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Implementation of toxicological data from other legal provisions (e.g. REACH)

An industry perspective

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Overview

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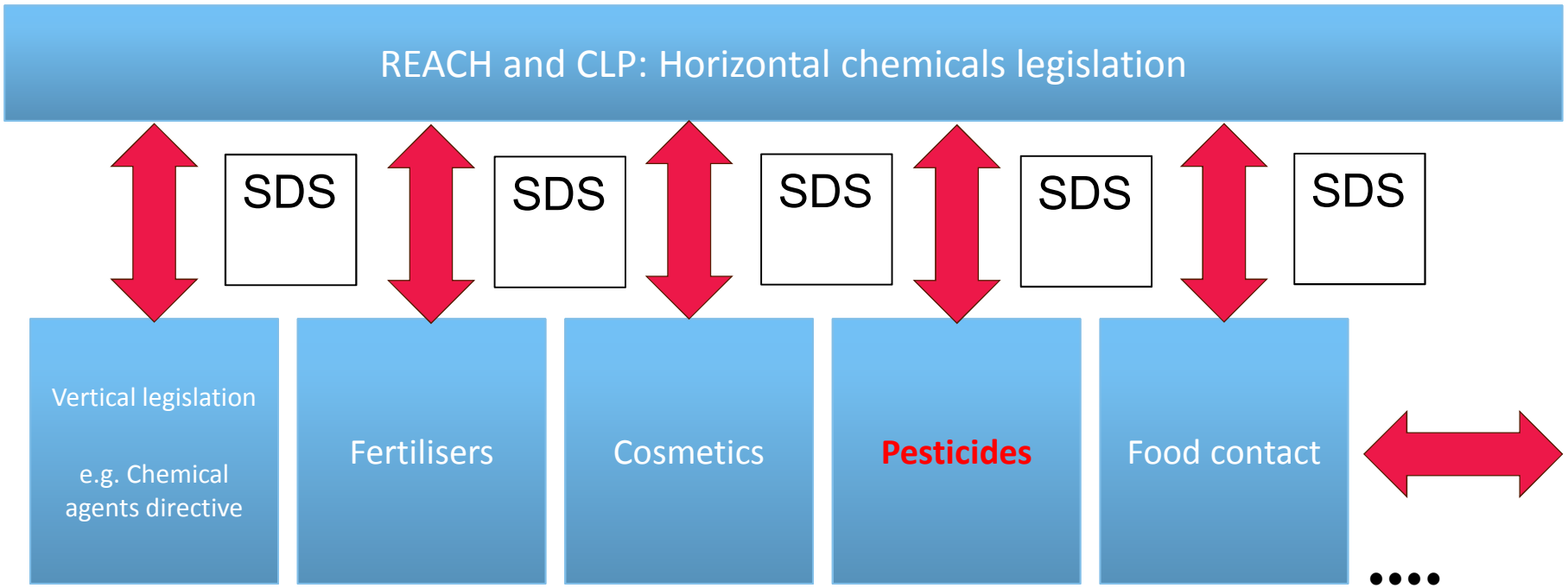
- EU chemicals framework
- Information available from REACH
- Legal considerations
- Use of available databases
- Established frameworks: hazard assessment, risk assessment, SDS

EU chemicals legislation



- Both REACH & CLP are horizontal pieces of legislation, with very few true exemptions.
- REACH & CLP deliver the majority of the common hazard information used by other vertical legislation – for both cut-offs and risk assessments.
- SDS is the legal instrument for hazard communication within the supply chain (and effectively between legislation).
  - Now includes risk management information in exposure scenarios.

Data on co-formulants provided by REACH

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- Co-formulants can either be substances, or mixtures.
- The framework for co-formulant data generation, cost sharing, data protection, prevention of repeated in vivo testing, is already available under REACH. Only the testing of active substances are exempt from these REACH provisions (Article 16(2)).
- Phase-in process ends 31st May 2018: all substances >1tpa must have a REACH registration*. Very likely to encompass all co-formulants supplied in the EU*. All substances >10tpa should have enough data for a quantitative human health risk assessment.
- This data should be made available via the supplier SDS and is intended for use under other vertical legislation, and via the ECHA webpages.
- Important to realise that REACH will not be “finished”. The data sets and interpretations are **dynamic**: continuously being (re)evaluated, generated, updated, with resultant changes in classification and risk assessment.

*Unless they have a valid exemption: e.g. polymers, Annex IV, Annex V, etc

Use of REACH data & information

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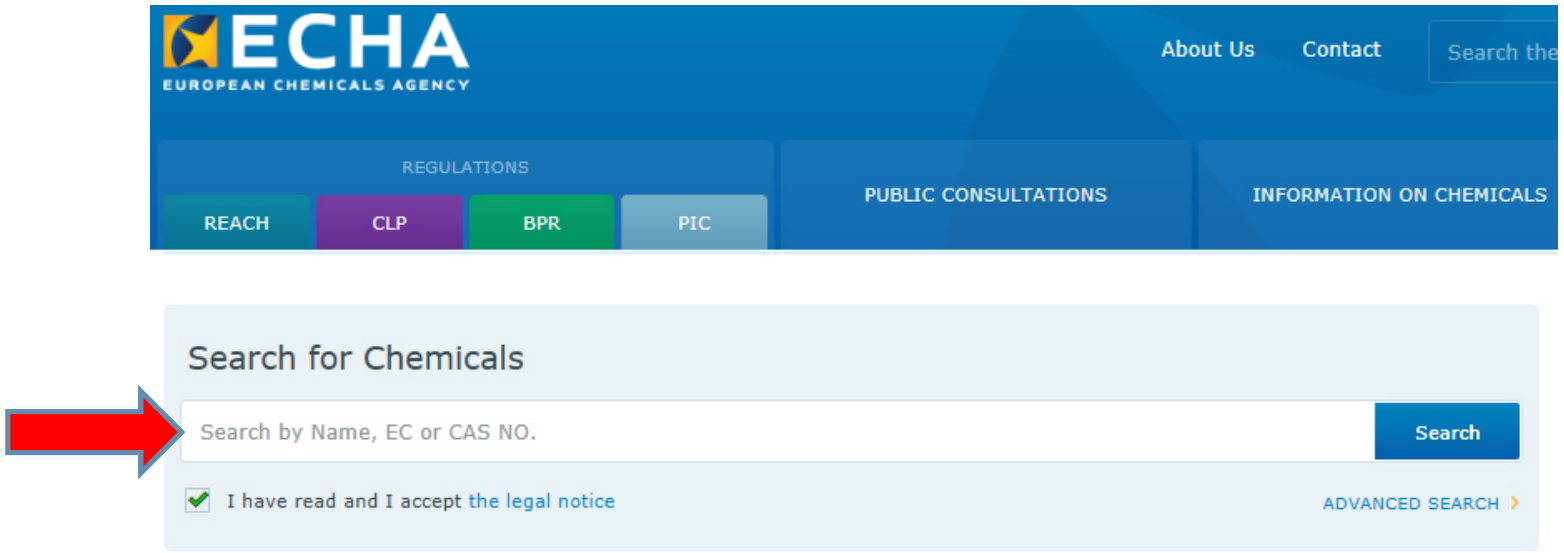
- **The two key publically accessible databases provided by ECHA:**
  - Disseminated REACH dossiers
    - Endpoint data (e.g. LD_{50}), selection of key studies, DNELs, etc
    - Consensus self-classification
  - Classification and labelling inventory
    - Only useful for harmonised classification
- **Supplier SDS: exposure scenarios resulting from confidential Chemical Safety Report.**
- **Indirect access to structured endpoint data in REACH dossiers (RSS) via the OECD:**
  - eChemPortal
    - Provides a way to query data across multiple substances (source must be restricted to ECHA).

Disseminated REACH Registration Dossiers



- Currently >16719 substances.
- Now the most complete and important chemical property database available worldwide.

Data vs Information vs…

- “Data is not information, information is not knowledge, knowledge is not understanding, understanding is not wisdom.”

- Data = Study report Robust Study Summaries (RSS)
- Information = Endpoint summaries – assessment of available data
- Knowledge = hazard conclusions, DNELs etc
- Understanding = combine with exposure for risk

For an efficient regulatory framework we need to leverage the evaluation performed under REACH: focus on transferring information, knowledge, and understanding, rather than underlying study reports and robust study summaries.

Disseminated REACH Registration Dossiers

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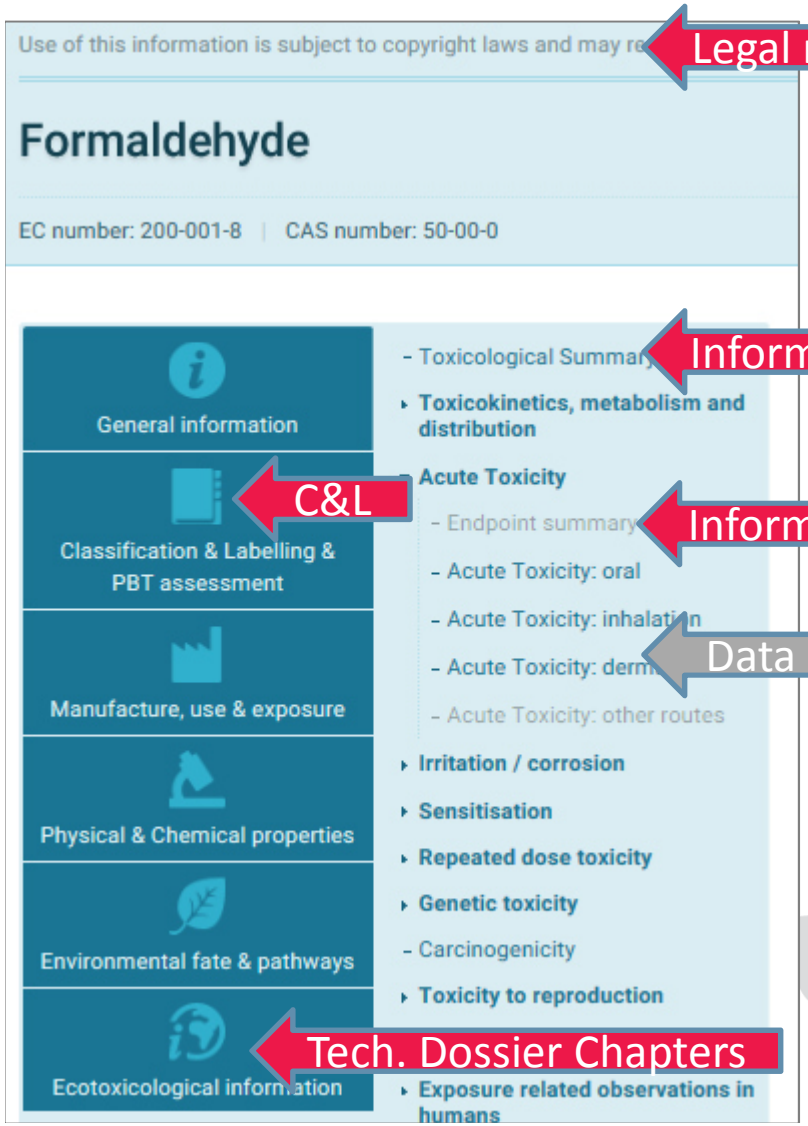

- **Legal notice**
- **Classification (C&L)**
- **Technical dossier chapters:**
  - **Toxicological summary:**
    - Data for quantitative risk assessment (DNEL derivation)
  - **Endpoint summary:**
    - Selection of data (key study, WoE) to carry forward for classification and DNEL derivation
    - Justification for classification
  - Robust study summaries:
    - Pool of available study results (data)

Disseminated REACH Registration Dossiers

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- "C&L", "Endpoint Summary" and "Toxicology Summary" sections contain the key information for use by other legislation.
  - Hazard assessment conclusions (self classification).
  - Exposure limit conclusions (DNELs).
- SDS information must be consistent with this registration information (REACH, Annex II). Only a few reasons for deviating:
  - Opt out due to company specific data (also disseminated).
  - Presence of impurities modifying the classification/risk profile.
- In practise, disseminated registration dossiers can complement (compensate) poor quality SDS, by providing missing information and explanation, or resolving contradictory information between suppliers.

Disseminated REACH Registration Dossiers - Challenges

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- Originally Endpoint Summaries were not disseminated.
  - Justification for selection of Endpoint data (key study, WoE, etc) and comparison against classification criteria were not visible publically.
  - Greyed out “Endpoint Summary” in previous example
- All new registrations publish the Endpoint Summary.
  - Released Endpoint Summaries are displayed as blue. Endpoint summaries are also released when existing registrations are updated.
- Recent changes to enforce one-substance one-registration (OSOR) have reduced the number of parallel dossiers, which was a source of confusion.
- Some substances of potential interest not yet within scope of REACH.
  - In particular polymers, however, this is fully expected sometime after 2018.

Legal Considerations

- Terms of use for the ECHA disseminated REACH data (webpages) are provided at the top of each dossier: https://echa.europa.eu/legal-notice.
- Within the REACH regulation, right to refer to study reports is clearly required. Data protection is lost after 12 years. However, this isn't relevant for other legislation.
- For other legislation, the minimum restriction is copyright which applies to all text/tables/graphics in a RSS or Endpoint Summary.
  - Permission required from rights holders for cut-and-paste (some Open Access exceptions for literature) of RSS or Endpoint Summaries in a PPPR formulation dossier. **Example: hexanol, acute oral tox, 7 RSS, 8 companies.**
    - In practise inclusion of all RSS in PPP dossiers would be unmanageable
  - Careful analysis required for possible additional restrictions on ownership in the receiving legislation.
  - However, the intrinsic properties of substances should not be subject to copyright (e.g. melting point, LD_{50}s, DNELs, classification, etc). They are also legally required to be placed on the SDS, and thus should be free for use in vertical legislation assessments.
- **Data generated on co-formulants for the purposes of PPPR, are not within the scope of PPPR Article 59(1) data protection. PPPR does not appear to place clear constraints on ownership of co-formulant data used.**

Classification & Labelling Inventory

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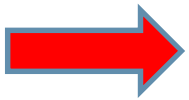
- Most useful information are the CLP Annex VI harmonised classifications.
- Less useful is the self-classification section which provides non-harmonised notifications.
- Most notifiers are not original data holders.



Summary of Classification and Labelling

Harmonised classification - Annex VI of Regulation (EC) No 127

General Information

Index Number	EC / List no.	CAS Number	
607-705-00-8	200-618-2	65-85-0	benzoic acid

ATP Inserted / Updated: ATP06

CLP Classification (Table 3)

Classification		
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(
Skin Irrit. 2	H315	H315
Eye Dam. 1	H318	H318
STOT RE 1	H372 (lungs) (Inhalation)	H372 (lungs) (Inhalation)

Classification & Labelling Inventory

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Notified classification and labelling

General Information

EC / List no.	Name	CAS Number
200-618-2	Benzoic acid	65-85-0

Notified classification and labelling according to CLP criteria

Classification		Labelling			Specific Concentration limits, M-Factors	Notes	Classification affected by Impurities / Additives	Additional Notified Information	Number of Notifiers	Joint Entries	
Hazard Class and Category Code(s)	Hazard Statement Code (s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)	Pictograms, Signal Word Code(s)							
Skin Irrit. 2	H315	H315		GHS08 GHS05 Dgr					5	✔	View details
Eye Dam. 1	H318	H318									
STOT RE 1	H372 (Lungs) (Inhalation)	H372 (H372 Causes dam...)									
Skin Irrit. 2	H315	H315		GHS05 GHS07 Dgr					797		View details
Eye Dam. 1	H318	H318									

REACH registration

Data recycling...

- **Always** use the REACH registration derived classification (**green tick**).
- Where multiple joint classifications, must refer back to REACH registration to understand the differences e.g. impurities, multiple dossiers, etc.
- Large number of notifiers usually just means severe data recycling, not reliability!

Established frameworks to utilize information on co-formulants

- **Hazard assessment:**
  - GHS as implemented by CLP.
  - Use of calculation methods for mixtures permits combination of co-formulant hazard information from REACH with AI information from PPPR.
    - Minimises animal testing.
    - Gives access to endpoints and hazard categories NOT covered by standard testing of formulations under PPPR e.g. co-formulants with STOT RE, CMR, chronic ecotox, PBT, etc.

- **REACH risk assessment of substances:**
- REACH co-formulant risk assessment is found in the confidential Chemical Safety Report. However, the results are communicated downstream in Exposure Scenarios, annexed to the SDS.
- Standard REACH exposure scenarios use exposure determinants which are relevant for industrial situations, but difficult to interpret in the PPP context: e.g. task duration, local exhaust ventilation, etc.
- ECPA REACH-IN tools were developed specifically to facilitate a robust and relevant co-formulant risk assessment for PPP*.
  - Co-formulant's maximum use rate calculated, and should be included in SDS exposure scenario.
  - Simple for a PPP formulator to perform a concentration weighted comparison with any formulation's critical GAP.

*More information on ECPA REACH-IN tools at the end of this slide deck.

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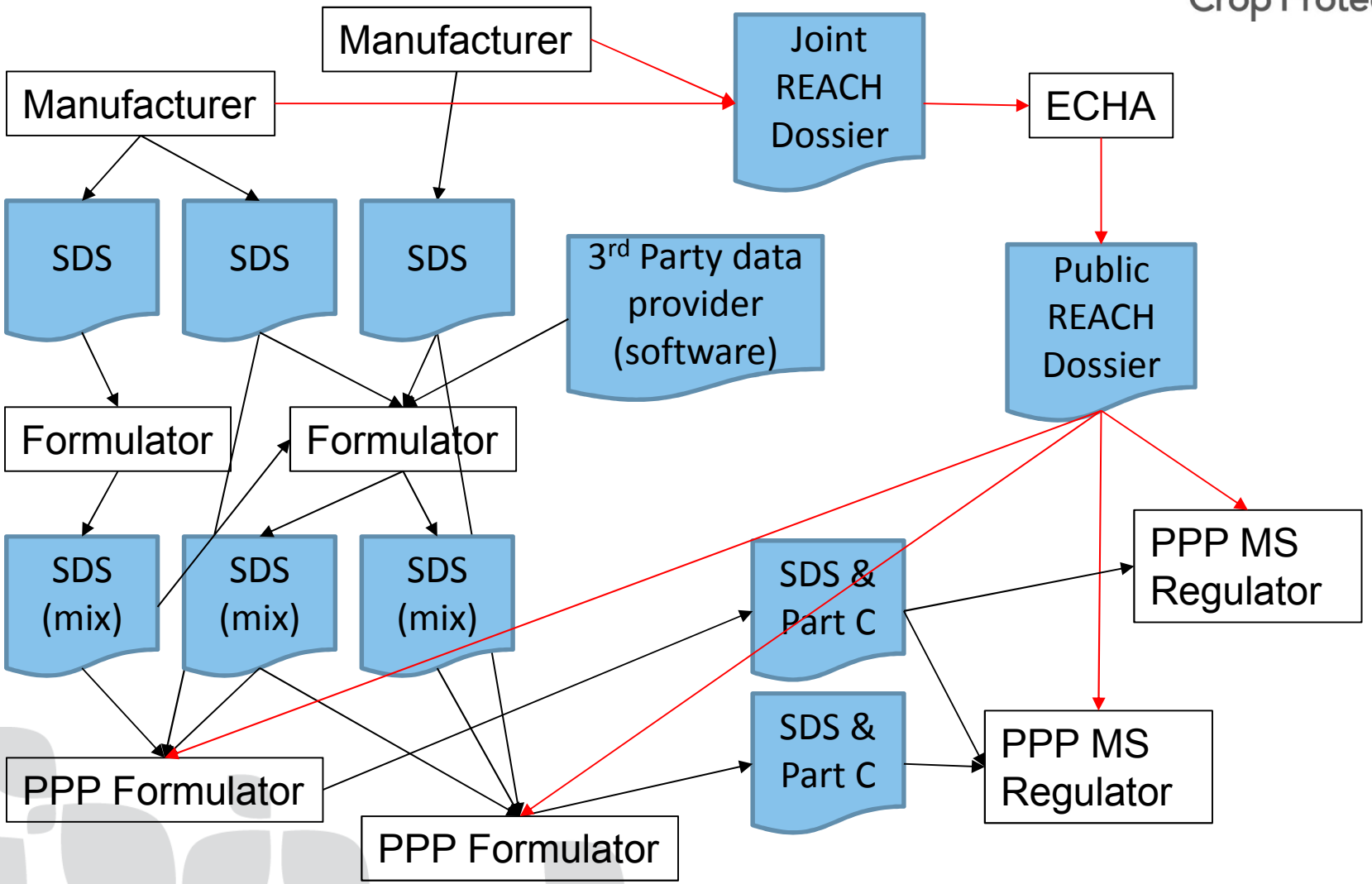
- **Risk assessment of mixtures (combining exposure scenarios):**
- Developing area under REACH: ENES workshops
- Two schemes: CLP+ (or DPD+) and Critical Component Approach (CCA)
- CLP+ picks lead substance by concentration weighted hazard classification.
- CCA picks lead substance by concentration weighted DNEL/PNEC.
  - In the PPP context, no DNEL or exposure scenarios for active substances, so direct comparison can't be made for lead substance.
  - ECPA REACH-IN tools (if used) make this unnecessary, just compare each formulation's critical GAP with each co-formulant's maximum use rate.
- A hybrid approach is likely to be required: standard PPP tools for active substance. REACH-IN tools for quantitative assessment of co-formulants.

Comparison of approaches for industrial example: https://academic.oup.com/annweh/article/58/7/793/156963

Substance data flow



- **Do ECHA databases offer an opportunity for simplified <u>substance</u> data flows?**

General Comments

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- Co-formulants are not active ingredients(!), and should not be viewed solely through the prism of PPP.
- Co-formulant “issues” are equally likely to affect other sectors, and thus should be dealt with under the horizontal legislation.
- Trust in the horizontal regulatory framework to deliver correct results is required.
- If there are perceived weaknesses, we should work to improve these rather than “reinventing the wheel” with yet more legislation.
- Convergence on substance properties/hazard classification is being driven by OSOR, but still needs improvement. CLP inventory needs some major changes.
- SDS quality is still a significant challenge, especially around provision of exposure scenarios.

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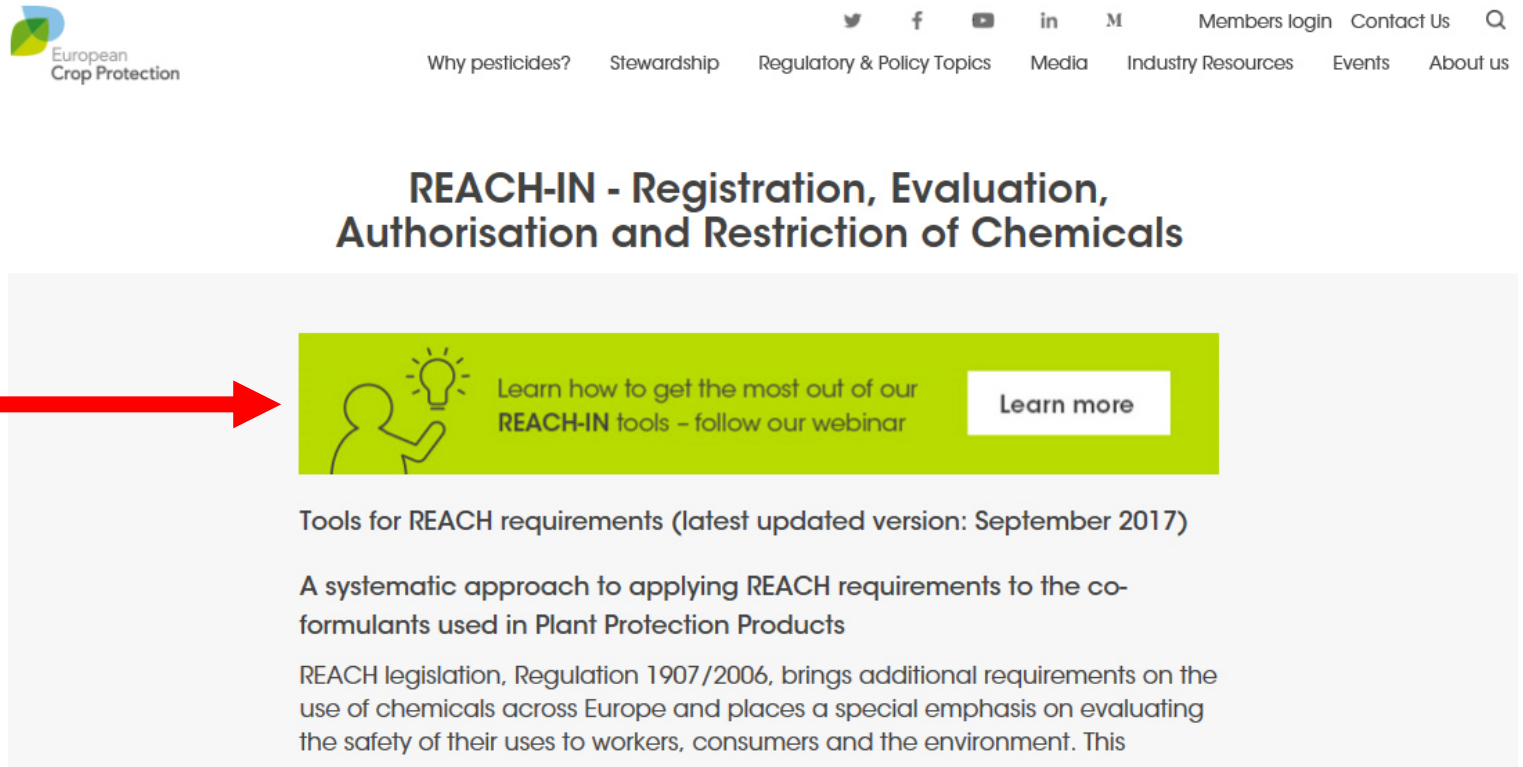
THANK YOU

ECPA REACH-IN tools for co-formulant risk assessment

Video



- Google “ECPA REACH-IN” or follow: http://www.ecpa.eu/industry-resources/reach-registration-evaluation-authorisation-and-restriction-chemicals

REACH-IN tools for co-formulant risk assessment

- Exposure models free for download.
- Full detailed description of models in the guidance document.
- Description of the development of Generic Exposure Scenarios:
- http://onlinelibrary.wiley.com/doi/10.1111/risa.12666/abstract

Risk Analysis DOI: 10.1111/risa.12666

Development of REACH Generic Exposure Scenarios for Substances Used as Coformulants in Plant Protection Products

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This article reviews the interactions between the REACH (Registration, Evaluation, Authorization and restriction of Chemicals) regulation and the plant protection product regulation for substances used as coformulants in the European Union, and describes generic exposure scenarios developed for their exposure and risk assessment. The REACH exposure scenarios describe the operational conditions and risk management measures used in the risk assessment of a coformulant, and as such these translate as the boundaries of safe use. The generic exposure scenarios are designed to be simple, and closely integrate with REACH use descriptors and customized exposure models. Clustering of application methods and exposure determinants resulted in four generic exposure scenarios, each covering professional workers or consumers, and application of products in liquid, granular form, or applied on seeds. When used in conjunction with appropriate exposure models, the generic exposure scenarios support efficient first-tier risk assessment of coformulants by utilizing a higher level of abstraction and conservatism than typically used in plant protection product assessments.

KEY WORDS: Exposure scenarios; pesticides; REACH

1. INTRODUCTION

The European Registration, Evaluation, Authorization and restriction of Chemicals (REACH) legislation requires a holistic risk assessment of all the potential uses of a substance across many industrial sectors, including use in plant protection products.[1] Within the boundaries laid out in the regulation, a manufacturer or importer of a substance must generate substance-specific data[2–4] and carry out a hazard assessment,[5] as well as exposure assessments of all identified uses for both human health[6,7] and the environment.[8] Finally, safe use must be demonstrated through risk characterization.[9] The risk assessment is documented in a chemical safety report, and communicated along with summaries of the data, to the European Chemicals Agency (ECHA) in a registration dossier. The conditions of safe use derived from this risk assessment must then be communicated within the supply chain to the downstream user via the extended Safety Data Sheet (SDS). For-