U.S. EPA Fragrance Technical Expert Meeting

Day 2

Understanding Biodegradation & Evaluating Environmental Toxicity

Session 3 : Evaluating Environmental Chronic Aquatic Toxicity

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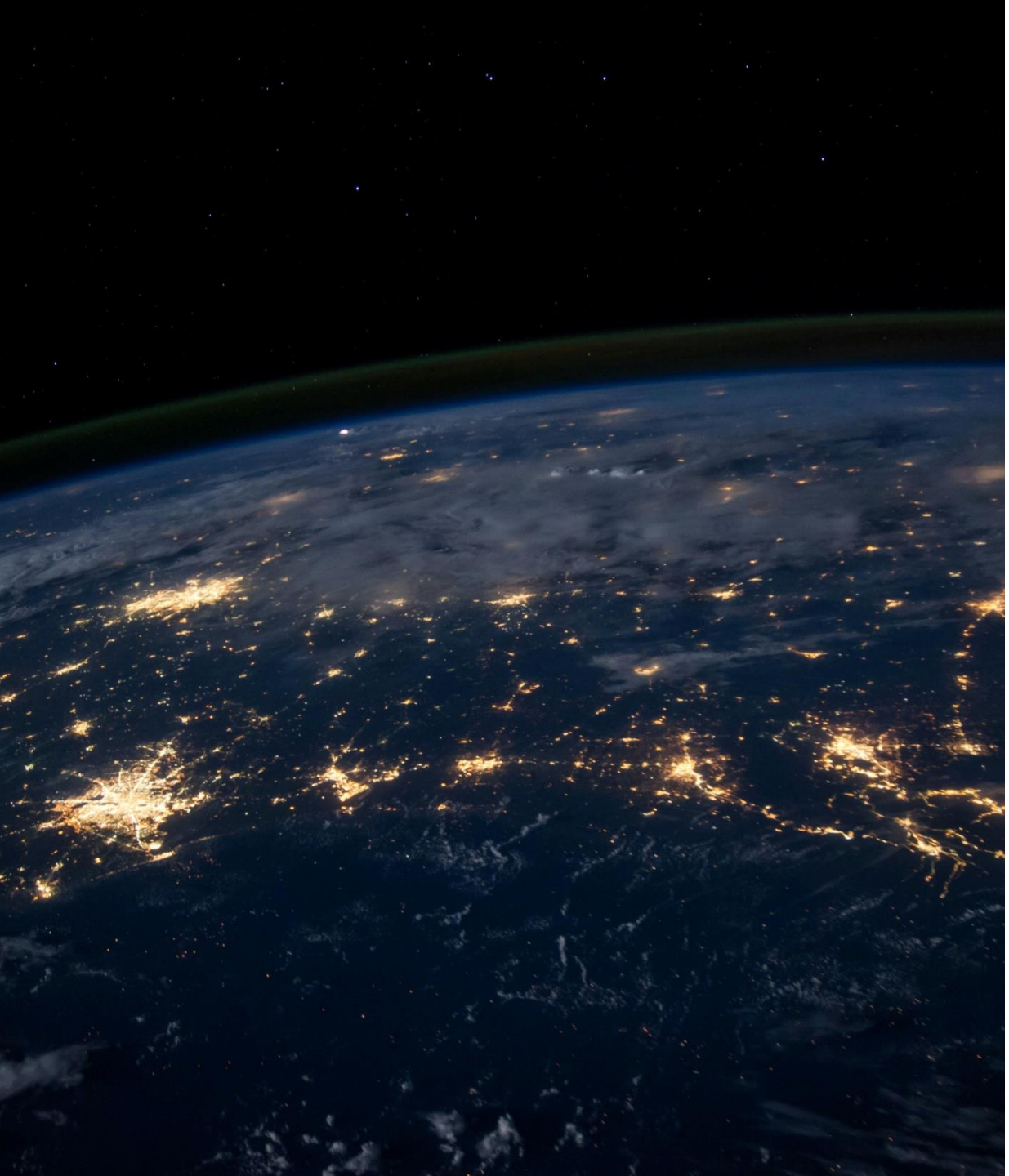
Chronic Aquatic Toxicity of Fragrance Ingredients :

Deriving Chronic-CoC Values
&
Linking this with Environmental Concern

Gordon Sanders

(Givaudan, CH – on behalf of FSAC)



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Chronic-Coc Values : Where do they come from ?

Several approaches ....

01. From Experimental Data

- Acute aquatic toxicity data (Fish, *Daphnia*, Algae) ➔ Measured data available for ALL Fragrance Ingredient PMNs
  - Fish, *Daphnia* : LC/EC50 ÷ 10 ➔ ChV ÷ 10
  - Algae : EC50 ÷ 4 ➔ ChV ÷ 10
- Chronic aquatic toxicity data (Fish, *Daphnia*, Algae) :
  - NOEC / EC10 ÷ 10
  - Geometric mean of NOEC and LOEC ÷ 10

02. QSAR Predictions - ECOSAR (v2.2)

- Fish, *Daphnia*, Algae ChV values ÷ 10
  - Use of manually entered LogKow preferred vs Default
  - Correct attribution of the ECOSAR chemical class
  - Reliability of the training set

PERSISTENCE	Not Persistent	Persistent	
Water, Soil, Sediment*	< 60 d	≥ 60 d	≥ 180 d
Air**	< 2 d	> 2 d	
BIOACCUMULATION	Not Bioaccumulative	Bioaccumulative	
Fish BCF*	< 1000	≥ 1000	≥ 5000
TOXICITY	Not Toxic	Toxic	
Fish ChV*	> 10 mg/L *or* No Effects at Saturation	0.1-10 mg/L	< 0.1 mg/L
Chronic-CoC	> 1000 ppb	10-1000 ppb	10 ppb

Consideration of <u>PROPORTIONALITY</u> of testing requirements :

- Data relatively sparse, but growing
- Sectorial animal testing bans
- Many fragrance ingredients (≈3000), low-volumes (65% < 1-tpa, 85% < 10-tpa) on US market
- High % of Fragrance Ingredients READILY Biodegradable

Opportunities to improve our comprehension of the aquatic chronic toxicity of Fragrance Ingredients :

More efficient use of what we already have today –

Short-Term advances

Guiding Principle : Use of PROPORTIONATE testing only when required

01. ECOSAR

- Is there a Standard Operating Procedure for the use of ECOSAR ?
  - Manually entered Phys-Chem values
  - Criteria for selection of most appropriate chemical class from output
  - Which values are finally selected ?
- Updates to ECOSAR and expanding data sets :
  - Frequency of updates ?
  - Data-mining and pulling of data to expand chemical class regression data

02. Read-Across

- AIM (Analog Identification Methodology)
  - When is “similar” really similar ?
- Is there a Good Read-Across Practice guidance for users : What would you consider as robust justification ?
- Availability of robust “source” studies limited

Opportunities to improve our comprehension of the aquatic chronic toxicity of Fragrance Ingredients :

What does the future hold ?

Mid- to Long-Term Perspectives

Guiding Principle : Avoid unnecessary vertebrate Testing

03. "Traditional" Aquatic Testing

- Chronic Fish testing as a last resort – Animal testing bans on cosmetics
- Freshwater Invertebrate Testing : + and – of testing with *Ceriodaphnia dubia* instead of *Daphnia magna* ?
  - EPA-8-21-R-02-013 : Method 1002.0
  - ISO 20665 : 2008
  - Connors *et al.* (2022), ETC, 41, 134 - 147
- Metabolite(s) – Is the Parent molecule the relevant entity to assess ?

04. New Approach Methodologies

- Develop fit-for-purpose and predictive NAMs for chronic aquatic toxicity (*c.f.* HESI Next Generation Ecological Risk Assessment Committee Workshop on alternatives to *In vivo* chronic fish testing, Paris, October 2023)

05. Other : Combinations of data as WoE

- Use combinations of existing data to PRIORITISE / DE-PRIORITISE need for further higher-tier testing
- Develop a Chronic EcoTTC for application to low tonnage ingredients
- MoAs – Fragrance ingredients predominantly Narcotics
- (Re)Analysis of Acute-to-Chronic ratios with increased data sets

Is there cause for concern ?

Linking Hazard to Risk –

A holistic view to assessing the safety of a Fragrance Ingredient

SUSTAINABLE FUTURES SUMMARY:			
Concern Level	HIGH	MODERATE	LOW
Persistence			X
Bioconcentration			X
Cancer Health Hazard			X
Non-Cancer Health Hazard			X
Aquatic Toxicity Hazard		X	
Is the chemical predicted to be a PBT by PBT Profiler?	No		
Overall Hazard Concern	Human Health Hazard: LOW Aquatic Hazard: MODERATE		
Overall Risk	Human Health Risk: LOW Aquatic Risk: LOW		

01. Focus on Rapid Biodegradability as a Priority Design Criteria vs Environmental Exposure

- Rapid Biodegradability = Readily, Inherently biodegradable i.e. total mineralisation of the Fragrance Ingredient
- $T_{1/2}$s of the order of 1 - 3 hours for Readily Biodegradable substances (https://www.epa.gov/sites/default/files/2015-09/documents/interim_guidance.pdf)

Using Ready and Inherent Biodegradability Data to Derive Input Data for WWT Models

The scheme in Table I is offered as an interim procedure for assigning activated sludge half-lives for input to models of activated sludge (AS)-based wastewater treatment (WWT) plants:

Table I Proposed Scheme

Ready test result	Inherent test result	Activated sludge half-life, hr
pass test	--	1
no pass, but >= 40 %	--	3
no pass: >= 20 but < 40 %	>= 70 %	10
--	>=20 but < 70 %	30
no pass: < 20 %	< 20 %	10,000, or current default for no biodeg if different

- Typical retention time in WWTP : 12 hours (industrial sites significantly longer)
- How much is actually removed from the emission related to the aqueous-phase during treatment?
  - Readily : 99.9% of input concentration of Parent removed
  - E-FAST outcome of #days Chronic-CoC exceedance << 20d

Developing the dialogue - The path towards safer and more sustainable Fragrance Ingredients

Robust science as an enabler

01. Thanks for organizing this initial meeting. There are many areas where we can collaborate and enrich one another's comprehension.

02. Understanding each others concerns – Building a dialogue on process, constraints, impacts and leveraging the science to build confidence.

03. Proposal of pathway forward :

- Obtain formal clearance and form an Environmental Expert Committee (EEC)
- Brainstorm and identify primary areas of concern on both the development of **intrinsic hazard** data as well as elements of **risk** and **exposure**
- Assimilate the fields of interest identified by EEC, rank subjects of highest priority, determine a "feasibility" score, determine timeframe and resources available to initiate
- Identify pool of Technical Experts (US-EPA and Fragrance Industry) willing to actively contribute to the identified Work-Streams
- Set short-, mid- and long-term agenda and objectives

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Contact for supplementary information :

gordon.sanders@givaudan.com
ngeorges@fsac.org

fsac
FRAGRANCE SCIENCE
& ADVOCACY COUNCIL