Recent Work of ECETOC Task Force (TF):

Moving Persistence (P) Assessments into the 21st Century

Webinar
13.00 – 15.00 CEST
29 September 2020

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Webinar practical information

- **This webinar will be recorded** for internal use only (not posted publicly)
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- Posted questions will be picked up by the **moderator** in the Q&A session Chat
- **Slides** will be shared after the event
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Webinar agenda

Objective: Share recent progress of this ECETOC Task Force with the scientific community, and also to provide timely input to support potential updates to the REACH PBT guidance

13.00 – 13.15	Introduction	**Aaron Redman**, ExxonMobil (TF Chair)
13.15 – 13.45	Presentation: Conceptual framework for improving P assessments	**Delina Lyon**, Concawe (TF member)
13.45 – 14.00	Q&A	Moderator: **Sylvia Jacobi**, Albemarle (ECETOC PBT EG rep)
14.00 – 14.30	Presentation: Scientific concepts and methods for improving P assessments	**Russell Davenport**, Newcastle University (TF member)
14.30 – 14.45	Q&A	Moderator: **Kathrin Fenner**, EAWAG (TF member)
14.45 – 15.00	Outlook and close	**Pippa Curtis-Jackson**, Environment Agency UK (TF member)

Introduction

Aaron Redman,
ExxonMobil,
TF Chair

13.00 – 13.15

What is ECETOC?

ECETOC is a collaborative space for leading scientists from industry, academia and governments to develop and promote practical, trusted and sustainable solutions to scientific challenges which are valuable to industry, as well as to the regulatory community and society in general

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Task force: terms of reference

- **Objective**: Develop an improved *framework* and best practices for persistence and degradation assessments based on *progress* in the scientific understanding of the underlying process
- **Timeline**: 18 months (initiated July 2019)

Task force

Name	Surname	Affiliation	
Aaron	Redman	ExxonMobil (TF Chair)	TF Members
Jens	Bietz	Clariant	
Jo	Chai	Dow	
Pippa	Curtis-Jackson	Environment Agency UK	
Philipp	Dalkmann	Bayer	
Russell	Davenport	Newcastle University	
Jordan	Davies	LyondellBasell	
John	Davis	Dow	
Kathrin	Fenner	EAWAG	
Laurence	Hand	Syngenta	
Kathleen	Mcdonough	Procter & Gamble	
Delina	Lyon	Shell/Concawe	
Jens	Otte	BASF	
Frédéric	Palais	Solvay	
John	Parsons	University of Amsterdam	
Andreas	Schäffer	RWTH Aachen University	
Cyril	Sweetlove	L'Oréal	
Neil	Wang	Total	
Tim	Gant	King's College London	TF Stewards
Johannes	Tolls	Henkel	
Amelie	Ott	Newcastle University	TF Scientific Secretary

Industry

Academia

Regulatory body

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Task force: main deliverables

- Two peer-reviewed papers:
  - **Perspectives paper**: strong focus on adapting OECD 2019 Weight-of-Evidence guidance for use in persistence assessment
  - **Methods paper**: review of recent experimental methods and strategies for evaluating absolute and relative degradation of chemicals
- Disseminations:
  - SETAC SciCon 2020: 1 platform & 2 poster presentations
  - Webinar 29 Sept 2020
  - Joint ECETOC/Cefic LRI/Concawe workshop – Helsinki May 2021

Task force: timeline for paper prep

TF Kick-off meeting July 2019	Q3 2019
TF drafting papers	Q4 2019
	Q1 2020
	Q2 2020
	Q3 2020
Inviting reviews from authorities and key stakeholders	Q4 2020
Revision and submission to peer-reviewed journal	

Acknowledgements

- Task force members (and Philipp Mayer, DTU)
- External co-authors
  - Erin Maloney, University of Saskatchewan
  - José Julio Ortega-Calvo, Spanish National Research Council
  - Stefan Trapp, DTU
- External regulators and selected experts for review of manuscripts
- ECETOC Secretariat and Scientific Committee

Conceptual Framework for Moving P Assessments into the 21st Century

Aaron Redman, Jens Bietz, John Davis, **Delina Lyon**, Erin Maloney, Amelie Ott, Jens Otte, Frédéric Palais, John Parsons, Neil Wang

13.15 – 13.45

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Definition of persistence

- "Propensity for a chemical to remain in the environment before being transformed by chemical and/or biological processes in a particular emission compartment (e.g., air, water, soil or sediment)"
- Persistence is inversely correlated to degradability
- ‘Degradability’ describes *how completely* and *how quickly* a chemical will degrade in a particular environment

Definition of persistence cont.

Persistence

=

Intrinsic properties of the substance (intrinsic persistence)

+

Environmental conditions (environment-dependent persistence)

How is persistence currently evaluated in Europe?

- Compartment-specific half-life criteria, with half-lives determined by biodegradation testing

Table R.11—5: Persistence (P/vP) criteria according to Annex XIII to the REACH Regulation and related simulation tests.

According to REACH, Annex XIII, a substance fulfils the P criterion when:	According to REACH, Annex XIII, a substance fulfils the vP criterion when:	Biodegradation simulation tests from which relevant data may be obtained include:
The degradation half-life in marine water is higher than 60 days, or The degradation half-life in fresh- or estuarine water is higher than 40 days, or	The degradation half-life in marine, fresh- or estuarine water is higher than 60 days, or	OECD TG 309: Simulation test – aerobic mineralisation in surface water
The degradation half-life in marine sediment is higher than 180 days, or The degradation half-life in fresh- or estuarine water sediment is higher than 120 days, or	The degradation half-life in marine, fresh- or estuarine sediment is higher than 180 days, or	OECD TG 308: Aerobic and anaerobic transformation in aquatic sediment systems
The degradation half-life in soil is higher than 120 days	The degradation half-life in soil is higher than 180 days	OECD TG 307: Aerobic and anaerobic transformation in soil

Challenges with current P assessment

1. Compartmental half-lives based POPs, from old studies

2. Screening and higher tier test methods are not broadly applicable to all chemical types

3. Half-lives are variable, depending on measurement method and test parameters

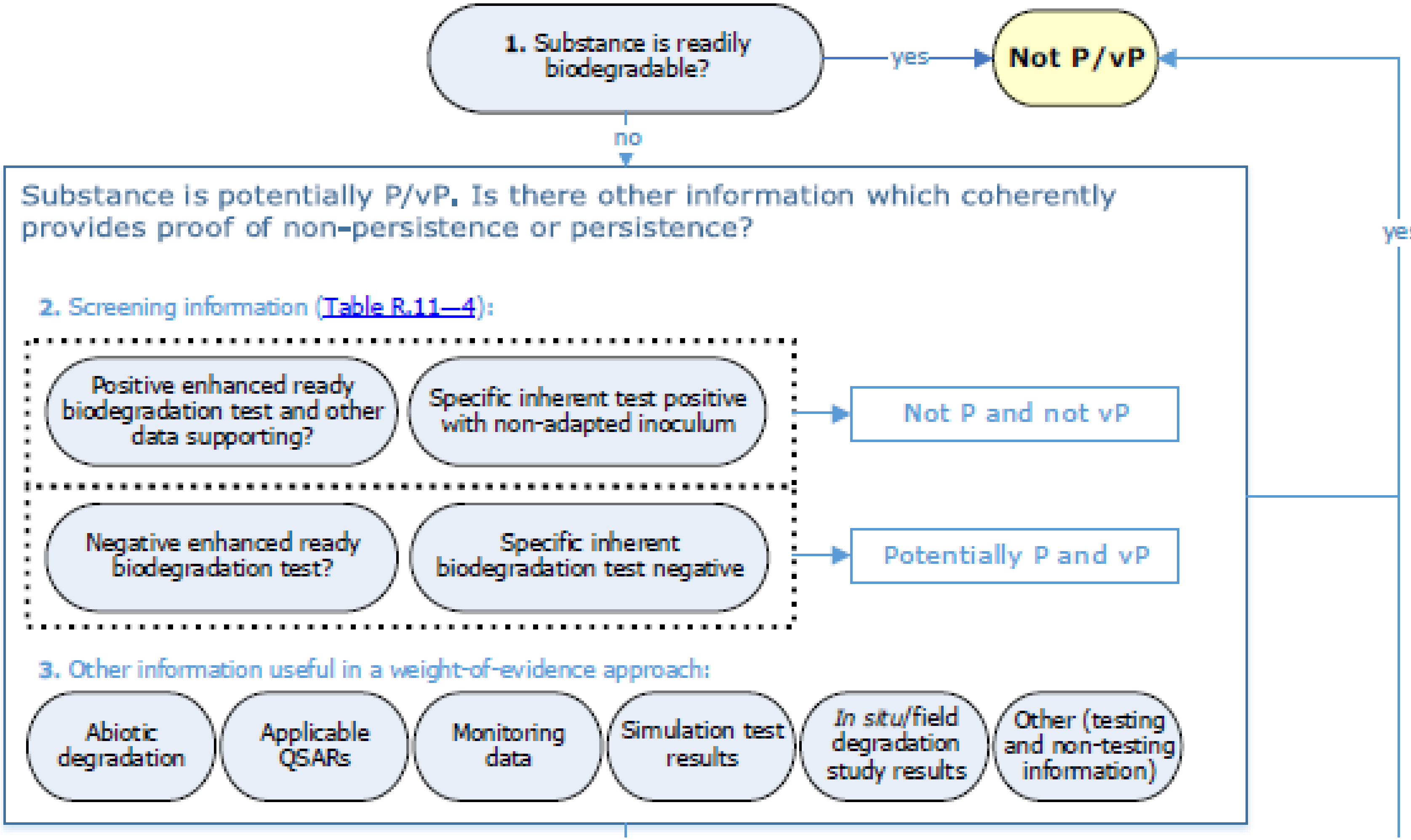
4. Single compartment behaviour does not reflect persistence in overall environment

5. Other degradation/fate processes overlooked, e.g., photolysis

Task force objective

- Propose an integrated assessment framework that combines **multimedia approaches** to organize and interpret data using a clear **WoE approach** to allow for a more **consistent, transparent and thorough assessment of persistence**

Weight-of-Evidence is recommended for P assessment in Europe



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Re-introducing the concept of overall persistence (P_{ov})

- P_{ov} → environment as a single, unified set of connected media

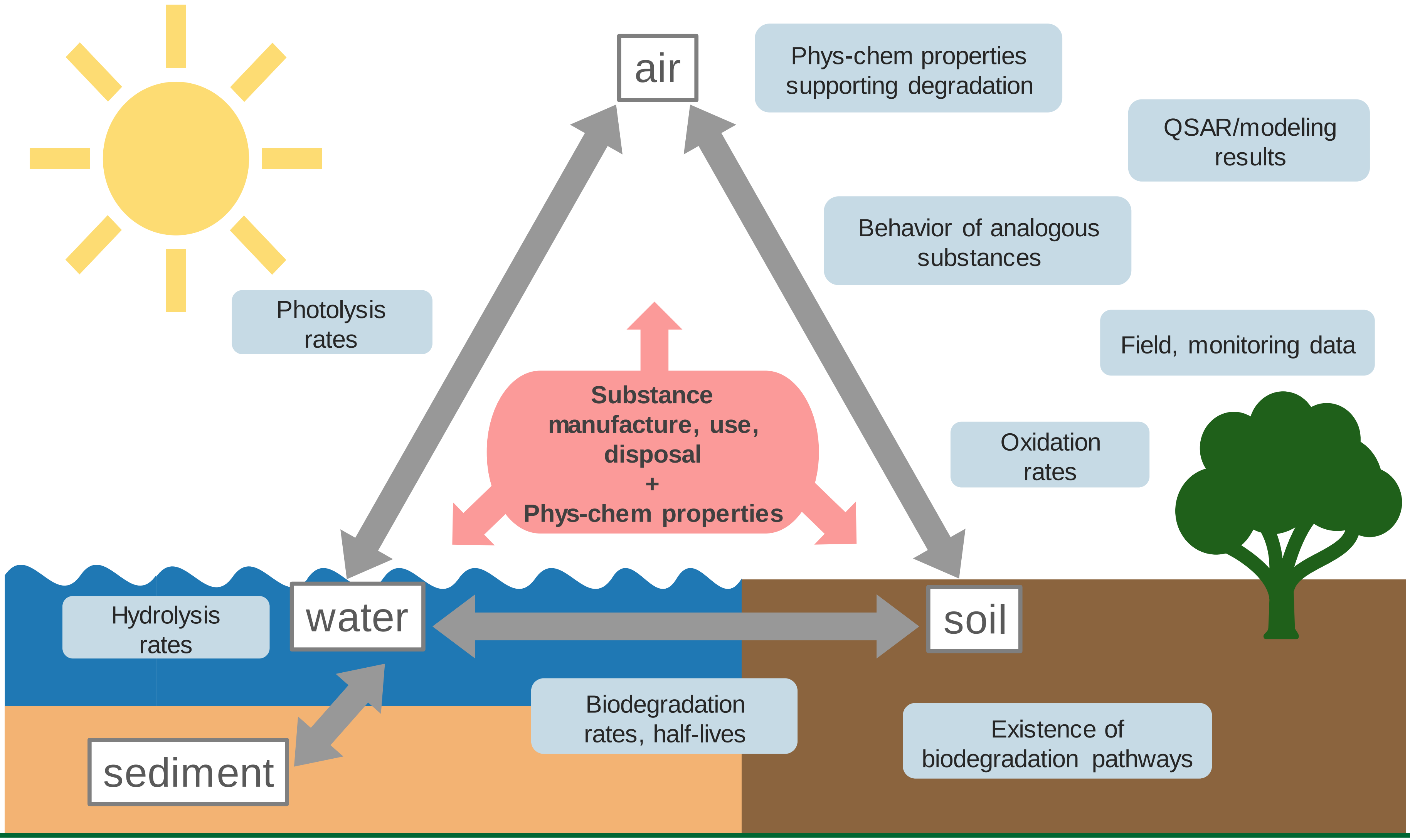
- P_{ov} calculation using multimedia fate and transport models (MFTMs)
  - multi-phase partitioning and environmental fate properties to determine residence time, predict persistence (P_{ov})
  - assume mass conservation across the entire system, while accounting for thermodynamics, inter-media transfer, input processes (emissions), and degradation

- Concept of P_{ov} raised many times since introduction in 1979 (incl. ECETOC 2003 Technical Report No. 90)

- OECD P_{ov} and LRTP Screening Tool - 2007

- P_{ov} recently proposed as suitable replacement for compartment-specific half-lives in P assessment (ECCC, 2016)

Data to feed into WoE for overall persistence



Proposed schematic of a WoE approach adapted for P assessment

(adapted from (OECD, 2019))

Step	Generic tasks	Application to P assessment
Problem formulation	▪ *Set the hypothesis* ▪ *Specific endpoints and/or final decisions*	• Hypothesis: substance is degradable (biotic or abiotic, any compartment) • Endpoints: P_{ov}, half-life in standard or nonstandard tests (Davenport et al 2021)
Evidence collection	▪ *Establish relevant lines of evidence* ▪ *Identify knowledge gaps*	• Assemble all lines of evidence • Use **unit world model** concept to identify relevant lines of evidence and data gaps
Evidence evaluation	▪ *Determine data reliability and uncertainty* ▪ *Determine relevance*	• Use established data quality metrics to screen evidence • Determine data relevance using **unit world** or **MFTM *(P_{ov})***
Evidence weighing	▪ *Score relevant lines of evidence* ▪ *Assign weight to evidence*	• Consider quantitative WoE
Evidence integration/ reporting	▪ *Evaluate consistency in evidence* ▪ *Assess impact of residual uncertainty*	• Complete Persistence Assessment based on unit world concept and WoE, • Determine persistence of substance using appropriate metrics (Pov, half-life, other relevant endpoints)

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Obtaining the right level of data for P_{ov} assessment

Initial P_{ov} assessment

- Using available or estimated parameters (Bonnell et al 2018; Gouin et al 2012)

Evaluation of P_{ov} result

- Identify the relevant compartments/processes
- Compare against benchmark, e.g., P_{ov} for POPs ≥195 days (Scheringer 2009)
- Uncertainty can be evaluated by sensitivity analysis and/or risk profile or proximity to thresholds

Refine P_{ov}

- Incorporate higher tier data as informed by intermediate analysis step

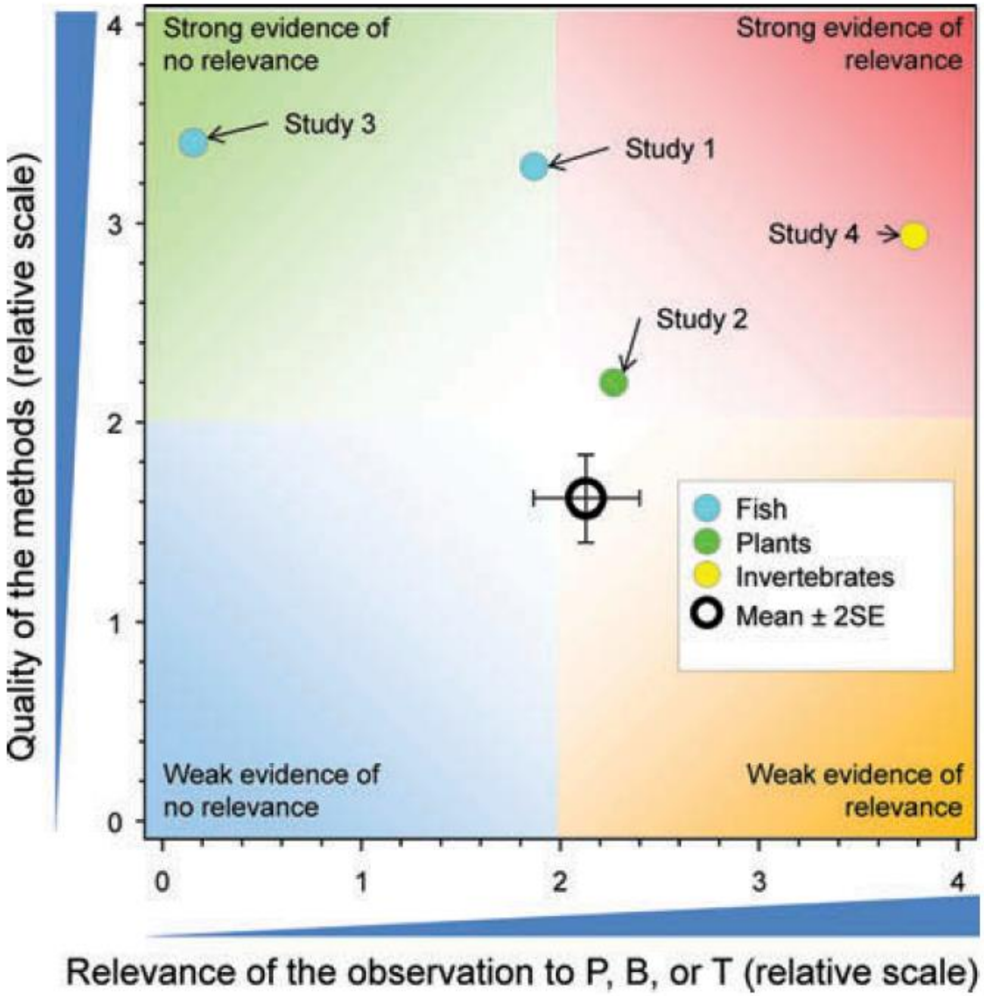
Previous examples of the use of WoE and P_{ov}

- Giesy et al. (2014) – chlorpyrifos
  - Plenty, variable data – Used geometric mean of half-lives
  - Field data
- Brandt et al. (2016) – substituted phenolic benzotriazoles
  - QSARs, biodegradation models, Environmental monitoring, Sediment core analysis
  - Summary narrative approach
- Bridges & Solomon (2016) – cyclic volatile methyl siloxanes
  - Environmental monitoring, laboratory data, field studies, MFTM
  - Proposed quantitative WoE (next slide)

Learnings & Comparison to OECD WoE approach

- Must first evaluate quality of studies (e.g., Klimisch scoring)
- Weight is to differentiate data sources, not for evaluating quality
- Final decision must be transparent

Quantitative WoE approach
(Bridges & Solomon, 2016)



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Goal: consistent, transparent and thorough P assessment

Problem formulation	▪ *Set the hypothesis* ▪ *Specific endpoints and/or final decisions*	• Hypothesis: substance is degradable (biotic or abiotic, any compartment) • Endpoints: P_{ov}, half-life in standard or nonstandard tests (Davenport et al 2021)
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Co-authors on "Conceptual Framework for Moving P Assessments into the 21st Century"

Name	Surname	Affiliation
Aaron	Redman	ExxonMobil (TF Chair)
Jens	Bietz	Clariant
Jo	Chai	Dow
John	Davis	Dow
Delina	Lyon	Shell/Concawe
Erin	Maloney	Shell/Uni. Saskatchewan
Jens	Otte	BASF
Frédéric	Palais	Solvay
John	Parsons	University of Amsterdam
Neil	Wang	Total
Amelie	Ott	Newcastle University

Q&A

Moderator: Sylvia Jacobi, Albemarle

13.45 – 14.00

Scientific Concepts and Methods for Moving P Assessments into the 21st Century

Russell Davenport, Pippa Curtis-Jackson, Philipp Dalkmann, Jordan Davies, Kathrin Fenner, Laurence Hand, Kathleen McDonough, Andreas Schäffer, Cyril Sweetlove, José Julio Ortega-Calvo, Amelie Ott, John Parsons, Stefan Trapp, Neil Wang, Aaron Redman

14.00 – 14.30

Content

- Introduction
- Major challenges by theme
- Current and future options
- Translating science into policy
- Conclusions

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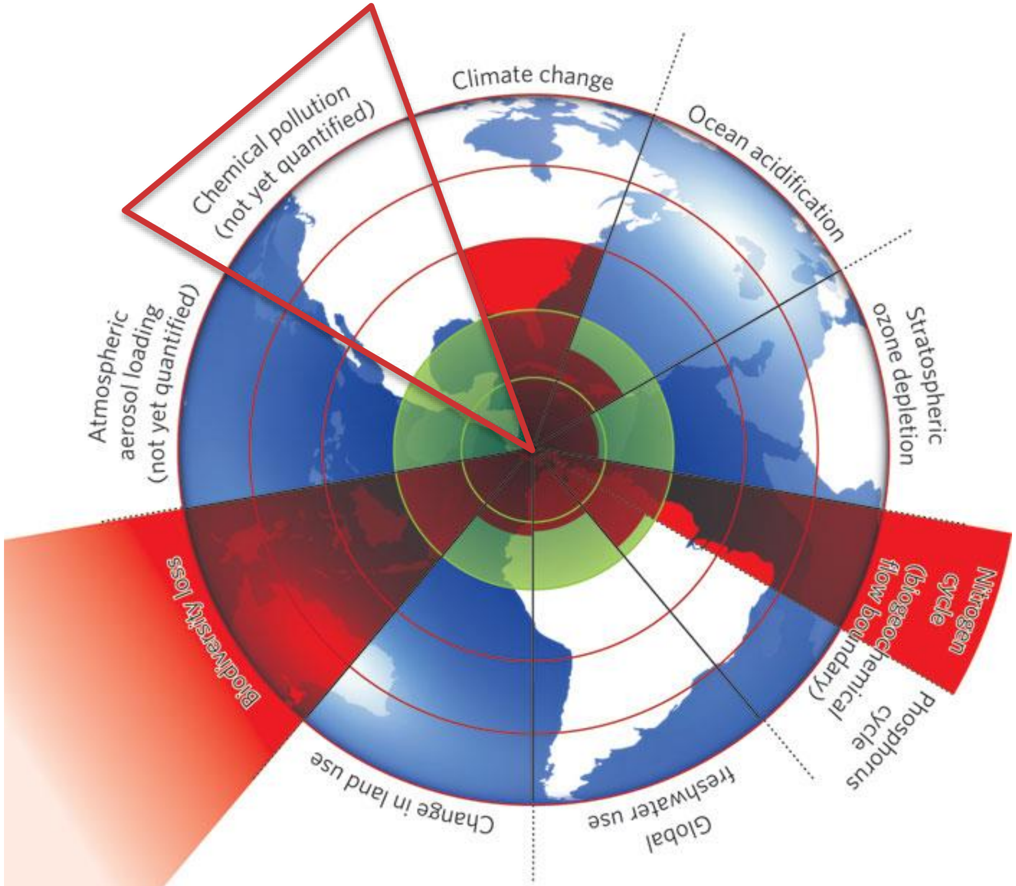
- Microbial characteristics
- Obstacles with test substance
- Testing/abiotic factors
- Linking lab to field

Modelling

Introduction
chemicals – an Earth system threat



- > 350,000 chemical & mixtures[1]
- Planetary Boundaries for Chemicals[2-4]
- Persistence central proxy for exposure[2-4]

A safe operating space for humanity in the "Anthropocene"

Rockström *et al.*, 2009 *Nature*

[1]Wang *et al.*, 2020 *EST*
[2]Diamond *et al.*, 2015 *EI*
[3]MacLeod *et al.*, 2014 *EST*
[4]Persson *et al.*, 2013 *EST*

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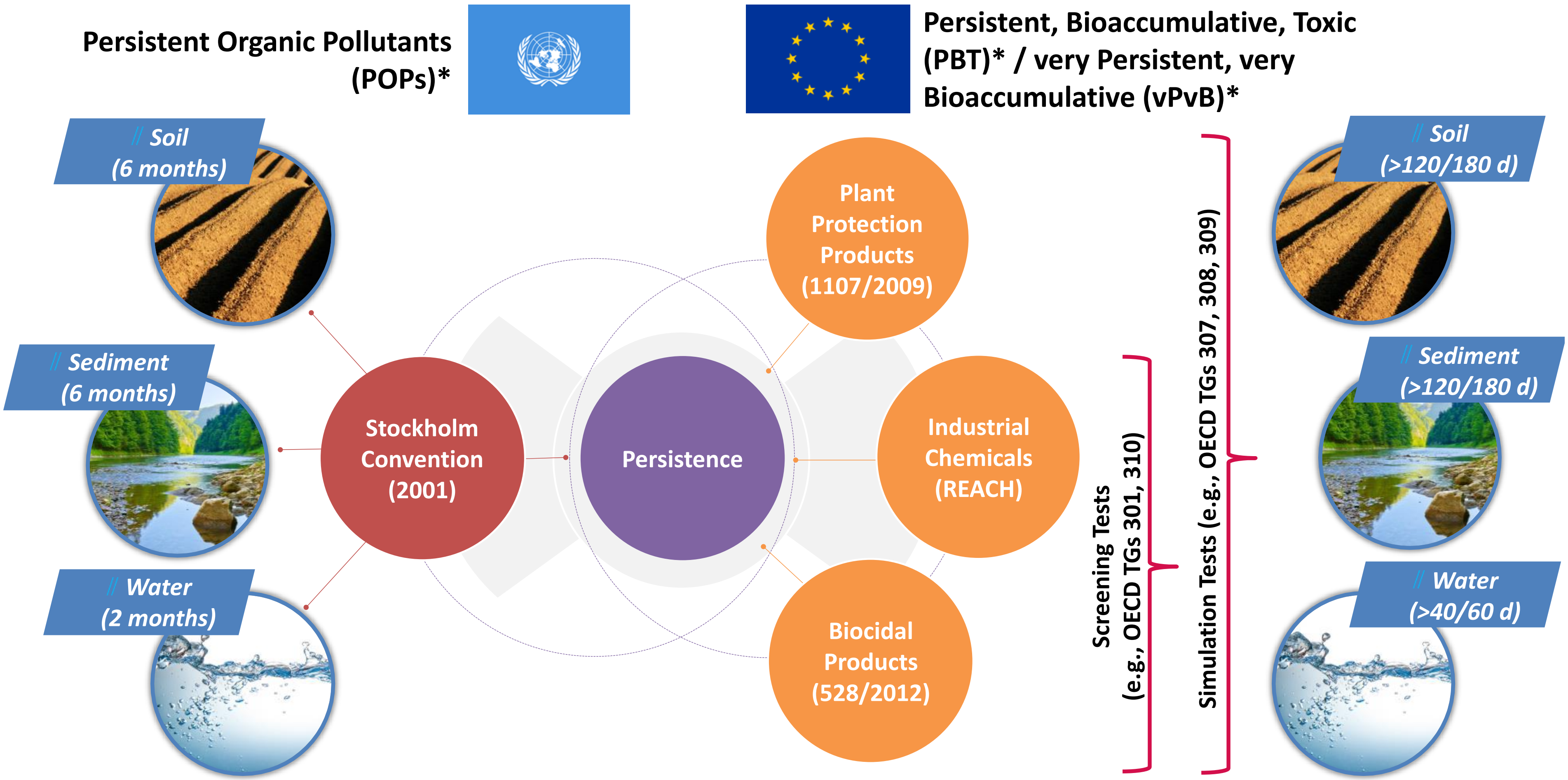
Introduction: importance and regulatory use



* Additional criteria to fulfill POP or PBT / vPvB classification: Bioaccumulation, long-range transport, (POP only), toxicity (PBT only)

Introduction: issues

- Current P assessment based on:
  - methods developed >30 years ago
  - a narrow range of chemical properties

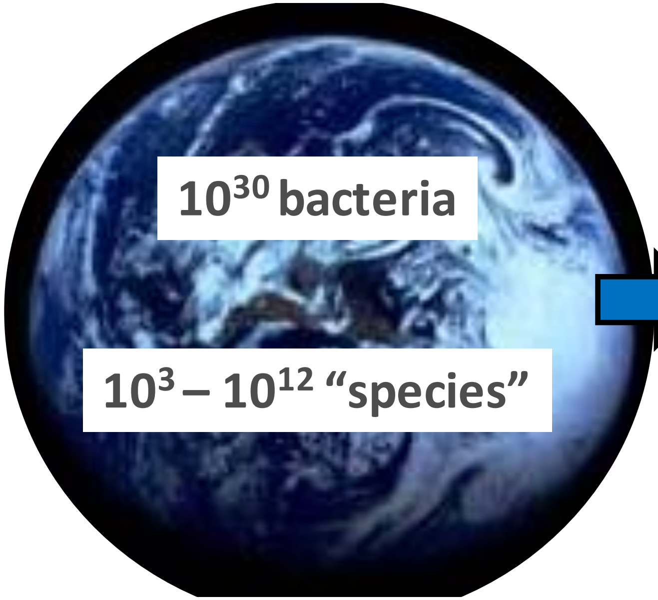
- Persistence not a single fixed physico-chemical property

  = intrinsic substance property + environmental conditions

- One test-one environmental condition ≠ real environment

Evaluate recent progress and future directions for improving such test methods

Challenge:
microbial source, sampling & characteristics



10^{30} bacteria

$10^3 – 10^{12}$ "species"

sediment

10^8 /mL

activated sludge

10^8 - 10^9 /mL

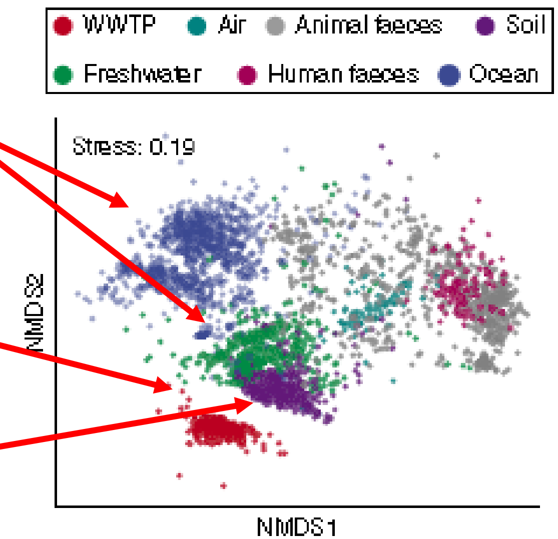
surface waters

10^5 - 10^7 /mL

soil

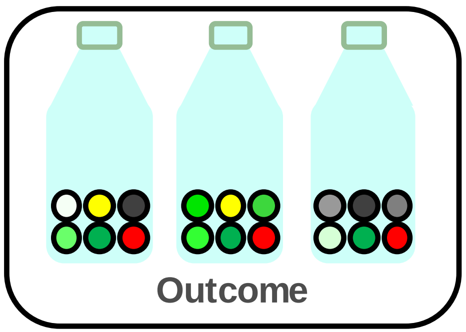
10^{10} /g

Microbial community similarity



Wu *et al.*, 2019 *Nat.Microbiol.*

Biodeg test:



Screening[1] ✓ X X

Simulation $t_{1/2}$ varies > x 10 [(2)]

Approx. cell concentrations:

$10^1 – 10^7$ /mL

$10^4 – 10^7$ /mL (OECD TG309)

Lifestyles and processes tests exclude:

Biofilms (40-80% of communities)[3]

Anaerobic[3]

Adaptation[4,5]

[1]Kowalczyk *et al.*, 2015 *EES*
[2]Latino *et al.*, 2017 *ESPI*

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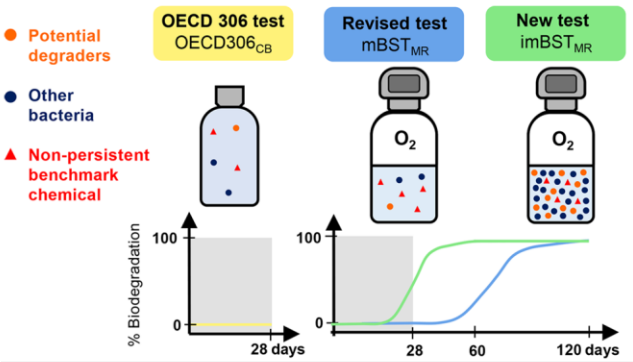
[3]Flemming & Wuertz 2019 *NRM*
[4]Poursat *et al.*, 2019 *CEST*
[5]Itrich *et al.*, 2015 *EST*

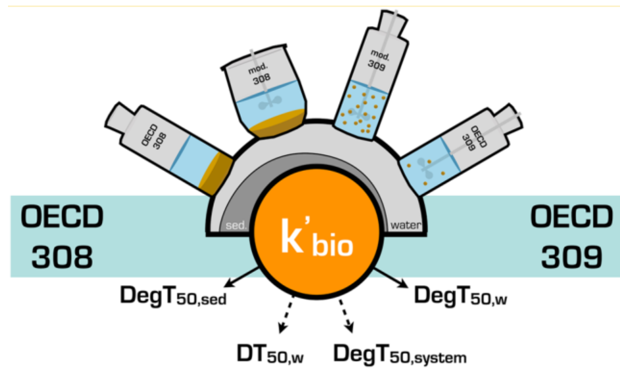
Current & future options: characterising microbial communities

Accounting for microbial abundance to improve tests

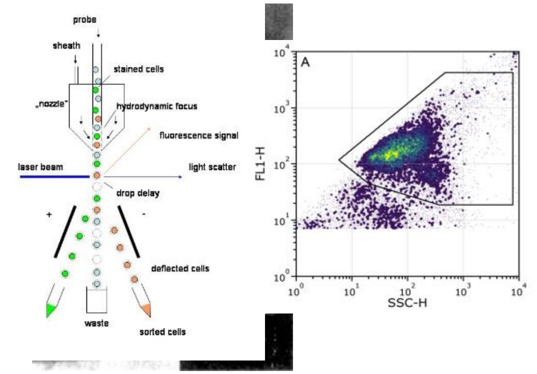
Screening tests[1]



Simulation tests[2]



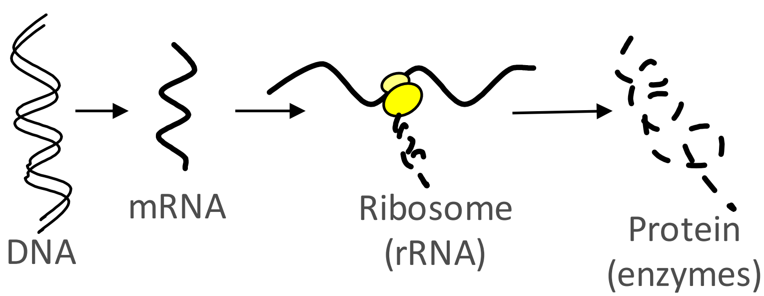
Methods



≥70 years old

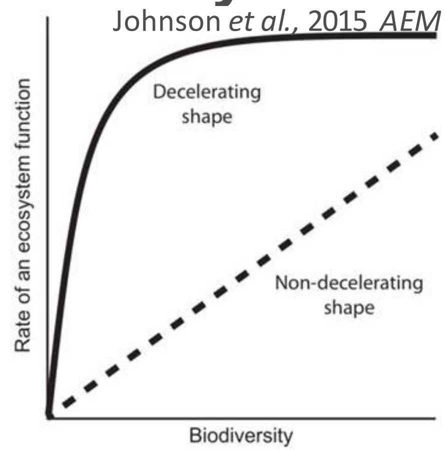
Flow cytometry[3]

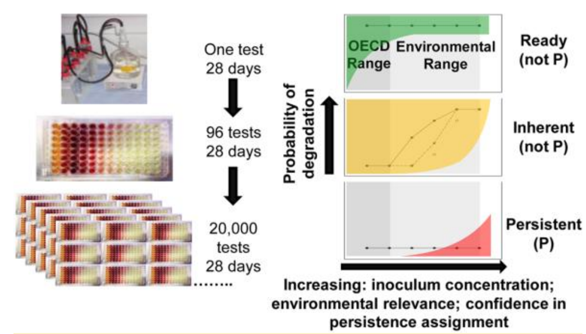
Characterising microbial diversity



'omics

Johnson *et al.*, 2015 *AEM*





Martin *et al.*, 2017 *EST*

[1]Ott et al 2020 *EST*
[2]Honti *et al.*, 2016 *CEST*
[3]Brown *et al.*, 2019 *JMM*

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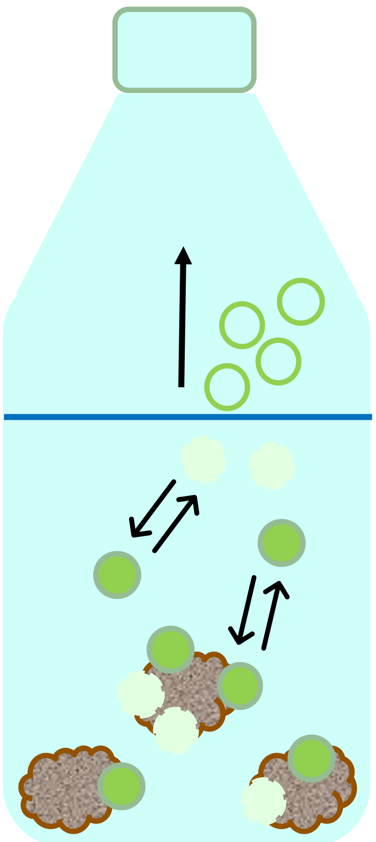
Obstacles with test substance

Simultaneous parallel processes to biodegradation



Volatility[1]

Solubility[2]

Sorption[2]

Non-extractable residues (NER)[3]

} Bioavailability

Additional issues

- Low substance concentrations
- Multiconstituent substances (e.g. UVCBs)[4]
- Substance toxicity[5]

[1]Shrestha *et al.*, 2019 *EST*
[2]Ortega-Calvo *et al.*, 2015 *EST*
[3]Schäffer *et al.*, 2018 *ESE*

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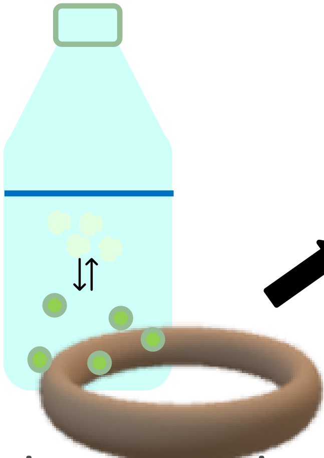
[4]Hammershøj *et al.*, 2019 *EST*
[5]Timmer *et al.*, 2020 *Chemos.*

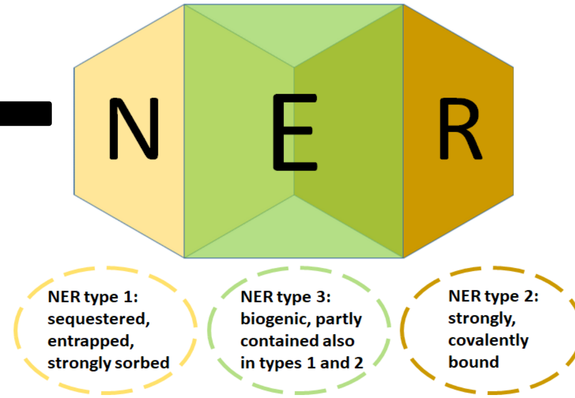
Overcoming obstacles with substances

Passive dosing for low solubility[1]



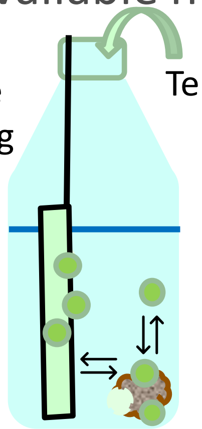
and/or

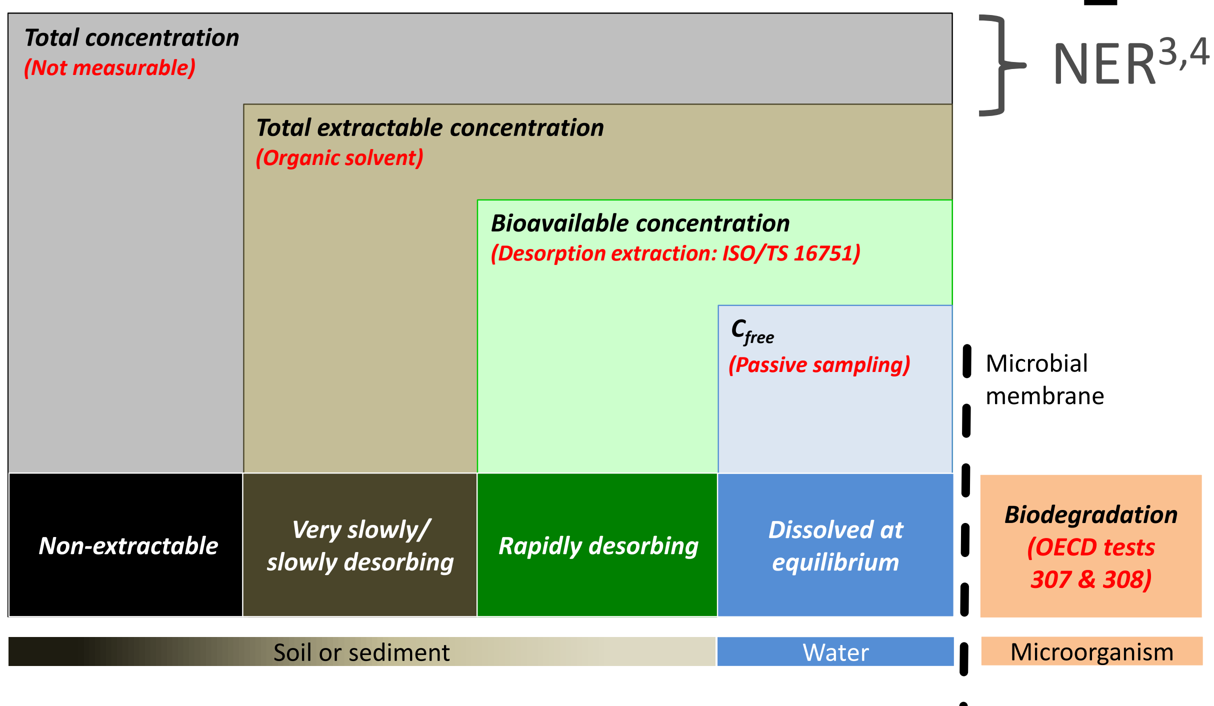
^{13}C or ^{14}C



Silylation derivatisation for type 1 and 2 NER[3]

Desorption extraction for bioavailable fractions[2]





[1]Birch *et al.*, 2018 *EST*
[3]Schäffer *et al.*, 2018 *ESE*
[4]ECETOC, 2013

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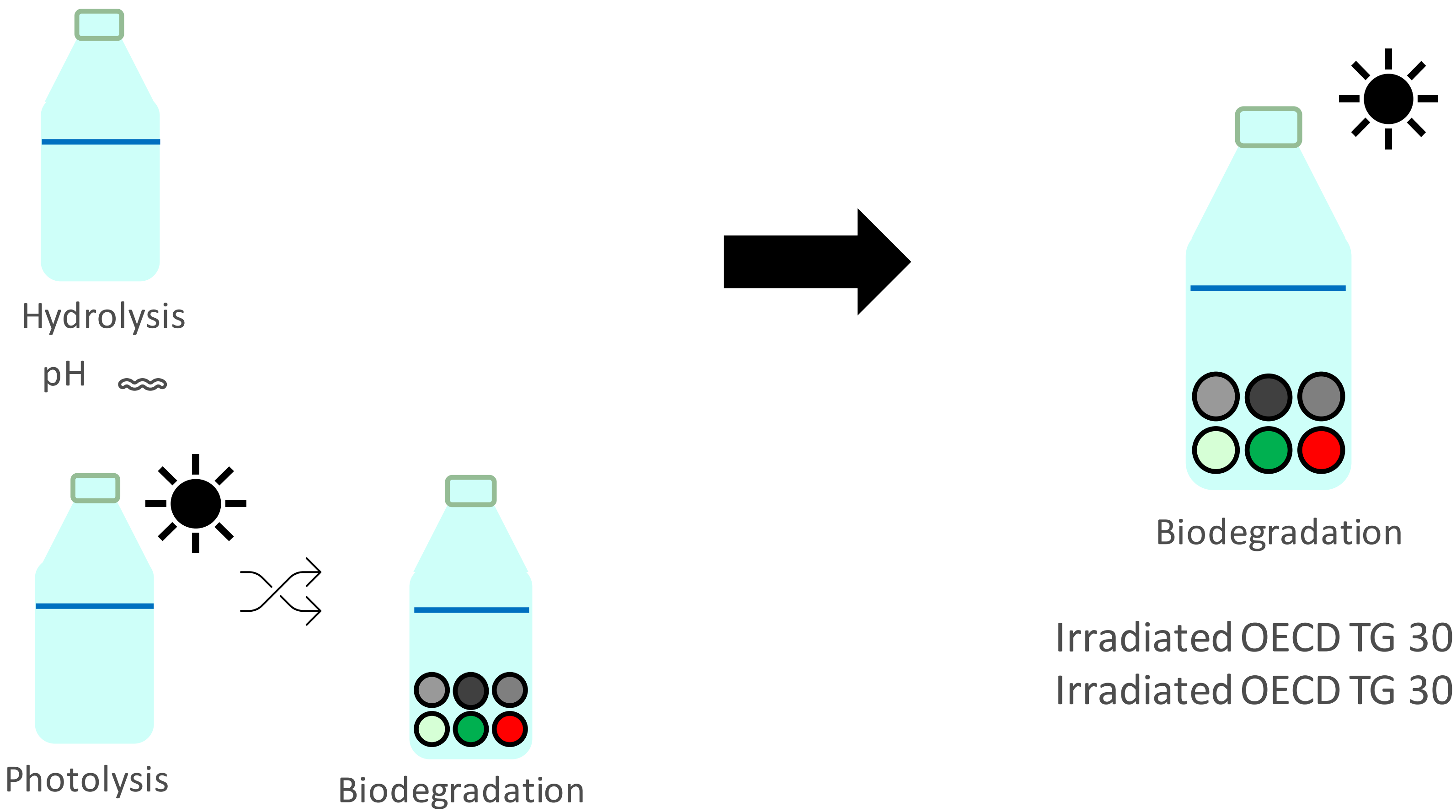
[2]Ortega-Calvo *et al.*, 2020 *EST*

Testing & abiotic factors

Siloed tests | **Combined test**



Irradiated OECD TG 308[1]
Irradiated OECD TG 309[2]

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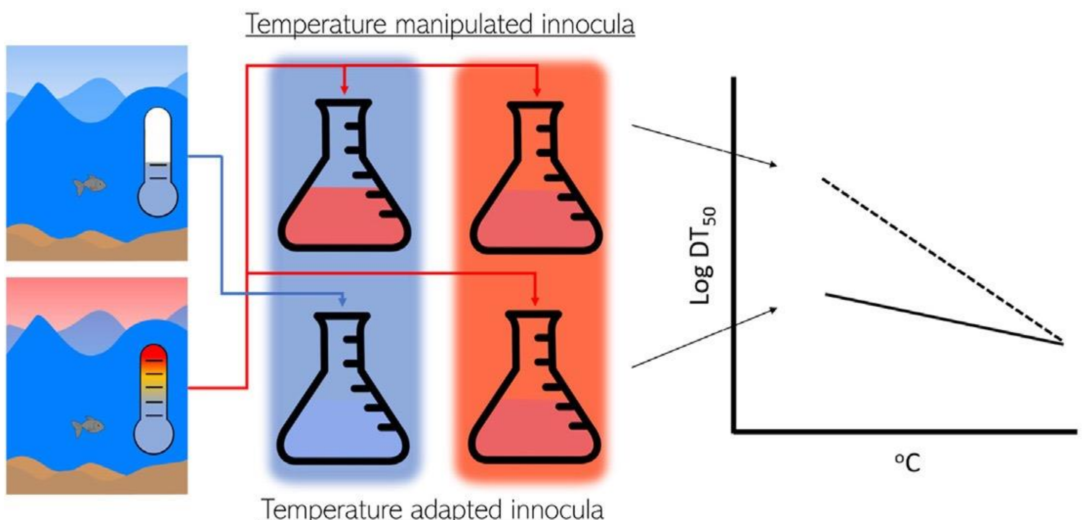
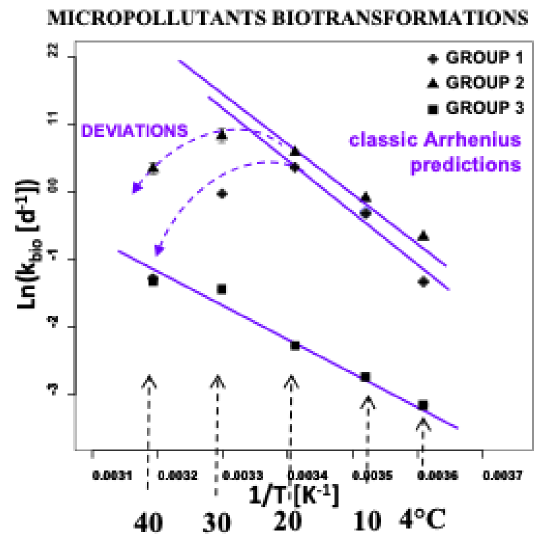
[1]EU, 2013
[2]Hand & Moreland, 2014 *ETC*

Testing & abiotic factors - temperature

- Chemical reaction temperature-dependence predicted by the Arrhenius equation
- ECHA guidance states OECD TG 309 to be carried out at 12 ^{0}C
- Q_{10} of 2.58 to correct for tests carried out at other temperatures (developed for pesticides in soil)
- Assumes a single *Ea* value for all environments and complex microbial communities



Brown *et al.*, 2020 *STOTEN*

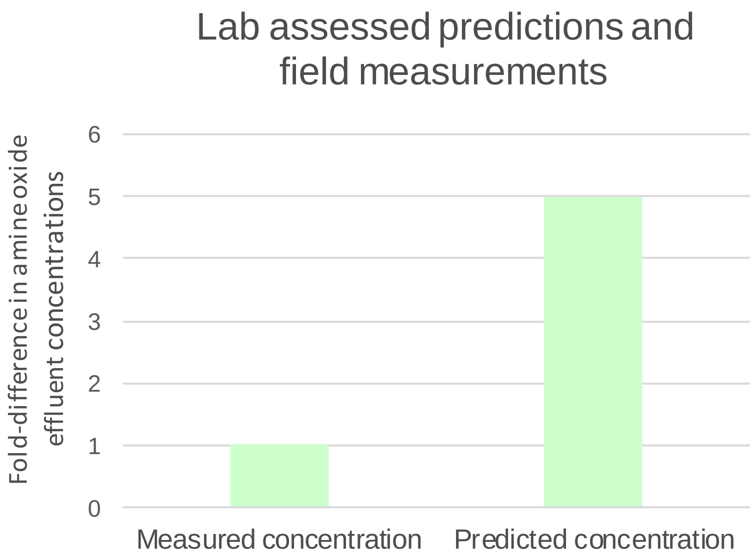


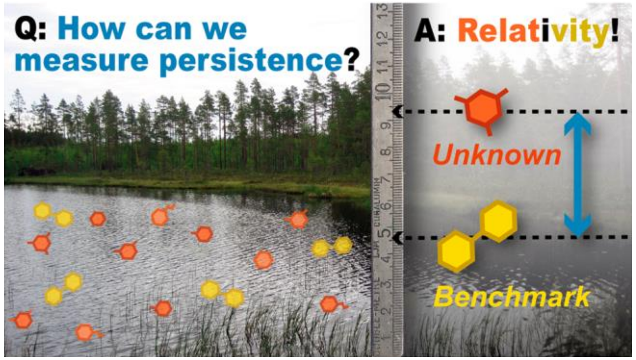
= different reaction types

Meynet *et al.*, 2020 *EST*

Linking lab P assessment to the field

- Persistence
  = intrinsic substance property + environmental conditions
- Lab assessments constrained by test design and conditions





McLachlan *et al.*, 2017 *EST*
Comber & Holt, 2010

McDonough *et al.*, 2018 *STOTEN*

Modelling

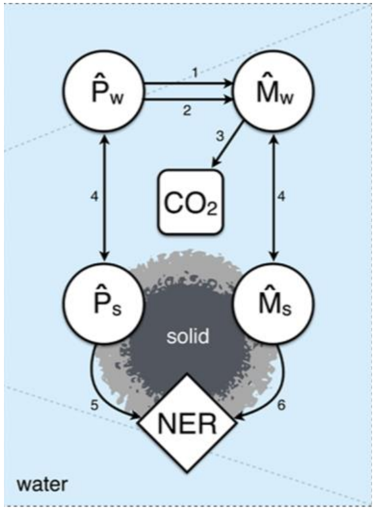
- Predict microbial biotransformation half-lives
- Predict microbial biotransformation products
    - Metabolites
    - NER

Databases

- Requirement for metadata
- Pathway data e.g. Eawag-BBD/PPS & envipath.org

Latino *et al.*, 2017 *ESPI*

Inverse modelling for biotransformation rates



Honti *et al.*, 2016 *EST*
Trapp *et al.*, 2018 *EST*

QSBRs

- Improvements in machine-learning
- Strategies to widen datasets through normalization e.g. biomass concentration.
- Group substances based on enzymatic transformation[1-3].

[1]Achermann *et al.*, 2018 EST
[2]Nolte et al 2018 *ESPI*
[3]Wang *et al.*, 2018 *Chemos.*

Translating science into policy

- Method validity and ratification
  - Reliability scores
  - Limitations in current test
  - Time to ratification
- Knowledge, skills and data discrepancies
  - Academia/industry versus guidelines
  - Contract Research Organisations (CROs)
  - Data reporting
- Early engagement

Conclusions

- Persistence is non-trivial and complex
- Scientific advances could improve the precision and accuracy of P assessments
- Time of implementing advances needs to be accelerated (< 10 years)
- More efficient collaboration between academia, regulators and industry

Q&A

Moderator: Kathrin Fenner, EAWAG

14.30 – 14.45

Outlook

Pippa Curtis-Jackson, UK Environment Agency

14.45 – 15.00

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Regulatory perspective

- Demonstrating the safety of a substance is the responsibility of the Registrant
- Persistence assessment evolves slowly
  - Integrated testing strategy (ECHA guidance)
  - Testing, Weight-of-Evidence, read-across
  - Guidance on interpretation (R7 and R11)

Regulatory perspective

- A global appetite for change amongst regulatory bodies must be inspired
- Regulators do recognise that advances have been made in science underpinning persistence assessment that may not be in the guidance
- Regulators realise that to assist in this change we must prioritise supporting the development of additional standardized intermediate tests (potentially ring tested at an OECD level), that could be read-across to the legal criteria, and do not undermine legacy conclusions

Regulatory perspective

- Always remember when working to improve the science of persistence assessment
  - The current assessment approach is precautionary
  - Any replacement standard and interpretation must be similarly precautionary
  - Before acceptance any new study or way of working must be proved i.e. introducing chemical benchmarking to studies and improving our microbial population understanding will need validating

Regulatory perspective

- Applicability, standardisation and agreement on interpretation between both registrants and regulators must be agreed
- Ideally new/replacement tests should ideally be quicker, more reproducible, accurate, reliable and comparable than that currently used for conclusion

OUTLOOK

- Set precedent
- Use the improved *framework*
- Use the improved *scientific understanding* and new methods

MOST CHEMICAL REGULATORS ARE SCIENTISTS TOO

We share a common language

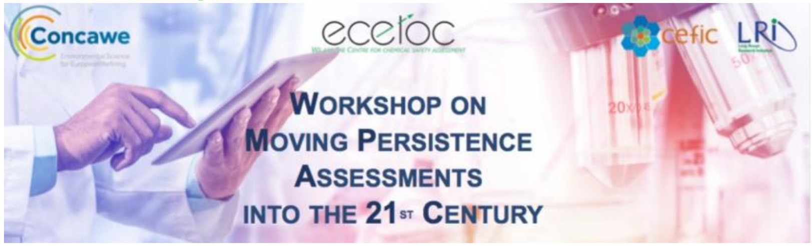
Regulatory perspective

Aims of this Task Force

- Develop an improved *framework* and best practices for persistence and degradation assessments based on *progress* in the scientific understanding of the underlying process

Ongoing & future work by ECETOC and Cefic LRI

- ECETOC/Cefic LRI/Concawe joint workshop on Moving P assessments into the 21st century – May 2021 - TBC



- Cefic LRI ECO 52: 'Bioavailability, complex substances and overall persistence (BCOP): Three themes to deliver a step-change in persistence assessments' - Christopher Hughes, Ricardo, UK
- Cefic LRI ECO 55: RfP title 'Assessing the impact of sample collection on microbial population and validity criteria in the OECD 309 surface water mineralisation test'
- Persistence Assessment Tool – next step to improve consistency, transparency & implementation of WoE

cefic LRI Long-Range Research Initiative

Thank you

ECETOC Task Force: Moving persistence assessments into the 21st Century

For more information, please contact:

Aaron Redman: aaron.d.redman@exxonmobil.com
Delina Lyon: delina.lyon@concawe.eu
Russell Davenport: russell.davenport@newcastle.ac.uk
Pippa Curtis-Jackson: pippa.curtisjackson@environment-agency.gov.uk
Amelie Ott: a.i.g.ott2@newcastle.ac.uk

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Connect with us
@ECETOC
linked.com/company/ecetoc
view our YouTube channel

Rue Belliard 40, Bte19
1040 Brussels
Belgium
Tel: +32 2 675 3600
Email: info@ecetoc.org