Risk Assessment and Exposure

ECETOC: Developing and promoting top quality science in the risk assessment of chemicals"

Chémia 2014

Liptovsky Jan, Slovakia, 24-26 September 2014

Madeleine Laffont, Health Scientist

Introducing ECETOC

1. What is ECETOC?
2. Purpose
3. Work Method
4. Programme in Action (Exposure Assessment)
5. Collaboration – Who we work with

What is ECETOC?

An Industry-funded THINK TANK that develops Tools and Guidance to improve Risk Assessment

- ✓ Scientific
- ✓ Non-political – *we do not lobby. We develop tools and guidance to improve RA*
- ✓ Non-profit
- ✓ Independent
- ✓ Pragmatic – *Practical, Fit For Purpose Tools & Guidance to improve EXISTING FRAMEWORKS*
- ✓Taps directly into industry's expertise, experience and data
- ✓ All Chemical Sectors - *Chemicals, agrochemicals, consumer products, pharmaceuticals, food & beverages, Oil companies*

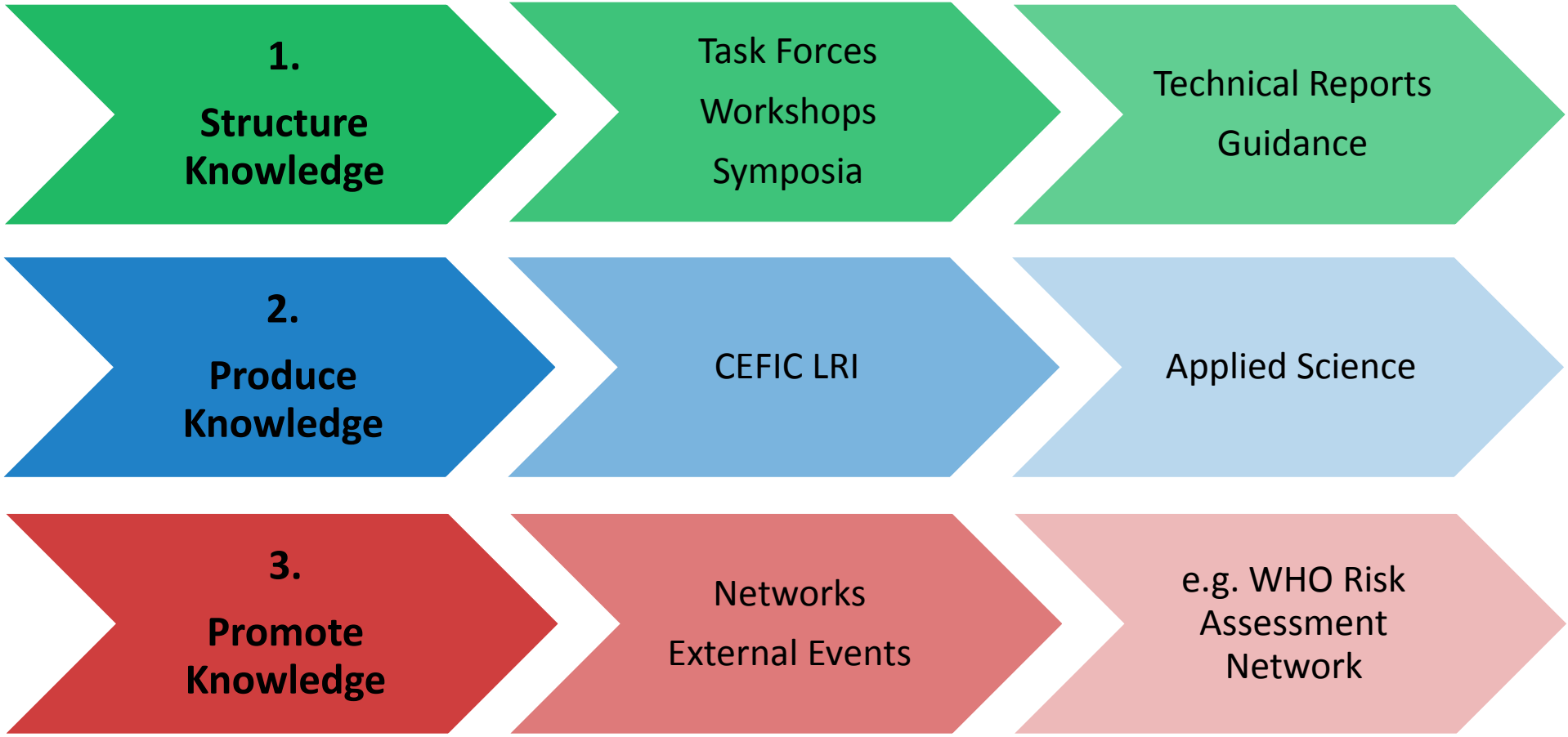
Industry's Voice on Risk Assessment:

A Partner for Regulators and Chemicals Management Institutions

ECETOC's Purpose: Improve Risk Assessment

Safer	(Re)evaluate risk assessment methodologies in light of emerging science.
Faster	**Targeted methods** and tools that fit into **existing frameworks** to speed up risk assessment.
Cost-Effective	ECETOC tools focus on **Regulatory Relevance** and are **Fit For Purpose.**
Save Animals	**New Science** to develop more efficient RA tools and reduce animal testing.
Enable Innovation	More efficient & cost effective RA frees up resources available for innovation.

Work Method:
Transparent Collaboration with Leading Experts



Work Method:
Transparent Collaboration with Leading Experts

Structure Knowledge → Task Forces, Workshops, Symposia → Technical Reports, Guidance

2013	Task Force Technical Reports:
Technical Reports	1. Understanding the relationship between extraction technique and bioavailability
	2. Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals
	3. Evaluation of systemic health effects following dermal exposure to chemicals
	4. Activity-Based Relationships for Aquatic Ecotoxicology Data: Use of the Activity Approach to Strengthen MoA Predictions
	5. Efficacy and Safety of Antidotes for Acute Poisoning by Cyanides
	6. Poorly Soluble Particles / Lung Overload
	7. Environmental Exposure Assessment of Ionisable Organic Compounds
Workshop Reports	1. Assessing Environmental Persistence
	2. 'Omics' and Risk Assessment Science
	3. Mode of Action: Recent Developments, Regulatory Applications and Future Work
	4. Expert Panel to better understand Endocrine Disrupter Low Doses Effects

Work Method:

Structure Knowledge → Task Forces / Workshops / Symposia → Technical Reports / Guidance

ECETOC TF: Potency in Carcinogenicity and Reproductive Toxicity Classification

Review Hypothesis

Journal of Applied Toxicology

Received: 20 March 2014, ... Published online in Wiley Online Library: 25 July 2014

(wileyonlinelibrary.com) DOI 10.1002/jat.3045

A proposal to improve clarity and communication in the EU Classification process for chemicals for carcinogenicity and reproductive and developmental toxicity

J. E. Doe*

ABSTRACT: There is an issue in the EU classification of substances for carcinogenicity and for reproductive or developmental toxicity which has brought difficulties to those involved in the process. The issue lies in the inability of the classification system to distinguish between carcinogens and reproductive toxicants with different levels of concern. This has its origins in the early years of toxicology when it was thought that a relatively small number of chemicals would be either carcinogens or reproductive toxicants, but this has turned out not to be the case. This can cause problems in communicating to the users of chemicals, including the public, the nature of the hazard presented by chemicals. Processes have been developed within the classification system for setting specific concentration limits which assess the degree of hazard for carcinogens and reproductive toxicants as high, medium or low. However these categories are not otherwise used in classification. It is proposed that their wider use would bring the advantages of transparency, clarity of communication, certainty of the process and would allow chemicals with a high degree of hazard to be identified and managed in an appropriate way. Copyright © 2014. The Authors. Journal of Applied Toxicology Published by John Wiley & Sons Ltd.

Keywords: carcinogenicity; reproductive toxicity; classification; degree of hazard; hazard characterization

What is the Issue?

The issue in the EU classification of substances for carcinogenicity and for reproductive toxicity is best summed up by the title of a paper by the inventor of the Ames test 'Chemical Carcinogenesis: Too many rodent carcinogens' (Ames and Gold, 1990). The system is seen to be too restrictive by many; it is seen to be too lenient by others; and it confuses the public. The origins of this issue are complicated and go back more than 40 years. The purpose of this article is to explore the issue and to suggest a way forward.

Background to Classification

Classification, labelling and packaging (CLP) in the EU was originally developed as a way of providing information for the packaging, labelling and sale of chemicals to occur (ECHA, 2012a). Before its introduction there was no agreed way of describing the potential hazardous properties of chemicals. Each company was at liberty to devise its own way of assessing and describing its products, making it difficult for purchasers to decide how to handle them. During the 1970s, individual countries started to develop classification schemes to harmonize activities within their own boundaries, but this did not address the problems of cross border trade. In the 1980s the EU developed a harmonized system across Europe, the 6th Amendment to Dangerous Substances Directive (EEC, 1979), which created one scheme for the whole European Community. In the 2000s attempts have been made to create one globally accepted scheme with the so-called Global Harmonization System (GHS, 2007) under the aegis of the United Nations. In turn, the GHS has been adopted by the EU into the new CLP Regulation introduced in 2008 (EC, 2008).

The range of hazardous properties that classification has embraced has expanded since its inception. Originally it focused on physicochemical hazards such as volatility, flammability and explosivity. The concept was then extended to the harm that chemicals could pose by their toxicity to humans or in the environment. This started with classification based on the results of acute toxicity tests for lethality and local toxicity tests for corrosivity, irritancy and sensitization. These tests have numerical outputs such as LD50, or scores from a rabbit skin or eye irritancy test, which made it possible to set criteria for classification which could be assessed objectively. There continues to be debate over whether the criteria are set in the correct place, but the classification can be determined from the data without relying on the judgement of the assessor.

Bringing Carcinogenicity, Mutagenicity and Reproductive Toxicity into Classification

During the 1980s and 1990s both the science of toxicology and the ambition of Classification grew. It was recognized that

*Correspondence to: J. E. Doe, Parker Doe Partnership LLP, Box 139, Frodsham, Cheshire, WA6 1AZ, UK.
E-mail: john.doe@parkerdoe.com

Parker Doe Partnership LLP, Box 139, Frodsham, Cheshire, WA6 1AZ, United Kingdom

ChemicalWatch
GLOBAL RISK & REGULATION NEWS

Home | News | Briefing | Events | Service Providers | Jobs | Forum | Consc

EU toxicology group pushes potency use in hazard classification

2 September 2014 / Europe, Risk assessment

Potency should become part of the EU classification process for carcinogenicity and reproductive toxicity, according to a paper published in the journal *Regulatory Toxicology and Pharmacology* and linked to by the European Centre for Ecotoxicology and Toxicology of Chemicals (Ecetoc).

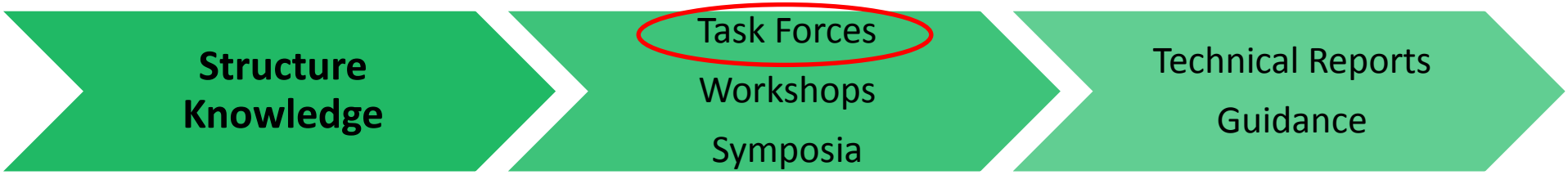
The paper, which stresses that potency is the most important indicator of degree of hazard, says that classification in the EU "does not discriminate across the wide range of potencies seen (six orders of magnitude) for carcinogenicity and for developmental toxicity and fertility. Therefore potency should be included in the classification process."

The study advocates using EU guidelines in order to avoid problems of hazard communication, which may have consequences downstream with the use of inappropriate chemicals.

Further information

- Journal
- Ecetoc

Work Method:



ECETOC TF: Human Health Exposure Data

(Internal dose, External dose, Aggregate/Multiple Exposures)

Develop a Best Practice framework on Human Exposure Data models (end 2014)

- ✓ What types of Exposure Data are required for current and future RA?
- ✓ Review current sources of Exposure Data
- ✓ Identify how more efficient use of Exposure Data can be achieved
- ✓ Using a case-study approach, develop a framework of best practices on how human Exposure Data might be reliably assessed (which exposure models might best be applied, when and with what purpose in mind)
- ✓ Workshop with key stakeholders

Work Method:

Structure Knowledge

Task Forces
Workshops
Symposia

Technical Reports
Guidance

Activities | Publications | News | Links | Members' Website

"Omics and Risk Assessment Science

start_date: 2013-02-25

end_date: 2013-02-26

Description:

'Omics and Risk Assessment Science

25-26 February 2013, Malaga (Spain)

Background

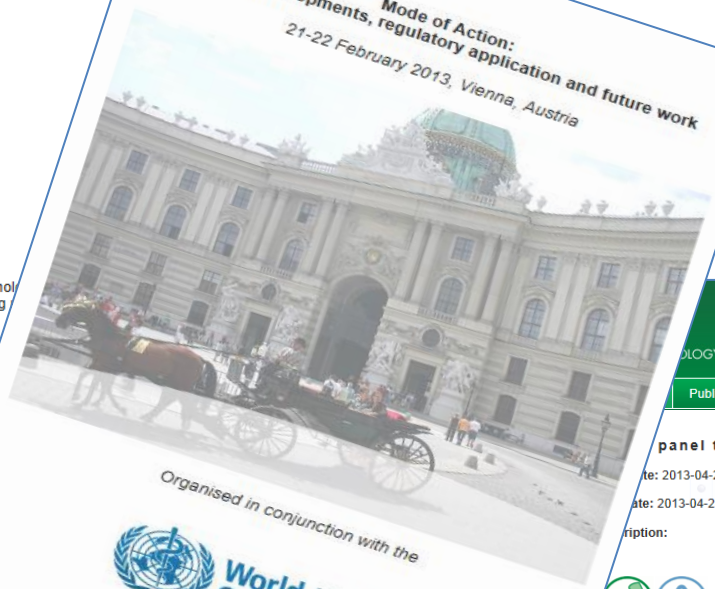
Two previous ECETOC workshops on "The Application of "Omics Technol
Studies and Risk Assessment" took place in 2007 and 2010, the results being
19 respectively. The workshop's main recommendations were:

1) to conduct studies in a more standardised form using reference che

2) to obtain a common and agreed definition of what constitutes a to

3) to study the toxicity dose and time dependent transition on re
through adaptive response, to adverse effect.

Mode of Action:
Recent developments, regulatory application and future work
21-22 February 2013, Vienna, Austria



Organised in conjunction with the
World Health Organization
International Programme on Chemical Safety

Workshop Reports are summaries of the discussions and conclusions derived from ECETOC's workshops. Unlike other ECETOC reports, they are not peer-reviewed by the Scientific Committee.

Choose your language

OLOGY OF CHEMICALS

Publications | News | Links | Members' Website | Search

panel to better understand endocrine disruptor low doses effects

te: 2013-04-22

ate: 2013-04-23

ription:

Environmental Sciences Manager {cms_selflink page="Environmental-Sciences-Manager" text="Malyka Galay Burgos"}

Administrative Assistant {cms_selflink page="secretariat" text="Sonia Pulinckx"}

Reproductive health / Risk, hazard and precaution

22-23 April 2013, Barcelona (Spain)

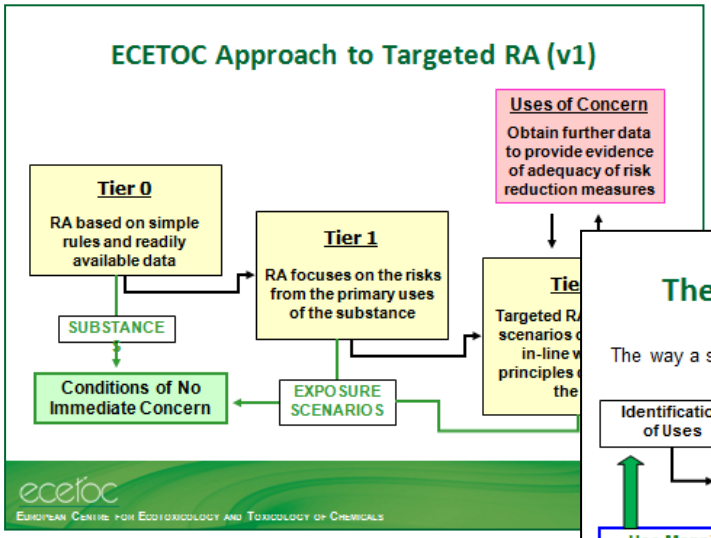
Background

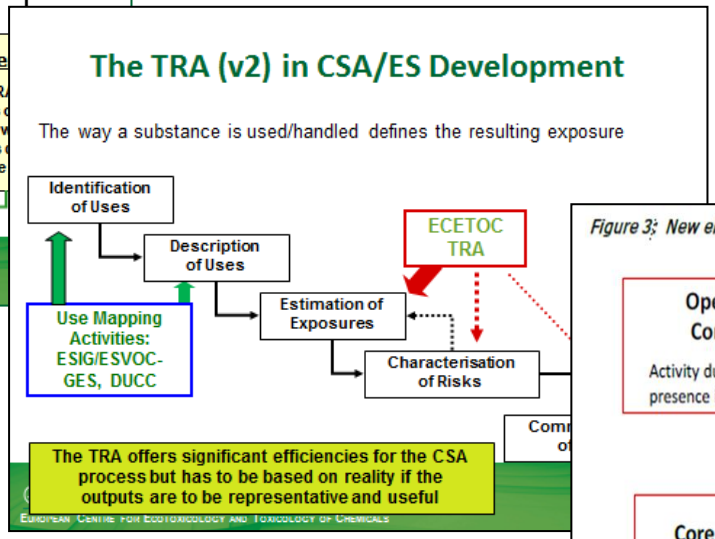
In the field of endocrine disruption, the so-called 'low dose' effects, non-monotonic dose responses (NMDRs), the existence or otherwise of toxic thresholds, mixture effects at low doses, and critical windows of exposure are challenging the current paradigm of toxicology and risk assessment of chemicals. Although the EFSA Opinion on the Hazard Assessment of Endocrine Active Substances (publ. 20 March 2013), and the earlier (June 2012, Parma) EFSA Scientific Colloquium on Low Dose Response in Toxicology and Risk Assessment, both suggest that there is no reason why endocrine active substances (EASs) should not be subject to risk assessment, the issues listed above imply a possible need to make modifications either to the risk assessment paradigm or to current test methods, or both. Furthermore, neither the EFSA Colloquium nor the more recent Workshop on Low Dose Effects and Non-Monotonic Dose Responses for Endocrine Active Chemicals (Sept. 2012, Berlin) were able to reach consensus about the importance, or even the existence, of these issues. This lack of consensus is partly due to uncertainty about the quality of data used to support these concepts, and partly due to a lack of understanding about putative underlying mechanisms of toxicity.

Work Method:

Structure Knowledge → Task Forces, Workshops, Symposia → Technical Reports, Guidance → e.g TRA, Targeted Risk Assessment

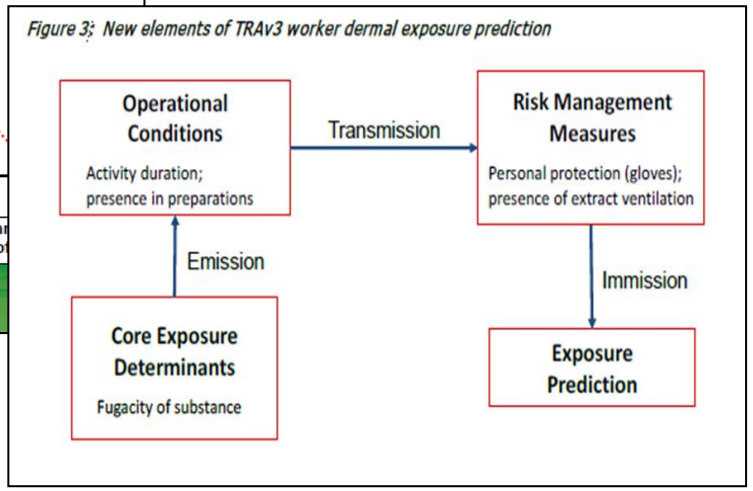
Targeted Risk Assessment Tool: TRA (Targeted Risk Assessment)





The TRA (v3.1) Sept 2014

The TRA (v3)



✓ > 80% of Phase 1 & 2 REACH CSAs are based on the TRA

✓TRA is currently being evaluated outside EU (China, Japan, Canada)

Work Method:

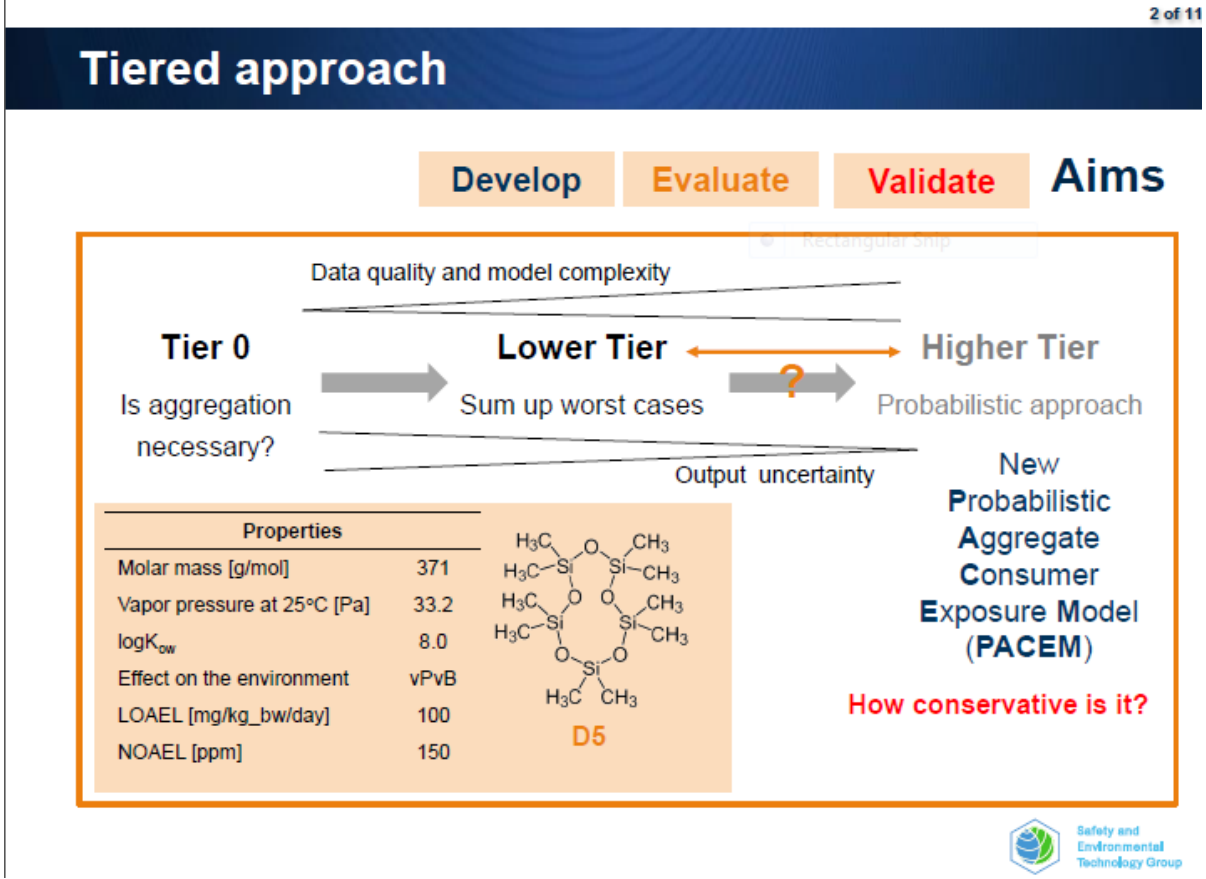
Produce Knowledge → CEFIC LRI → Applied Science

Ongoing	LRI Exposure Projects:
Human Health	1. Predicting indoor air exposure to chemicals/non-chemicals
	2. Computation of tiered aggregate exposure
	3. Consumer exposure to chemicals from multiple sources
	4. Dermal Exposure Assessment
	5. Integrated Assessment Tool (INTEGRA)
	6. Exposure via Dust
	7. In vitro metabolism & mechanisms of action + PBPK modeling
	8. Study of co-exposure (mixtures) to endocrine disruptors at high and low doses
	9. Variability in HBM spot samples – address casual interpretation that one biomonitoring result might result in "B" categorisation
Environment	1. Environmental relevance of biodegradation
	2. Fish bioaccumulation assessment
	3. Tiered approach to assessing trophic magnification factors
	4. Improving OECD 308 tests
	5. Passive sampling & toxicity profiling in surface waters
	6. Bioavailability of non-extractable residues in soil
	7. Prediction of NERs from chemical structures

Work Method:

Produce Knowledge → CEFIC LRI → Applied Science → e.g Aggregate Expousure Models

Tiered approach to Aggregate Exposure Modelling for Consumer Products: Guidance for Exposure Modelling using Case Studies



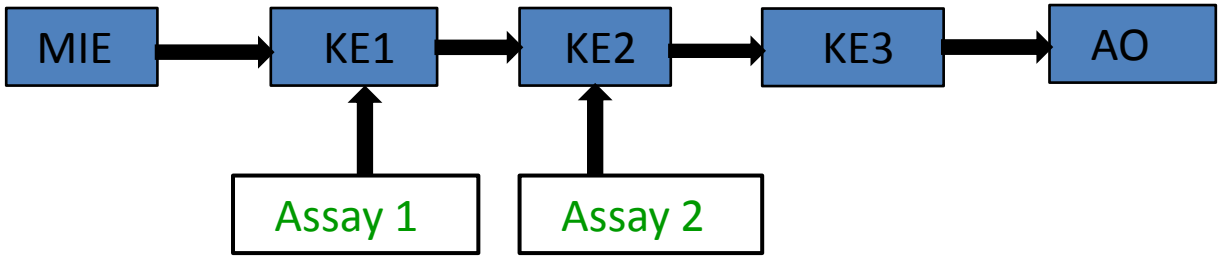
- Is aggregate exposure to consumers really necessary?
- If yes, to which extent should it be aggregated?
- High Tier tools are either not well developed or not publically available
- Develop new tool: publicly available, maintained

Work Method:

Produce Knowledge → CEFIC LRI → Applied Science → e.g AOP for Reproductive Toxicity

LRI Project (Scoping): Qualitative AOP for Reproductive Toxicity

Objective: Use the AOP/MoA Framework as a predictive tool to support read across of reproductive toxicants



Industry & Regulatory Value:

Animal use: Fulfil commitment to reduce animal testing

Time: Weeks rather than years

Financial: 10 of thousands versus 100 of thousands

Data: Reduce concerns about incomplete data sets

Efficiency: Robust Read Across for reproductive toxicants

Collaboration – Who We Work With

33 full member companies, 7 associate member companies

ECHA EUROPEAN CHEMICALS AGENCY

JRC EUROPEAN COMMISSION

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

OECD

World Health Organization

✓Academia

✓NGOs (3R)

Thank you

Madeleine.Laffont@ecetoc.org