Moving towards ‘One substance, one assessment’:

Case study with plant extract registrations

Sabine Navis

Thanks to: An Vanden Bosch, Leen Jansen, Sarah Croonenborghs

ABIM Conference – 25 Oct. 2022

Presentation outline

EU Regulatory framework

Case study: plant extract registrations

Moving towards 1S1A

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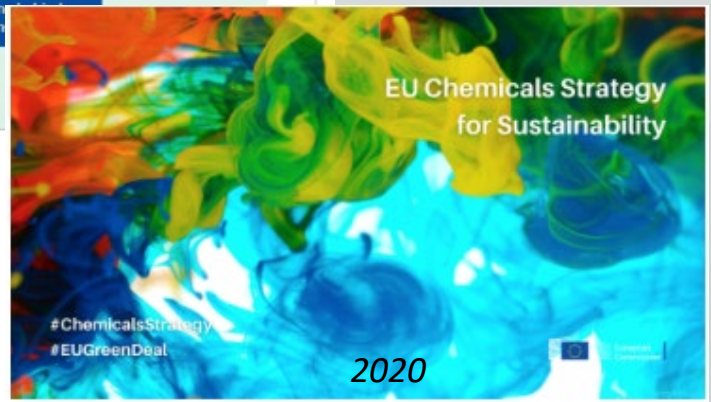
Chemicals Strategy for Sustainability

2019

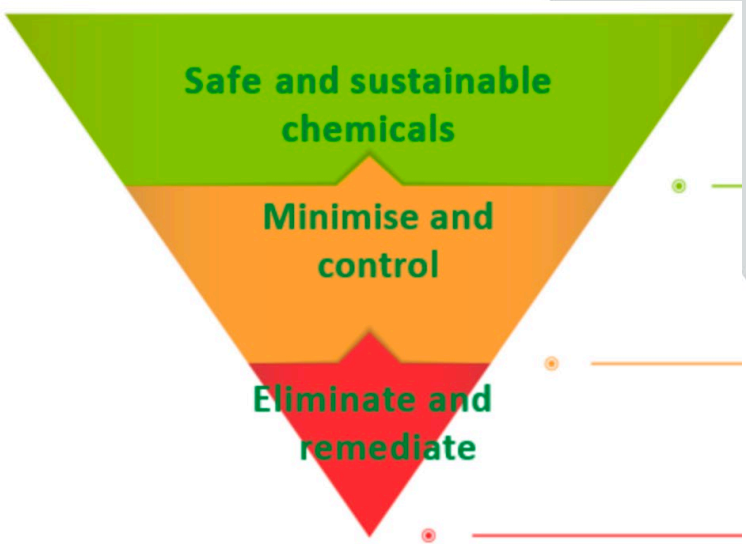


2020

EU Action Plan: Towards zero pollution for air, water and soil (2021)

Chemicals Strategy for Sustainability (CSS)

CSS: Paradigm shift for EU Chemicals policy, towards **Safe and Sustainable by Design**



The toxic-free hierarchy – a new hierarchy in chemicals management

In line with the European Green Deal, the strategy strives for a **toxic-free environment**, where chemicals are produced and used in a way that **maximises their contribution to society** including achieving the green and digital transition, while **avoiding harm to the planet and to current and future generations**.

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One substance, one assessment (1S1A)

Aim: To improve effectiveness, efficiency and coherence of the safety assessment of chemicals across chemical legislation.

1S1A Expert working group: Commission services (chair = DG ENV), EU Agencies (ECHA, EFSA, EEA, EMA…) and Member States

Three legal proposals:

1. Reattribution of tasks on chemicals to EU Agencies (2022)
2. Transparency and re-use of data allowing EU and national authorities to commission testing (2023)
3. Strengthen the governance of the European Chemicals Agency

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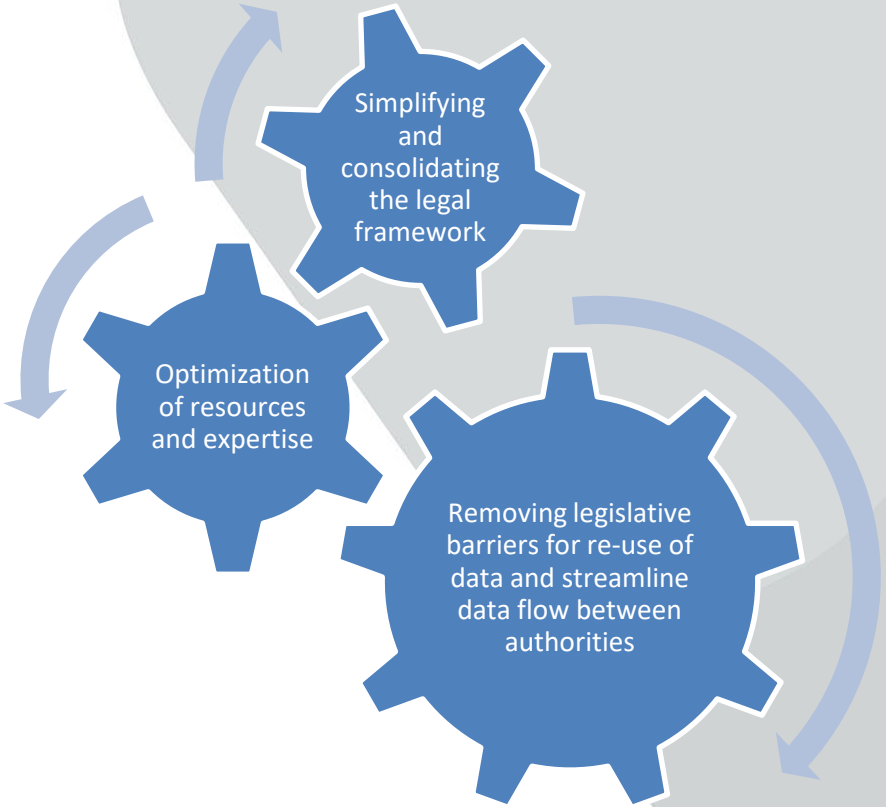
One substance, one assessment (1S1A)



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Current EU registration frameworks

- Plant protection products: PPPR, Regulation (EC) No 1107/2009
- Biocides: Biocidal Products Regulation (BPR), Regulation (EU) No 528/2012
- Industrial chemicals: REACH, Regulation (EC) No 1907/2006
- Medicinal products: Regulation (EC) No 726/2004
- Fertilizing products: FPR, Regulation (EU) 2019/1009
- …

=> Different strategies for hazard, exposure and risk assessment might lead to different outcomes for **similar or even identical chemicals**

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Case study:
Registration of plant extracts (geraniol)

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Current EU registration frameworks

The total number of chemicals under each framework that were registered at time of the analysis (i.e. autumn/winter 2019) and for which CAS-numbers were identified. The total amount of substances that were also registered under one or more other registration frameworks are shown.

	Total number of Registered Chemicals with CAS	Total number of chemicals also registered under other frameworks	Overlapping chemicals per framework				
			Biocides	Industrial Chemicals	Pesticides	Medicines for Human Use	Veterinary Medicines
Biocides	148	73	–	49 (33%)	28 (19%)	1 (0.7%)	5 (3.4%)
Industrial Chemicals	9518	97	49 (0.5%)	–	28 (0.3%)	23 (0.2%)	5 (0.1%)
Pesticides	393	53	28 (7%)	28 (7%)	–	6 (2%)	2 (0.5%)
Medicines for Human Use	752	42	1 (0.1%)	23 (3%)	6 (0.8%)	–	16 (2%)
Veterinary Medicines	130	29	5 (4%)	5 (4%)	2 (2%)	16 (12%)	–
Non-approved Biocides	35	17	–	15 (43%)	3 (9%)	0	0
Non-approved Pesticides	743	114	19 (3%)	94 (13%)	–	5 (0.7%)	3 (0.4%)

J. Van Dijk et al (2021)

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Differences: hazard assessment

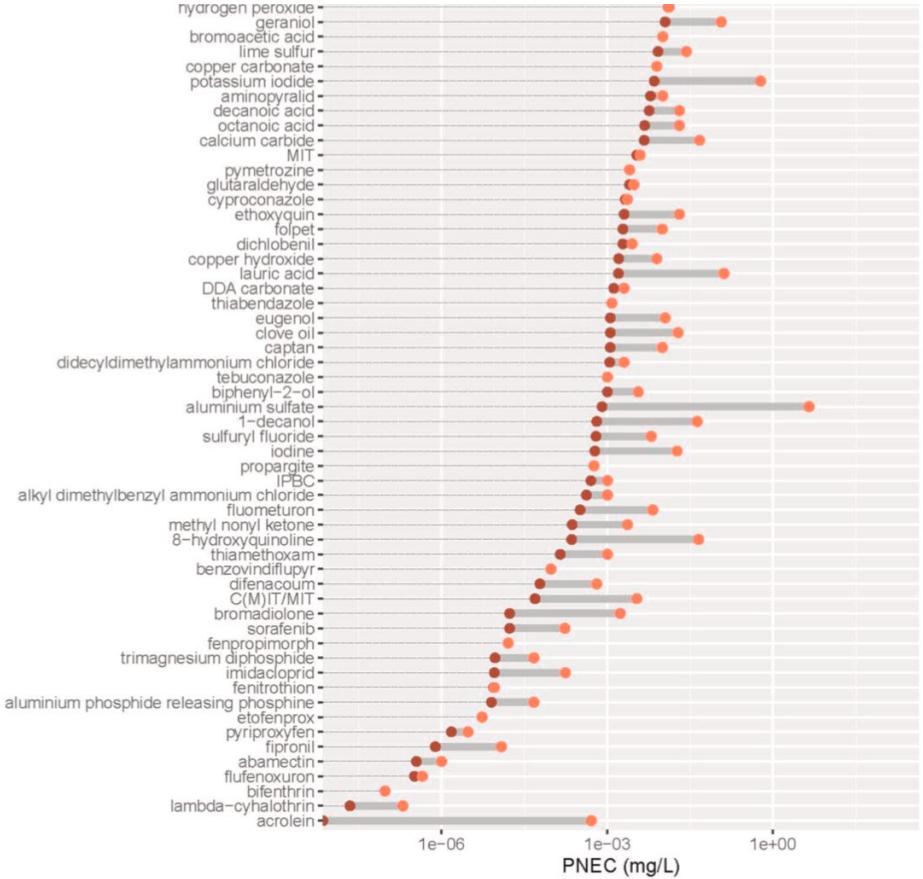
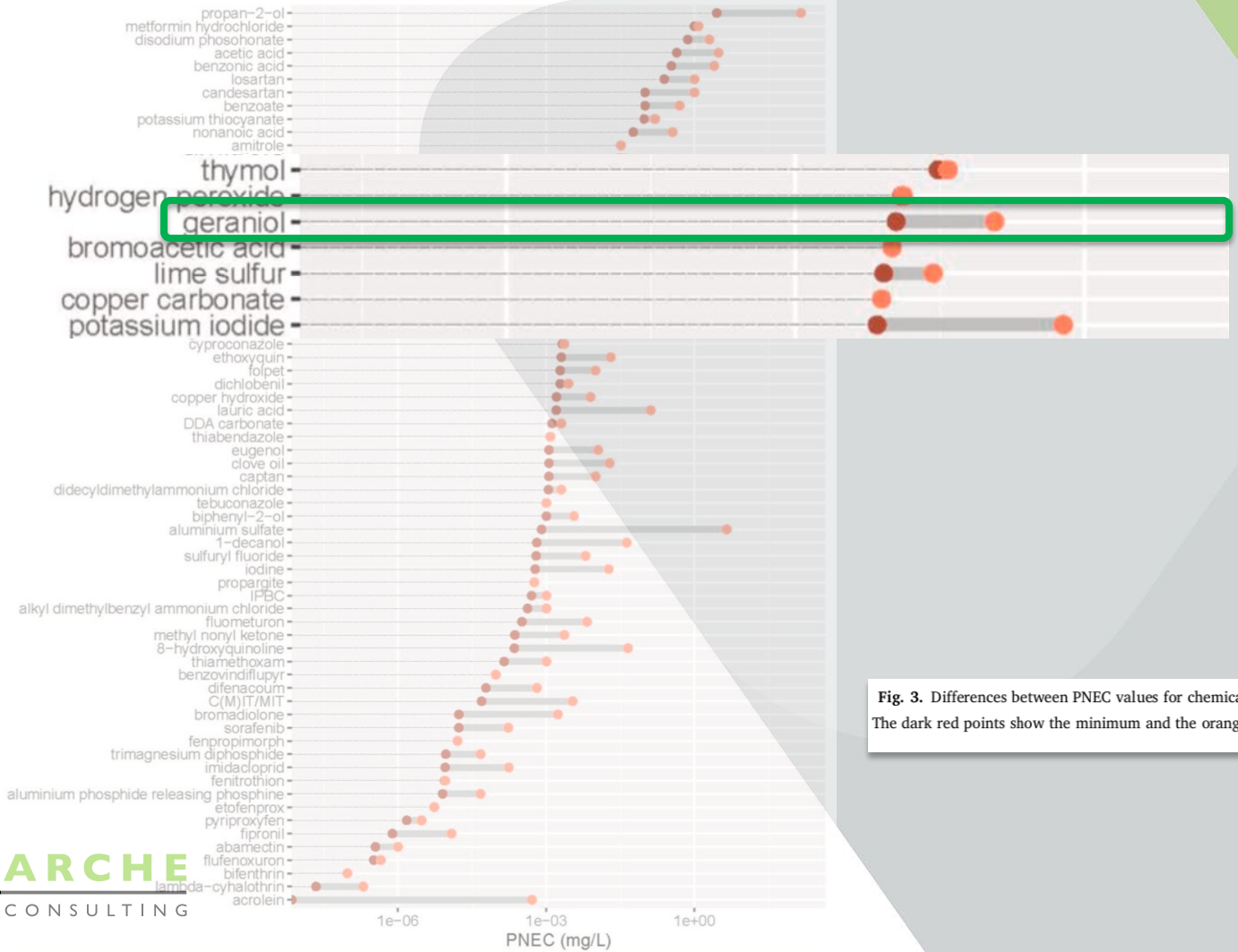


Fig. 3. Differences between PNEC values for chemicals registered under 2 or more frameworks. The dark red points show the minimum and the orange points the maximum reported PNEC value.

J. Van Dijk et al (2021)



Case study: Geraniol

Fig. 3. Differences between PNEC values for chemicals registered under 2 or more frameworks. The dark red points show the minimum and the orange points the maximum reported PNEC value.

J. Van Dijk et al (2021)

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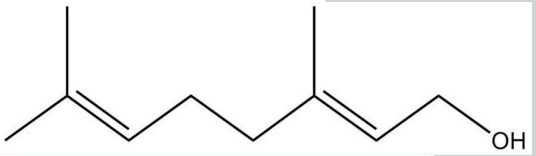
Case study: plant extract geraniol

- Geraniol: plant extract, naturally occuring in fruits, vegetables, herbs and spices
- Currently approved/under approval under different EU regulatory frameworks
  - REACH registration ≥ 1 000 tonnes
  - PPPR: fungicide in grapes
  - BPR: under approval, PT18/19 (insecticide/repellent in textile)
  - Cosmetics PR: perfume, tonic
  - Flavouring agent in food
- Harmonized CLP C&L: H317 (Skin Sens. 1)



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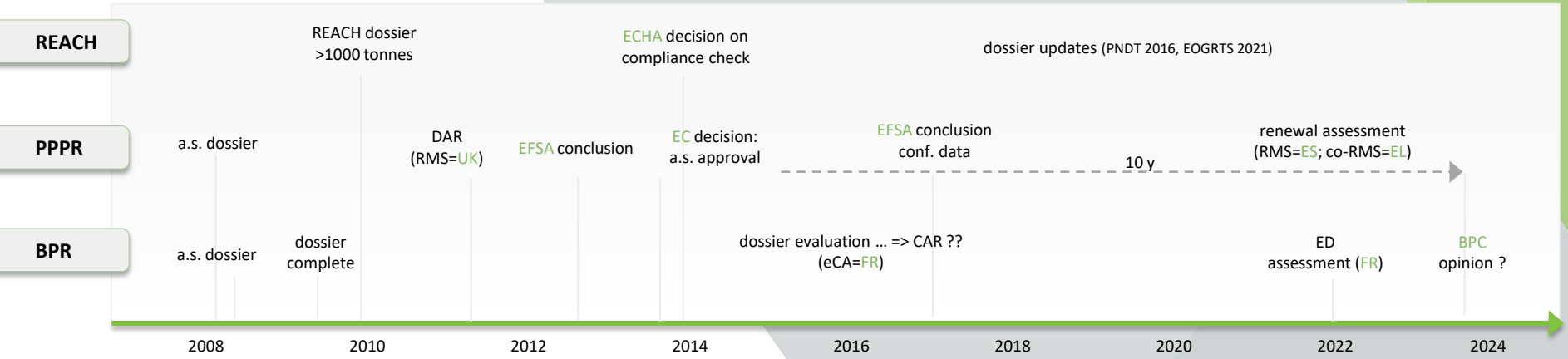
Case study: plant extract geraniol - timeline



Consideration of substances under different legislations is neither synchronized, nor harmonized in terms of data requirements, nor overseen by a single competent authority

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Case study: plant extract geraniol – env. risk assessment

Differences in studies and derived threshold levels

- REACH
  - **PNECaqua = 0.011 mg/L** (*Daphnia magna* most sensitive, EC_{50} = 10.8 mg/L; AF = 1000)
  - No chronic aquatic toxicity studies
- PPPR
  - EFSA conclusion (2012):
    - **"PNECaqua" = 0.116 mg/L** (calculated based on fish acute EC_{50} = 11.6 mg/L, AF = 100)
    - Confirmatory data on chronic aquatic toxicity requested
  - New studies aquatic toxicity in CLH report + Application for renewal (2021)
    - BUT issues with maintaining steady test concentration due to volatilty
- Biocides: No information publicly available

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Transparency & confidentiality

Data protection

- Data protection rules are specific to a regulatory framework
- Data sharing is generally only mandatory for vertebrate data (exception: Art 95 BPR)

Transparency

- Availability of data across regulations is often not clear
- Data eligible for mandatory data sharing: no cross-check between agencies
- Introduction **Transparency Regulation** (March 2021, PPPR)

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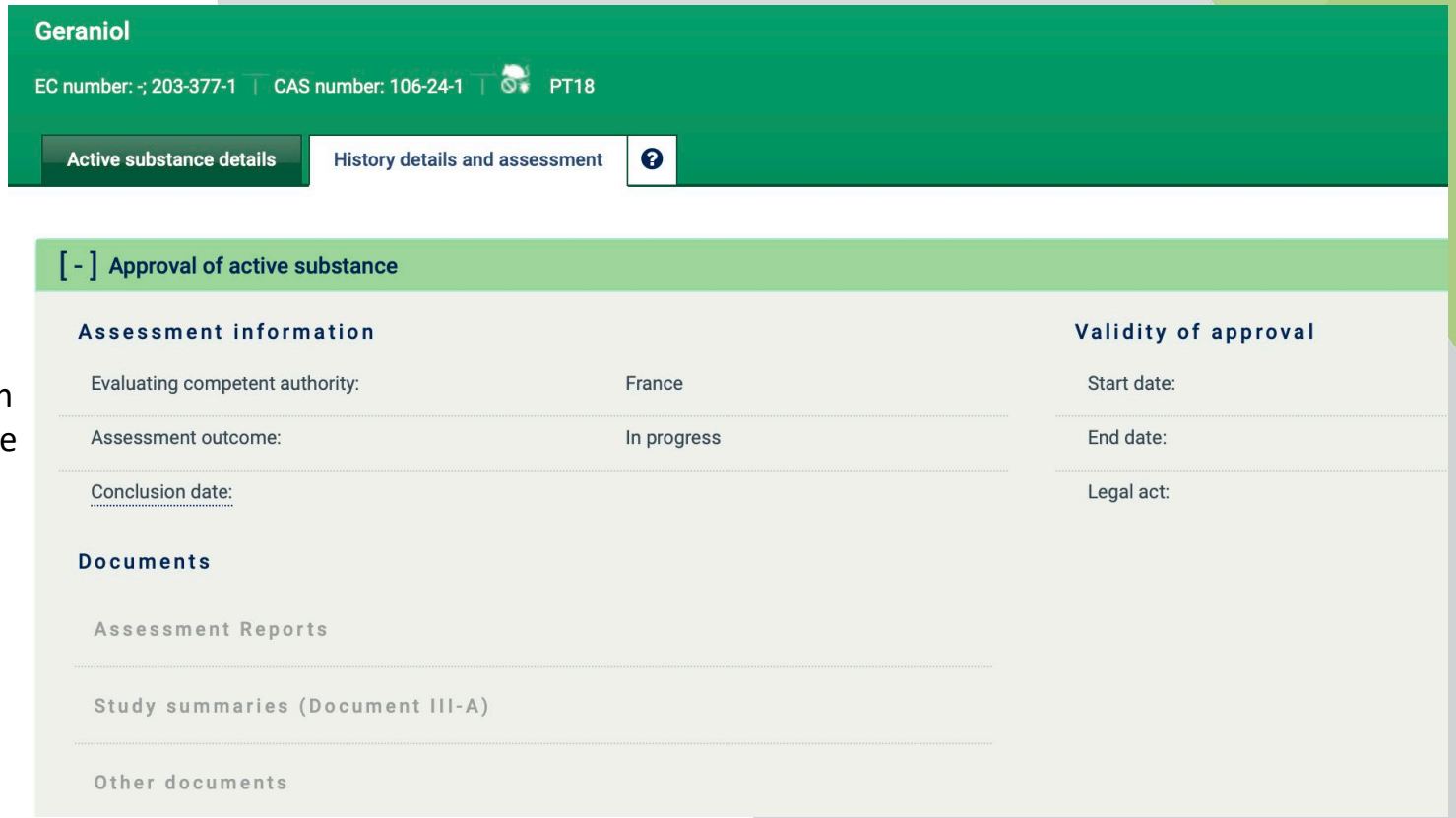
Transparency - BPR

ECHA website BPR:
Available information on biocidal active substance assessment



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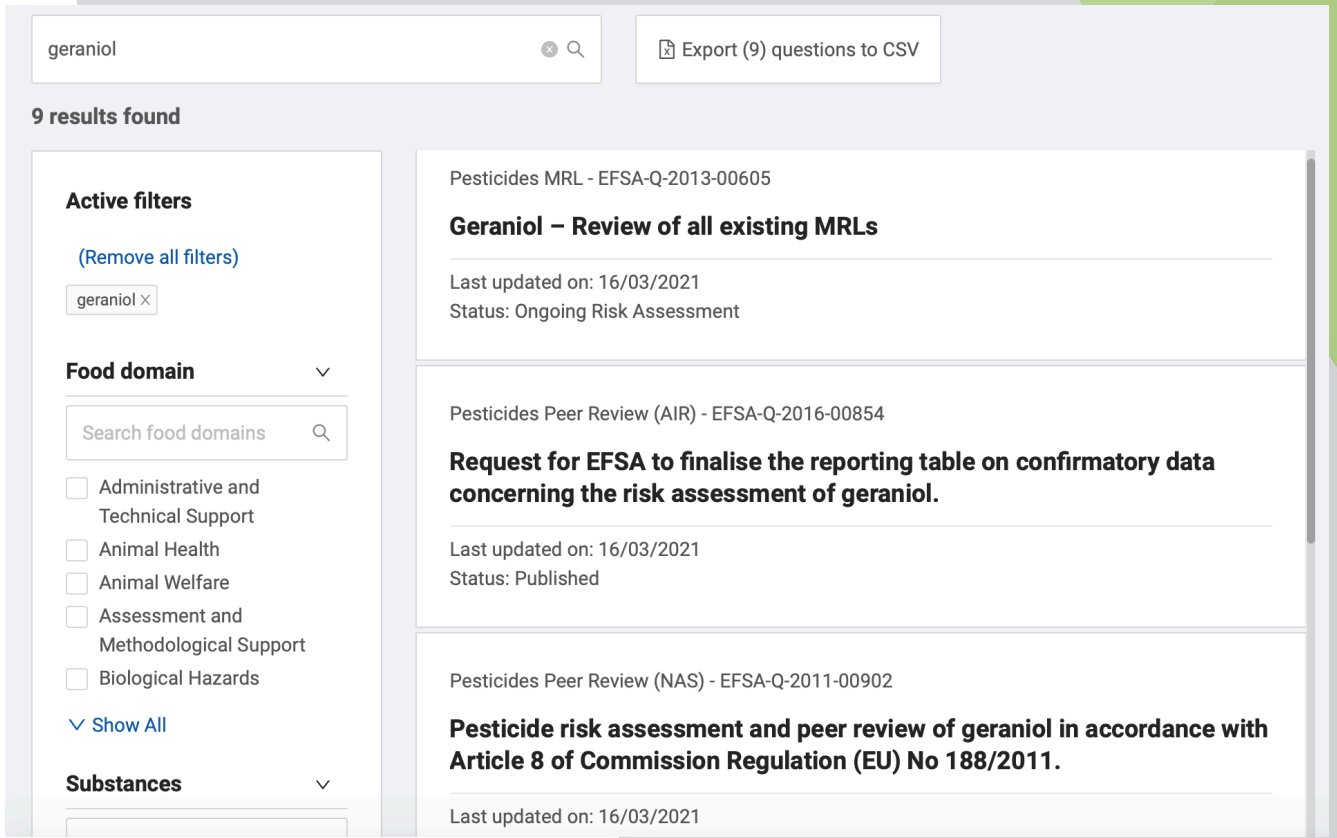
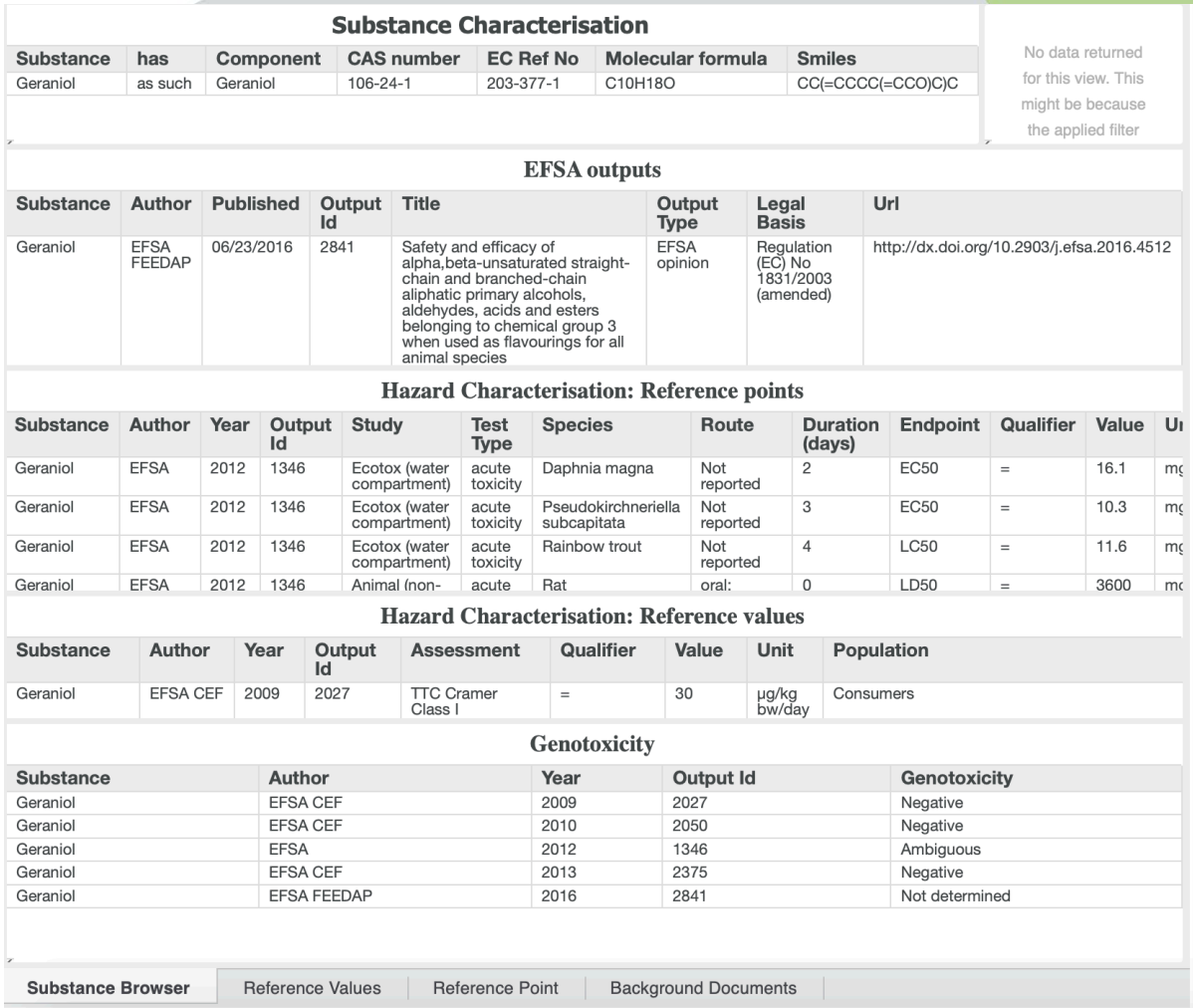
Transparency - PPPR

[Open EFSA website]



Transparency

[EFSA Open Food Tox]



Substance Characterisation

Substance	has	Component	CAS number	EC Ref No	Molecular formula	Smiles
Geraniol	as such	Geraniol	106-24-1	203-377-1	C10H18O	CC(=CCCC(=CCO)C)C

No data returned for this view. This might be because the applied filter

EFSA outputs

Substance	Author	Published	Output Id	Title	Output Type	Legal Basis	Url
Geraniol	EFSA FEEDAP	06/23/2016	2841	Safety and efficacy of alpha,beta-unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids and esters belonging to chemical group 3 when used as flavourings for all animal species	EFSA opinion	Regulation (EC) No 1831/2003 (amended)	http://dx.doi.org/10.2903/j.efsa.2016.4512

Hazard Characterisation: Reference points

Substance	Author	Year	Output Id	Study	Test Type	Species	Route	Duration (days)	Endpoint	Qualifier	Value	Ur
Geraniol	EFSA	2012	1346	Ecotox (water compartment)	acute toxicity	Daphnia magna	Not reported	2	EC50	=	16.1	mg
Geraniol	EFSA	2012	1346	Ecotox (water compartment)	acute toxicity	Pseudokirchneriella subcapitata	Not reported	3	EC50	=	10.3	mg
Geraniol	EFSA	2012	1346	Ecotox (water compartment)	acute toxicity	Rainbow trout	Not reported	4	LC50	=	11.6	mg
Geraniol	EFSA	2012	1346	Animal (non-	acute	Rat	oral:	0	LD50	=	3600	mg

Hazard Characterisation: Reference values

Substance	Author	Year	Output Id	Assessment	Qualifier	Value	Unit	Population
Geraniol	EFSA CEF	2009	2027	TTC Cramer Class I	=	30	µg/kg bw/day	Consumers

Genotoxicity

Substance	Author	Year	Output Id	Genotoxicity
Geraniol	EFSA CEF	2009	2027	Negative
Geraniol	EFSA CEF	2010	2050	Negative
Geraniol	EFSA	2012	1346	Ambiguous
Geraniol	EFSA CEF	2013	2375	Negative
Geraniol	EFSA FEEDAP	2016	2841	Not determined

Substance Browser | Reference Values | Reference Point | Background Documents

Substance (1 Selected)

Geraniol

Search Substance

Synonym

Search Synonym

CAS number

Search CAS number

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Case study: plant extract geraniol - conclusions

- Different **timelines** and procedures for additional information
- Differences in **transparency** of the process and available/requested studies

- Differences in effect **thresholds** for human health and environment:
  - Different data requirements
  - Limited access to data/studies performed under other regulatory frameworks
  - Different assessment factors applied (different protection levels?)

- Differences across regulations due to distinct use pattern and exposure routes => one substance, one **hazard** assessment?

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Moving towards ‘one substance, one assessment’

What can we learn from existing EU chemical regulations?

REACH	Medicinal Products	PPPR	BPR
Tonnage based data requirements	Regulatory support at development phase (PRIME scheme)	Transparent evaluation process and requests for data	Simplified authorisation for specific substances of natural origin (Annex 1)
Specific guidance on substance ID (UVCBs)	Specific assistance for SME’s		

Moving towards ‘one substance, one assessment’

- Interesting building blocks from 1S1A approach:

  - Re-attribution of tasks (existing agencies)
  - Data generation mechanism?
  - Increased transparency, notification of studies
  - Data sharing (legislative barriers for re-use; improve uptake of academic data)

  - **Repository of health-based limit values**
  - **EU Common data platform on chemicals**

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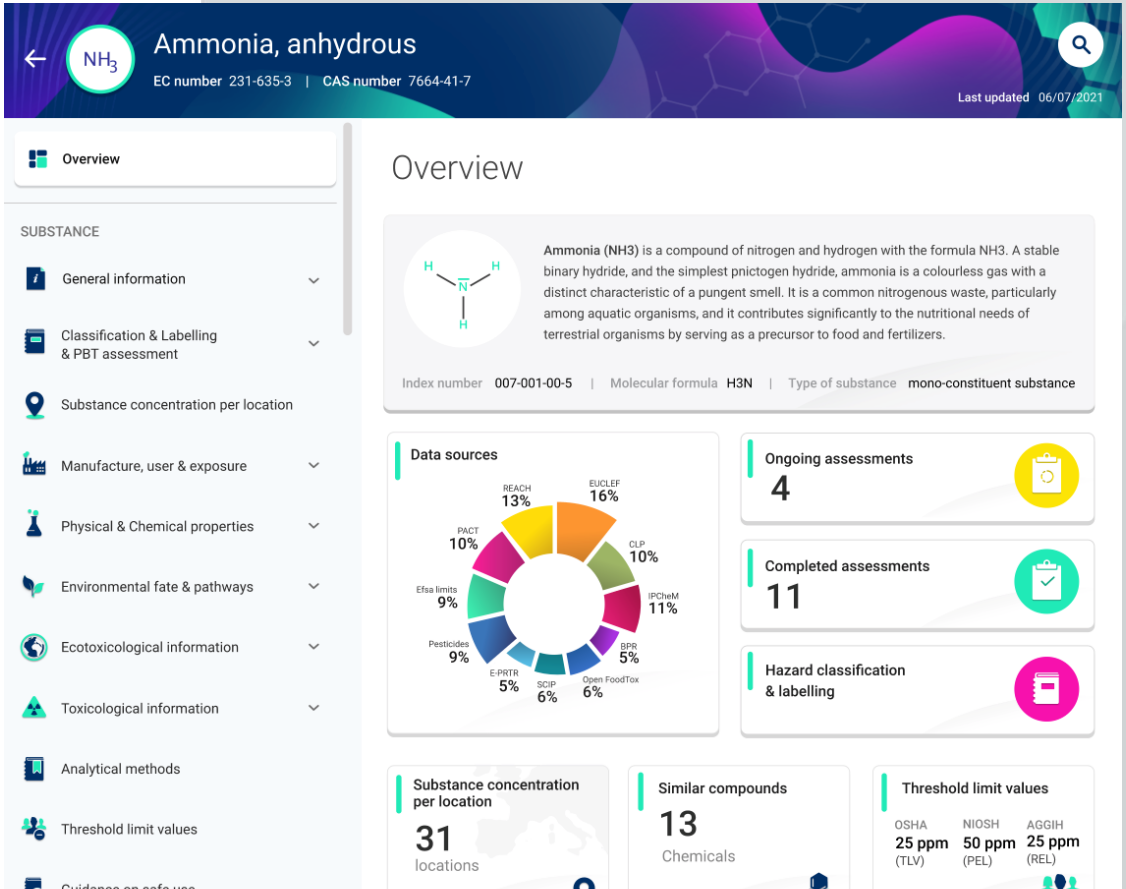
Development common data platform on chemicals



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Moving towards ‘one substance, one assessment’

- Current EU chemicals legislation was designed for chemical active substances. Data requirements, exposure models and risk assessment strategies, have all been drawn up with synthetic chemicals in mind.
- One substance, one assessment is targeting ‘chemicals’, but is equally relevant for microbials, natural substances, semiochemicals, etc.
- **Transition towards 1S1A could be an opportunity to improve assessment framework for biocontrol solutions.**

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Thanks for your attention!

For more information or further discussion: **booth 110**

Contact details: sabine.navis@arche-consulting.be

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