology and Risk Assessment

Ref. ECRAN IED/Chemicals WG
Montenegro
13-15 May 2014

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Chemicals & Hazards


explosive


corrosive


environmental danger


flammable

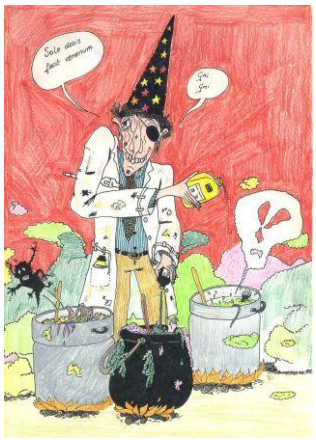

oxidative

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

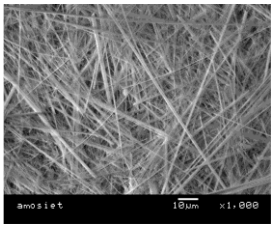
Environment and Climate Regional Accession Network ECRAN

Chemicals and Toxicity



Paracelsus:"Dosis Sola Facit Venenum"
(it is the dose which makes the poison)

Substance	LD50 (mg/kg bw)
Ethanol	7000
Sodium chloride	3000
Cupric sulphate	1500
DDT	100
Nicotine	60
Tetrodotoxin	0.02
Dioxin (TCDD)	0.02

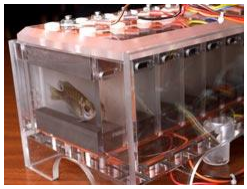


Asbestos

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

VARIOUS TEST SYSTEMS AND ANIMALS



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Case determine LC50

Dose (mg/l)	% alive	% mortality
0	100	
1.9	90	
2.69	84	
4.28	62	
8.51	16	
15	0	

Step:

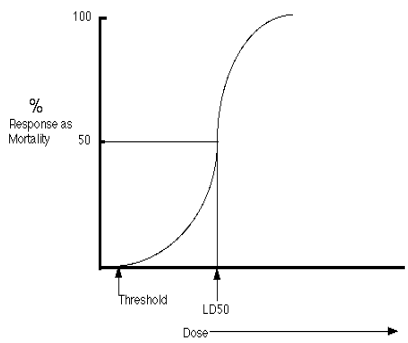
1. Draw graphic

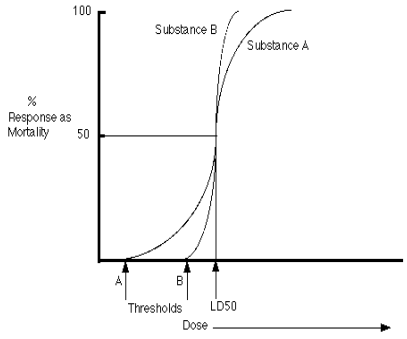
2. Read out the LC50

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

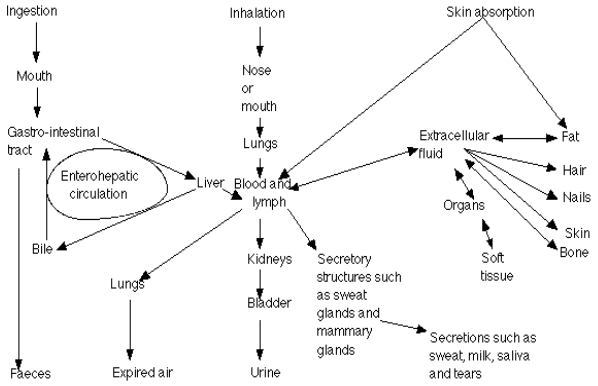
The Relationship of Dose or Concentration of a Toxicant to the Response Produced in Terms of Mortality





Environment and Climate Regional Accession Network ECRAN

Routes of absorption, distribution and excretion of potentially toxic substances



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Accidents & chemicals

Minamata -MeHg

Bhopal- MIC

Seveso- TCP/Dioxins

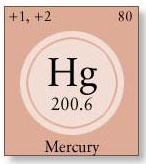
Basel (Sandoz)- pesticides

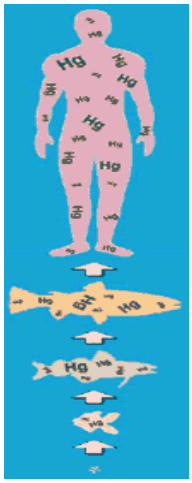
This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Minamata disease



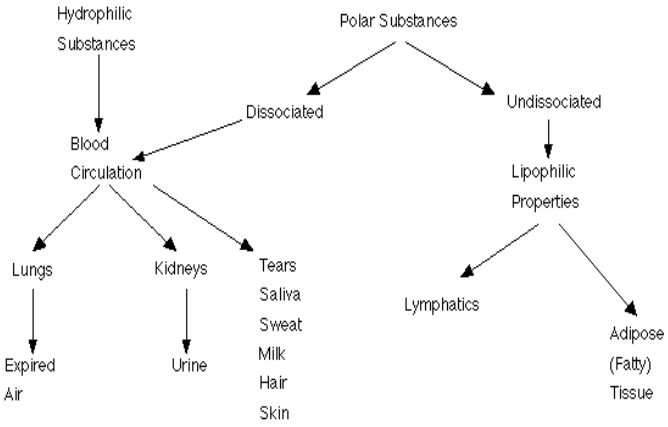


This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

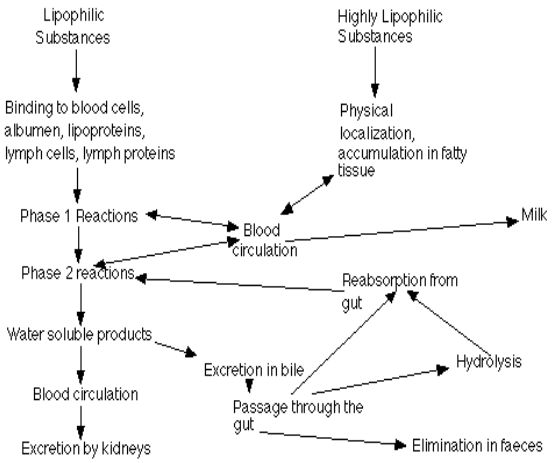
Distribution and excretion of potentially toxic substances which are hydrophilic or polar



1

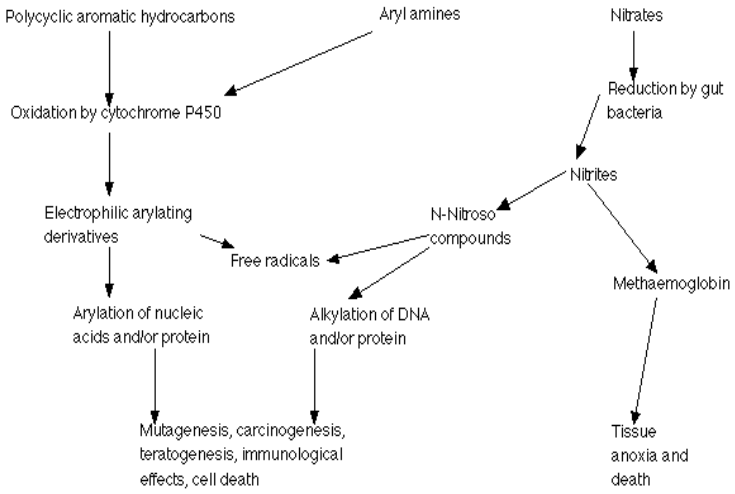
Environment and Climate Regional Accession Network ECRAN

Distribution and excretion of potentially toxic substances which are lipophilic



Environment and Climate Regional Accession Network ECRAN

Examples of biotoxification

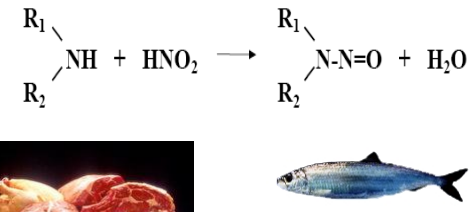


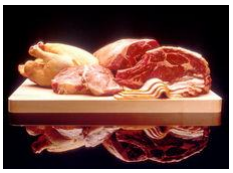
Environment and Climate Regional Accession Network ECRAN

NITRATE/NITRITE/NITROSAMINES

Nitrate ***mouth bacteria*** Nitrite

Stomach





This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

"Lethal Synthesis (rat poison-fluoro-acetic acid)"

Fluoroacetic acid (ingested)

↓

Fluorocitric acid

↓

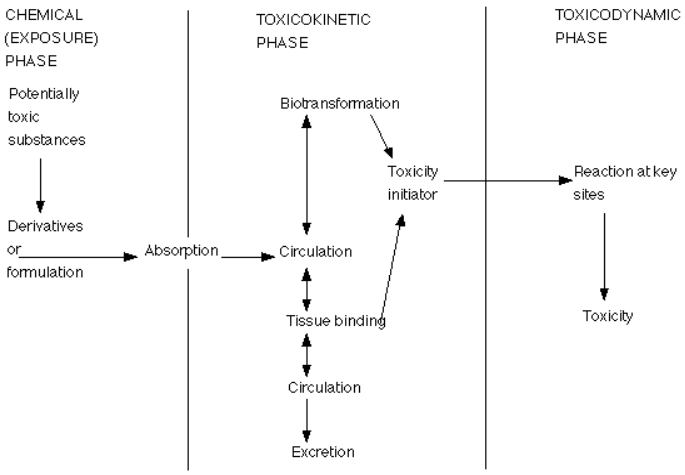
Inhibition of aconitase

↓

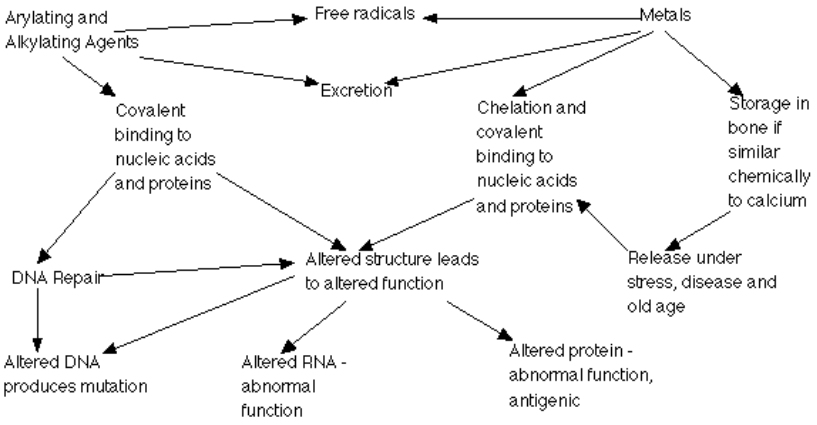
Citric acid cycle block

Environment and Climate Regional Accession Network ECRAN

Phases in the production of toxicity

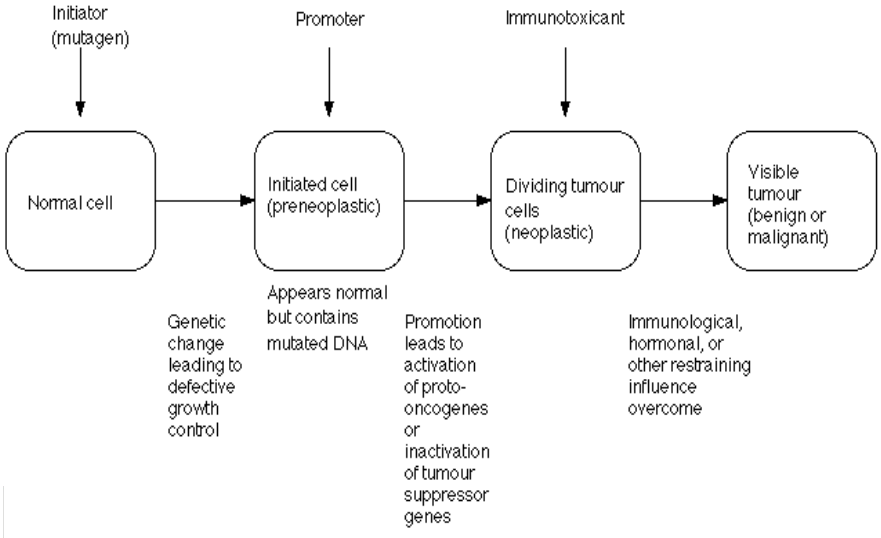


Main steps in biotransformation of potentially toxic substances which are arylating or alkylating agents or metals



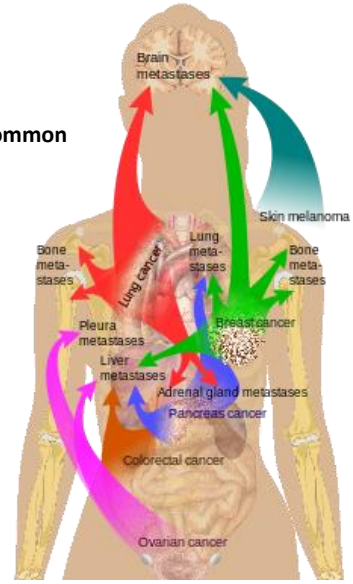
Environment and Climate Regional Accession Network ECRAN

Steps in the development of tumors



Environment and Climate Regional Accession Network ECRAN

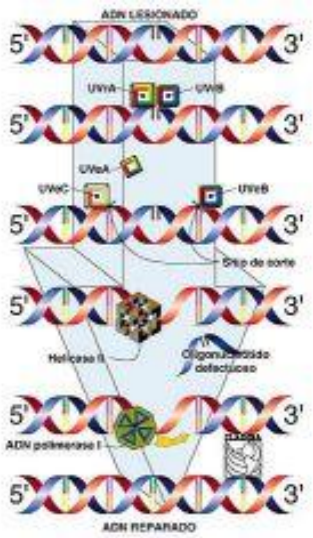
Metastases for common cancer types



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

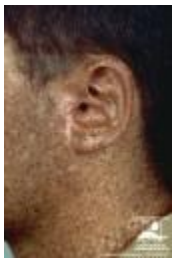
Environment and Climate Regional Accession Network ECRAN



EXCISSION REPAIR MECHANISM

DNA lesions

(missing enzyme:example people sufferingfrom Xeroderma Pigmentosum)

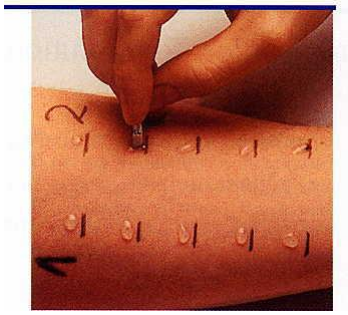


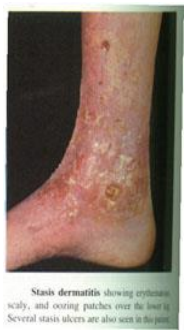
This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Allergic reactions

chemical → combine with proteins → allergen → antibodies





Stasis dermatitis showing erythema, scaly, and oozing patches over the lower leg. Several stasis ulcers are also seen in this joint.

Environment and Climate Regional Accession Network ECRAN

Interactions in toxicity

1 + 1 = 2, 1 + 5 = 6 (additive: eg. organophosphate pesticides)

1+ 1= 4, 1+ 5= 10 (synergistic: eg. asbestos and cigarette smoke increase risk of lung cancer with factor 40)

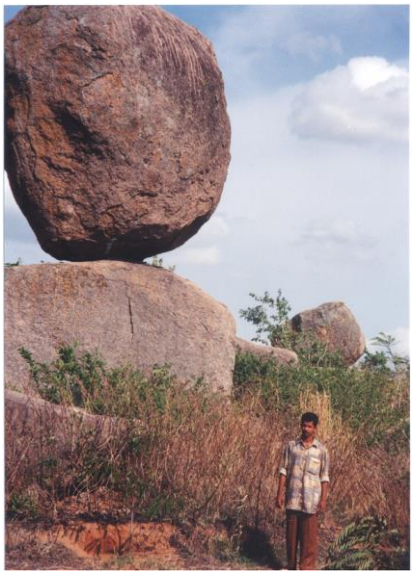
1+1=0, 1+5= 2 (antagonism: eg. some metals)

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

HAZARD and RISK



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

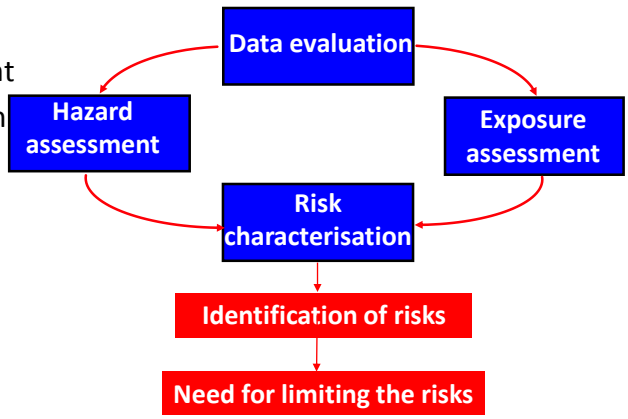
Principles of Health Risk assessment

Data evaluation: hazard identification

Hazard assessment

Exposure assessment

Risk characterisation



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Hazard identification - step 1

Hazards include:

- Physico-chemical hazards (main hazards are fire and explosion in this group)
- Hazards to health (divided in acute and chronic effects; local and systemic effects and; reversible an irreversible effects).

For example, skin irritation is an acute, local, reversible effect, whereas liver cancer is chronic, systemic and irreversible

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Hazard/Effects Assessment - step 2

Effects human health

- ✓ acute toxicity;
- ✓ irritation;
- ✓ corrosivity;
- ✓ sensitisation;
- ✓ repeated dose toxicity;
- ✓ mutagenicity;
- ✓ carcinogenicity;
- ✓ toxicity for reproduction.

Laboratory NELs converted to DNELs
by applying “uncertainty factors” (range 10 - 10,000)

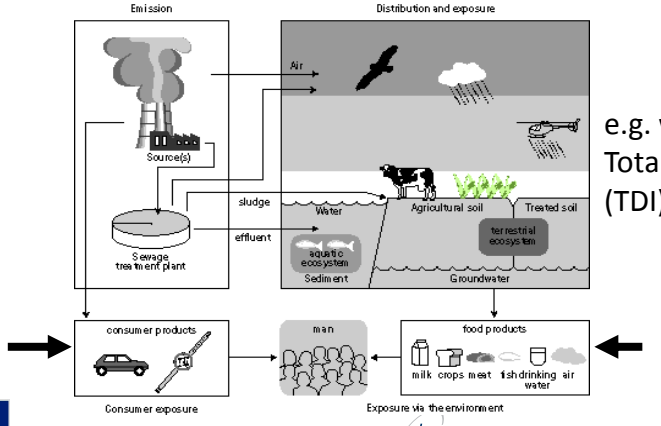
This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure Assessment - step 3.1

1. Consumers
2. Human exposure via the environment



e.g. what is the Total Daily Intake (TDI)?

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure Assessment - step 3.2

3. Workers (occupational exposure)

e.g. What is the exposure concentration 8-hr TWA in mg/m3 as percentage of the TLV, PEL or MAK)?

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Risk Characterization - step 4

Risk characterization is the estimation of the incidence and severity of the adverse effects likely to occur in the human population due to actual or predicted exposure.

= integration of step 1-3

When risk is not neglegible (eg TDI higher than 0.1(NEL or DNEL))

→ **Acceptable, tolerable or not?**

Is 1 in 50 000 risk of death each year acceptable, or should it be 1 in 100 000, or more?

= Risk Management ←

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

EU regulatory framework (REACH/CLP)

INTRODUCTION Human Health Risk Assessment

(REACH Guidance)

This Project is funded by the European Union

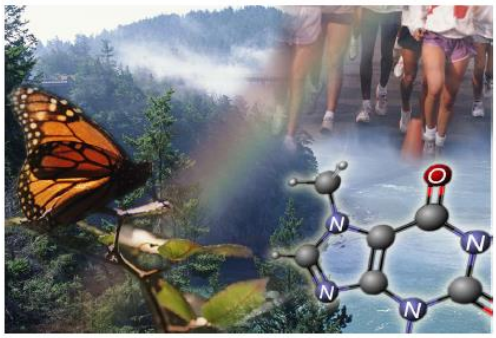
Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

ECHA

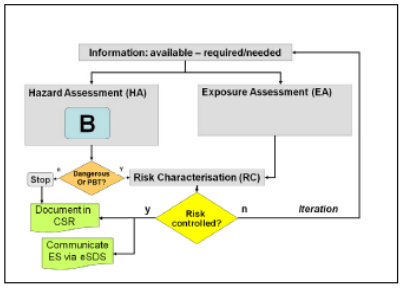
Guidance on information requirements and chemical safety assessment

Part B: Hazard Assessment



May 2008

Guidance for the implementation of REACH

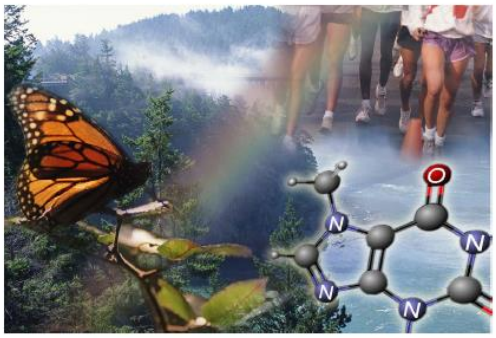


Environment and Climate Regional Accession Network ECRAN

ECHA

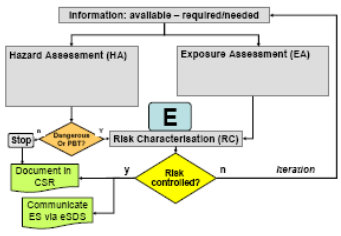
Guidance on information requirements and chemical safety assessment

Part E: Risk Characterisation



May 2008

Guidance for the implementation of REACH



Environment and Climate Regional Accession Network ECRAN

Steps in the hazard assessment

Step 1: Evaluation of non-human information
Step 2: Evaluation of human information
Step 3: Classification and Labelling
Step 4: Derivation of DNELs* (or DMELs*)

- DNEL: Derived No Toxic Effect Level*
- DMEL: Derived Minimal Effect Level (for non-threshold Carcinogens)*

This Project is funded by the European pps.nl Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Information Gathering and Evaluation

Step 1: Gather and share existing information
Step 2: Consider information needs
Step 3: Identify information gaps
Step 4: Generate new information or propose a testing strategy

Information sources

- *in-house company and trade association files (including test data)*
- *databanks and databases of compiled data*
- *agreed data sets such as the OECD HPV Chemicals Program*
- *published literature*
- *internet search engines and relevant websites*
- *(Q)SAR models (Section R.6.1)*
- *data sharing in the substance information exchange forum (SIEF)*

This Project is funded by the European pps.nl Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Reliability of data

Klimisch code (scoring system) for 4 catagories

1. Reliable without restrictions
2. Reliable with restrictions
3. Not reliable
4. Not assignable

New toxicology and ecotoxicology tests must be based on GLP (OECD and EU protocols)

Others must be carefully evaluated

This Project is funded by the European pps.nl

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Registrations requirements (1)

- Registration dossier:
  - ≥1 tonne: Technical dossier
  - ≥10 tonnes: with Chemical Safety Report (CSR)
- Information requirements:
  - 1-10 tonnes: available phys-chem, tox and ecotox information + Phys-chem properties in Annex VII (full Annex VII for substances meeting Annex III criteria)
  - 10-100 tonnes: Annex VII & VIII
  - 100-1000 tonnes: Annex VII & VIII; test proposals for information in Annex IX
  - ≥ 1000 tonnes: Annex VII & VIII; test proposals for information in Annex IX & X

This Project is funded by the European pps.nl

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

Manufacture/import of 1 tonne or more/year

- State of the substance at 20 oC and 101,3 kPa
- Melting/freezing point (Section R.7.1.2)
- Boiling point (Section R.7.1.3)
- Relative density (Section R.7.1.4)
- Vapour pressure (Section R.7.1.5)
- Surface tension (Section R.7.1.6)
- Water solubility (Section R.7.1.7)
- Partition coefficient in-octanol/water (Section R.7.1.8)
- Flash-point (Section R.7.1.9)
- Flammability (Section R.7.1.10)
- Explosive properties (Section R.7.1.11)
- Self-ignition temperature (Section R.7.1.12)
- Oxidising properties (Section R.7.1.13)
- Granulometry (Section R.7.1.14)

Physico-chemical properties

Manufacture/import of 100 tonnes or more/year

-Stability in organic solvents and identity of relevant degradation products (only if stability of the substance is considered to be critical)

Dissociation constant (Section R.7.1.17)

- Viscosity (Section R.7.1.18)

Environment and Climate Regional Accession Network ECRAN

European Commission - DG Environment

Registration Requirements (2)

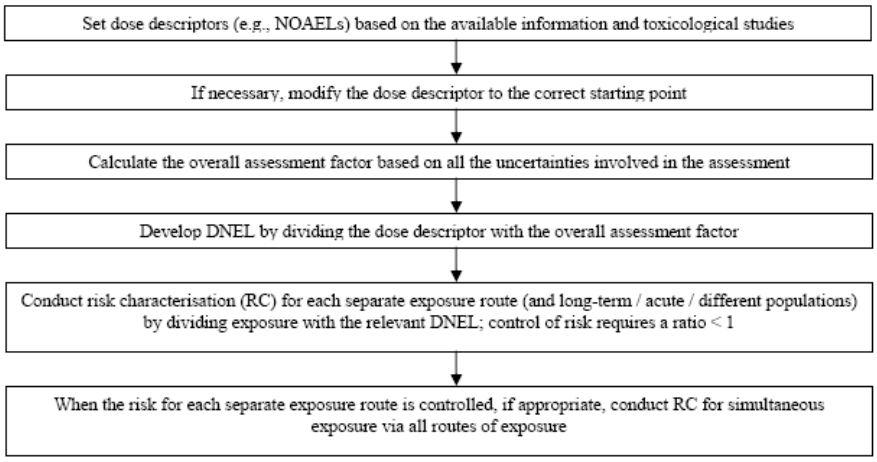
	Health	Environment
1-10t prioritised	❑ *In vitro* skin and eye irritation ❑ Skin sensitiation ❑ *In vitro* mutagenicity ❑ Acute toxicity (one route)	❑ Acute aquatic toxicity – Daphnia ❑ Biodegradation – biodegradability and hydrolysis ❑ Acute aquatic toxicity – Algae
10-100t	❑ *In vivo* skin and eye irritation ❑ Further *in vitro* mutagenicity ❑ Sub acute toxicity (28 days) ❑ Reproductive toxicity screen	❑ Acute aquatic toxicity – Fish ❑ Activated sludge ❑ Adsorption/desorption screening
100-1000t	❑ Further mutagenicity tests ❑ Sub-chronic toxicity (90-days) ❑ Further reproductive toxicity tests	❑ Long term aquatic toxicity daphnia and fish ❑ Further degradation and fate/behaviour studies ❑ Short term effects on terrestrial organisms
>1000t	❑ Further mutagenicity tests ❑ Carcinogenicity ❑ Chronic toxicity ❑ Further reproductive toxicity tests	❑ Further degradation and fate/behaviour studies ❑ Long term effects on terrestrial organisms

This Project is funded by the European pps.nl

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Illustration of the different steps of the quantitative human health risk assessment for threshold endpoints



This Project is funded by the European pps.nl

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

How to derive DNEL(s)

1. Identifying dose descriptors and deciding on mode of action

As part of the evaluation of the toxicity studies, dose descriptors (e.g., NOAEL, NOAEC, BMD, LD50, LC50, T25) should be identified for the endpoint concerned.

If no treshold mode of action (eg. Geno-toxic carcinogen)

→ **DMEL** derivation

This Project is funded by the European pps.nl

human dynamics public sector consulting Project implemented by Human Dynamics Consortium

How to derive DNEL(s)

2. Application of Assessment Factors (AFs)
To compensate for uncertainties (intra-/interspecies, Quality, exposure duration etc.)

$$Endpoint-specific \quad DNEL = \frac{NOAEL_{corr}}{AF_1 * AF_2 * \_ * AF_n} = \frac{NOAEL_{corr}}{Overall \quad AF}$$

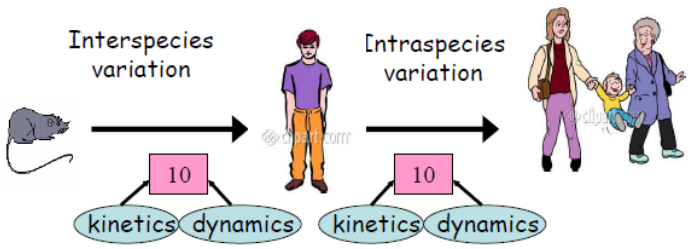
This Project is funded by the European pps.nl

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

ECHA European Chemicals Agency

Basic assessment factors



This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Local vs Systemic Health Effects

A **Local effect** refers to an adverse health effect that takes place at the point or area of contact. The site may be skin, mucous membranes, the respiratory tract, gastrointestinal system, eyes, etc. Absorption does not necessarily occur.

Examples: strong acids or alkalis.

Systemic effect refers to an adverse health effect that takes place at a location distant from the body's initial point of contact and presupposes absorption has taken place.

Examples: arsenic effects to the blood, nervous system, liver, kidneys and skin; benzene effects to the bone marrow.

Environment and Climate Regional Accession Network ECRAN

How to derive DNEL(s)

3. Select the leading health effect(s) for relevant exposure patterns

The critical DN(M)EL, used for the (semi-)quantitative risk characterisation, should be the lowest DN(M)EL obtained for the relevant combination of population/route/exposure pattern.

For both **acute and long-term local effects**, DNELs may need to be set for workers and the general population exposed via the dermal and inhalation routes (i.e., four local DNELs).

For **systemic, long-term effects**, long-term DNELs are needed for worker dermal and inhalation exposure routes.
Additionally, three long-term DNELs may need to be set for the general population (dermal, oral and/or inhalation) (ref consumer products and environmental contaminants)

This Project is funded by the European pps.nl Project implemented by Human Dynamics Consortium

Risk characterisation ratios (RCRs)

RCR = Exposure /DNEL

If Exposure < DNEL → Risk is adequately controlled

If Exposure > DNEL → Risk is NOT controlled

Environment Human health

$$RCR = \frac{PEC}{PNEC} \text{ or } \frac{Exposure}{DNEL}$$

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Risk Assessment under REACH

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Basic risk assessment principles

Hazard Assessment →	Hazard identification Dose - effect assessment	DNEL/DMEL PNEC
Exposure Assessment →	Quantification of exposure (direct and indirect)	Upper exposure level PEC
Risk Characterisation →	Assessment of actual risk	Upper exposure level/DNEL < 1 PEC / PNEC < 1

** DNEL: Derived No Toxic Effect Level*
** DMEL: Derived Minimal Effect Level (for non-threshold Carcinogens)*
** PNEC: Predicted No Effect Concentration (for the environment)*

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Steps in Hazard Assessment

Step 1: Evaluation and integration of available information

Step 2: Classification and Labelling

Step 3: Derivation of the hazard threshold levels for human and the environment (DNEL/DMEL, PNEC)

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Hazard Assessment
- Step 1: Evaluation and integration of available information

- Registration dossier:
  - ≥1 tonne: Technical dossier
  - ≥10 tonnes: with Chemical Safety Report (CSR)

- Information requirements:
  - 1-10 tonnes: available phys-chem, tox and ecotox information + Phys-chem properties in Annex VII (full Annex VII for substances meeting Annex III criteria)
  - 10-100 tonnes: Annex VII & VIII
  - 100-1000 tonnes: Annex VII & VIII; test proposals for information in Annex IX
  - ≥ 1000 tonnes: Annex VII & VIII; test proposals for information in Annex IX & X

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

REACH Registration Requirements

Tonnage	Physico-chemical properties
≥ 1 t/y	State of the substance at 20 °C and 101,3 kPa Smelting/freezing point Boiling point Relative density Vapour pressure Surface tension Water solubility Partition coefficient in-octanol/water Flash-point Flammability Explosive properties Self-ignition temperature Oxidising properties Granulometry
≥ 100 t/y	Stability in organic solvents and identity of relevant degradation products Dissociation constant Viscosity

Tonnage	Health	Environment
1-10 t/y prioritised	In vitro skin and eye irritation Skin sensitiation In vitro mutagenicity Acute toxicity (one route)	Acute aquatic toxicity-Daphnia Biodegradation-biodegradability and hydrolysis Acute aquatic toxicity-Algae
10-100 t/y	In vivo skin and eye irritation Further in vitro mutagenicity Sub acute toxicity (28 days) Reproductive toxicity screen	Acute aquatic toxicity-Fish Activated sludge Adsorption/desorption screening
100-1000 t/y	Further mutagenicity tests Sub-chronic toxicity (90 days) Further reproductive toxicity tests	Long term aquatic toxicity daphnia and fish Further degradation and fate/behaviour studies Short term effects on terrestrial organisms
> 1000 t/y	Further mutagenicity tests Carcinogenicity Chronic toxicity Further reproductive toxicity tests	Futher degradation and fate/behaviour studies Long term effects on terrestrial organis

Environment and Climate Regional Accession Network ECRAN

Step 1: Evaluation and integration of available information

Information Gathering

1: Gather and share existing information
2: Consider information needs
3: Identify information gaps
4: Generate new information or propose a testing strategy

Information sources

- ✓ *in-house company and trade association files (including test data)*
- ✓ *databanks and databases of compiled data*
- ✓ *agreed data sets such as the OECD HPV Chemicals Program*
- ✓ *published literature*
- ✓ *internet search engines and relevant websites*
- ✓ *(Q)SAR models (Section R.6.1)*
- ✓ *data sharing in the substance information exchange forum (SIEF)*

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Step 1: Evaluation and integration of available information

Evaluation of available information

- ✓ Relevance
- ✓ Reliability

Klimisch code (scoring system) for 4 categories

1. Reliable without restrictions
2. Reliable with restrictions
3. Not reliable
4. Not assignable

- ✓ Adequacy
  - ➢ Test data
  - ➢ Non-testing data
  - ➢ Human data

✓*New toxicology and ecotoxicology tests must be based on GLP (OECD and EU protocols)*

✓*Others must be carefully evaluated*

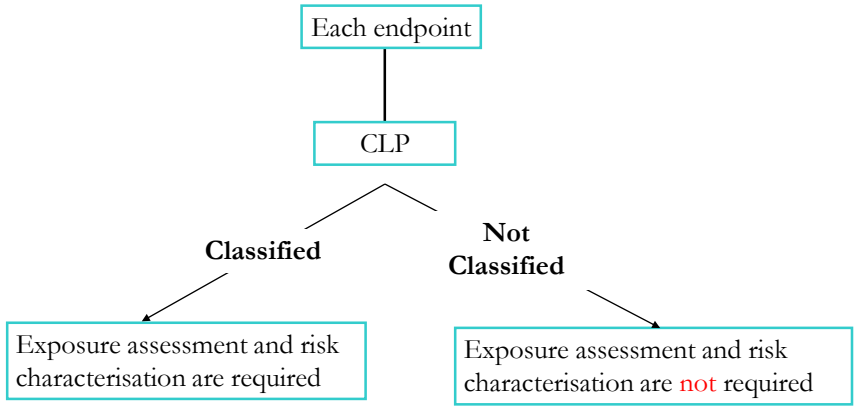
The weight of evidence (WoE) approach

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Step 2: Classification and Labelling



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

Environment and Climate Regional Accession Network ECRAN

Step 3: Derivation of the hazard threshold levels - DNEL(s)/DMEL

1. Identifying dose descriptors and deciding on mode of action

As part of the evaluation of the toxicity studies, dose descriptors (e.g., NOAEL, NOAEC, BMD, LD50, LC50, T25) should be identified for the endpoint concerned.

→ DMEL derivation

If no treshold mode of action (eg. Geno-toxic carcinogen)

2. Application of Assessment Factors (AFs)

To compensate for uncertainties (intra-/interspecies, Quality, exposure duration etc.)

$$Endpoint-specific \quad DNEL = \frac{NOAEL_{corr}}{AF_1 * AF_2 * \_ * AF_n} = \frac{NOAEL_{corr}}{Overall \quad AF}$$

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

Environment and Climate Regional Accession Network ECRAN

Step 3: Derivation of the hazard threshold levels - DNEL(s)/DMEL

Local *vs* Systemic Health Effects

A **Local effect** refers to an adverse health effect that takes place at the point or area of contact. The site may be skin, mucous membranes, the respiratory tract, gastrointestinal system, eyes, etc. Absorption does not necessarily occur.

Examples: strong acids or alkalis.

Systemic effect refers to an adverse health effect that takes place at a location distant from the body's initial point of contact and presupposes absorption has taken place.

Examples: arsenic effects to the blood, nervous system, liver, kidneys and skin; benzene effects to the bone marrow.

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Step 3: Derivation of the hazard threshold levels - DNEL(s)/DMEL

3. Select the leading health effect(s) for relevant exposure patterns

The critical DN(M)EL, used for the (semi-)quantitative risk characterisation, should be the lowest DN(M)EL obtained for the relevant combination of population/route/exposure pattern.

For both **acute and long-term local effects**, DNELs may need to be set for workers and the general population exposed via the dermal and inhalation routes (i.e., four local DNELs).

For **systemic, long-term effects**, long-term DNELs are needed for worker dermal and inhalation exposure routes.

Additionally, three long-term DNELs may need to be set for the general population (dermal, oral and/or inhalation) (ref consumer products and environmental contaminants)

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Step 3: Derivation of the hazard threshold levels - PNEC

$$PNEC_{comp} = \frac{\text{Min } \{EC_{comp}\}}{AF}$$

The lowest valid effect concentration for organisms from the compartment i.e. EC50 or LC50, EC10/NOEC

Assessment factor

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Step 3: Derivation of the hazard threshold levels - PNEC

Data set	Assessment factor (AF)
Lowest short-term L(E)C50 from freshwater or saltwater representatives of three taxonomic groups (algae, crustaceans and fish) of three trophic levels	10,000
Lowest short-term L(E)C50 from freshwater or saltwater representatives of three taxonomic groups (algae, crustaceans and fish) of three trophic levels, + two additional marine taxonomic groups (e.g. echinoderms, molluscs)	1000
One long-term result (e.g. EC10 or NOEC) (from freshwater or saltwater crustacean reproduction or fish growth studies)	1000
Two long-term results (e.g. EC10 or NOEC) from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish)	500
Lowest long-term results (e.g. EC10 or NOEC) from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels	100
Two long-term results (e.g. EC10 or NOEC) from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish) + one long-term result from an additional marine taxonomic group (e.g. echinoderms, molluscs)	50
Lowest long-term results (e.g. EC10 or NOEC) from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels + two long-term results from additional marine taxonomic groups (e.g. echinoderms, molluscs)	10

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure Assessment

- The exposure should, where possible, be described using both **reasonable worst-case** and **typical exposures**
- Actual exposure measurements
- Exposure estimates should be developed by collecting **all necessary information**
- In carrying out the exposure estimation the risk reduction/control measures (RMMs) that are **already** in place **should be taken into account**

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure estimation with measurements and modelling approaches - Occupational Exposure Estimation

Tier 1:

- ✓ ECETOC Targeted Risk Assessment (ECETOC TRA) tool
- ✓ Easy-to-use workplace control scheme for hazardous substances (EMKG/BauA-COSHH) www.baua.de

Higher Tier:

Currently no validated higher Tier exposure tools

- ✓ Stoffenmanager exposure model (Netherlands)
- ✓ RISKOFDERM dermal model
- ✓ Advanced tool for occupational exposure assessment

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure estimation with measurements and modelling approaches - Consumer Exposure Estimation

Tier 1:

ECETOC TRA Consumer tool

Lower tier:

ConsExpo computer tool www.consexpo.nl

Higher tier:

Advanced refinements for ECETOC TRA consumer tool

Others:

US EPS E-Fast model

Web-based GExFRAME system
http://gexframe.jrc.ec.europa.eu/Default.aspx

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Exposure estimation with measurements and modelling approaches - Environmental Exposure Estimation

EUSES http://ecb.jrc.it/euses - Tier 1 assessment

TGD excel sheet (EU TGD 2003 Risk Assessment Spreadsheet Model) – Tier 1 and higher Tiers

Others:

- ✓ FOCUS-models (surface water, agricultural soil)
- ✓ CHARM (offshore installation e.g. drilling and production chemicals, or completion/workover)
- ✓ Emission scenario documents for biocides (ESDs) http://ecb.jrc.it/biocides/

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

Risk characterisation ratios (RCRs)

Environment Human health

$$RCR = \frac{PEC}{PNEC} \text{ or } \frac{Exposure}{DNEL}$$

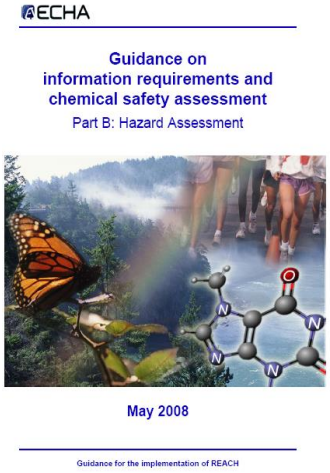
If RCR < 1 → Risk is adequately controlled
If RCR > 1 → Risk is NOT controlled

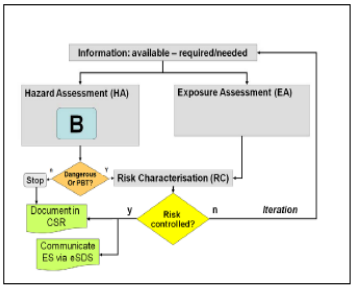
This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

ECHA Guidance - Hazard Assessment





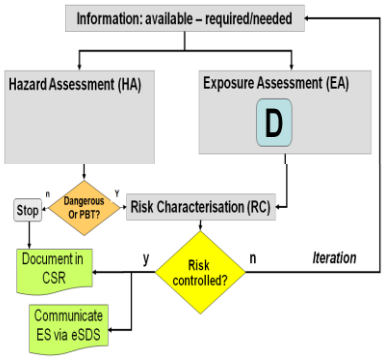
R.7: Endpoint specific guidance
R.8: Characterisation of dose [concentration]-response for human health
R.9: Physico-chemical hazards
R.10: Characterisation of dose [concentration]-response for environment
R.11: PBT Assessment

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

ECHA Guidance – Exposure Assessment



R.12: Use descriptor system

R.13: Risk management measures and operational conditions

R.14: Occupational Exposure Estimation

R.15: Consumer Exposure Estimation

R.16: Environmental Exposure Estimation

R.17: Estimation of exposure from articles

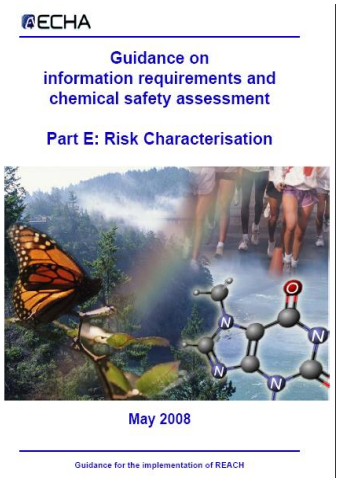
R.18: Estimation of exposure from waste life stage

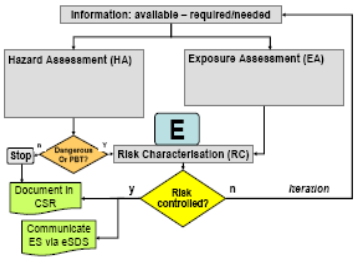
This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Environment and Climate Regional Accession Network ECRAN

ECHA Guidance – Risk Characterization





R.13: Risk management measures and operational conditions

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Chesar stands for Chemical Safety Assessment and Reporting. The tool has been developed by the European Chemicals Agency (ECHA) for supporting registrants under REACH. It suggests a workflow for carrying out exposure assessments and risk characterisations, thereby facilitating the generation of a Chemical Safety Report (CSR) and exposure scenarios for communication.

Note: Chesar includes exposure models for workers and consumers (ECETOC-TRA) and environment (EUSES)

website: http://chesar.echa.europa.eu/

This Project is funded by the European Union

Project implemented by Human Dynamics Consortium

Box 1 Manage substance

Box 2 Report uses

Box 3 Manage exposure estimation

Box 4 Build exposure scenarios for the CSR

Box 5 Build exposure scenarios for the extended SDS

Box 6 Library

Box 7 User 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