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REACH: Guidance and Methods for the Identification and Assessment of PMT/vPvM Substances

2nd Edition

by:
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Abstract: REACH: Guidance and Methods for the Identification and Assessment of PMT/vPvM Substances

This is an update of the 2019 guidance and methods for the identification and assessment of Persistent, Mobile and Toxic (PMT) and very Persistent and very Mobile (vPvM) substances. The PMT/vPvM assessment in this report uses a traffic light colour scheme to represent the conclusion of the assessment and the associated uncertainty level.

As of September 2019, there were 22400 substances in the REACH registration database, from which 13405 unique chemical structures could be identified and assessed. Over 27 % (3595 of 13405) did not meet the PMT/vPvM criteria. No final PMT/vPvM conclusion was possible for 67 % (9047 of 13405) due to either insufficient data for 41 % (5542 of 13405) or ambiguous assessments for 26 % (3504 of 13405). There were 3.1 % (421 of 13405) that met the criteria for persistence and mobility but with currently no high-quality consensus conclusions that the criteria for toxicity was met. Only 2.6 % (343 of 13405) met the PMT/vPvM criteria.

The guidance and methods were applied to REACH registered substances using both the PMT/vPvM criteria proposed by Neumann and Schliebner (2019) under REACH published as UBA TEXTE 127/2019, and those proposed by the European Commission (EC) in 2021. When using the less stringent PMT/vPvM criteria proposed by the EC, the number of identified PMT/vPvM substances is reduced to 1.9% (259 of 13405).

That already 4358 out of 13405 unique chemical structures in the REACH registered database could be assessed with the guidance indicates that the PMT/vPvM criteria are fit-for-purpose for integration in the CLP and REACH regulation. However, no final PMT/vPvM conclusion being possible for 67 % (9047 of 13405) confirms that there are also substantial data gaps in the REACH registration database that should immediately be addressed through an update of the existing REACH registration requirements.

This guidance and methods can be immediately used by REACH registrants, to ensure safety of their substances, to close data gaps, and when necessary to seek safer alternatives or develop risk mitigation measures (RMM). In addition, Member States and ECHA can use this guidance when identifying PMT/vPvM substances as substances of very high concern (SVHC) following Article 57f of REACH.

Kurzbeschreibung: REACH: Leitlinien und Methoden für die Identifizierung und Bewertung von PMT/vPvM-Stoffen

Dies ist eine Aktualisierung der Leitlinien und Methoden für die Identifizierung und Bewertung von persistenten, mobilen und toxischen (PMT), sowie sehr persistenten und sehr mobilen (vPvM) Stoffen aus dem Jahr 2019. Die PMT/vPvM-Bewertung in diesem Bericht verwendet ein Ampelfarbschema, um die Schlussfolgerung und das verbundene Unsicherheitsniveau darzustellen.

Im September 2019 befanden sich 22400 Stoffe in der REACH-Registrierungsdatenbank, aus denen 13405 einzigartige chemische Strukturen identifiziert und bewertet werden konnten. Über 27 % (3595 von 13405) erfüllten nicht die PMT/vPvM-Kriterien. Für insgesamt 67 % (9047 von 13405) war keine abschließende Bewertung möglich, entweder aufgrund unzureichender Daten (41 %; 5542 von 13405) oder aufgrund nicht eindeutiger Bewertungen (26 %; 3504 von 13405). Für 3,1 % (421 von 13405) waren zwar die Kriterien für Persistenz und Mobilität erfüllten, aber es fehlt eine abschließende Bewertung, ob das T-Kriterium erfüllt ist. Nur 2,6 % (343 von 13405) erfüllten die PMT/vPvM-Kriterien.

Die Leitlinien und Methoden wurden angewendet auf REACH-registrierte Stoffe sowohl unter Einsatz der von Neumann und Schliebner (2019), veröffentlicht als UBA TEXTE 127/2019, im Rahmen von REACH vorgeschlagenen PMT/vPvM-Kriterien, als auch unter Einsatz der von der Europäischen Kommission im Jahr 2021 im Rahmen von CLP vorgeschlagenen Kriterien. Bei Verwendung der von der Europäischen Kommission vorgeschlagenen weniger strengen PMT/vPvM-Kriterien reduziert sich die Zahl der identifizierten PMT/vPvM-Stoffe auf 1,9 % (259 von 13405).

Dass bereits 4358 von 13405 einzigartigen chemischen Strukturen in der REACH-Registrierungsdatenbank mit diesen Leitlinien bewertet werden könnten, deutet darauf hin, dass die PMT/vPvM-Kriterien für die Integration in die CLP- und REACH-Verordnung geeignet sind. Allerdings Keine endgültige PMT/vPvM-Schlussfolgerung für 67 % (9047 von 13405) bestätigt jedoch, dass es auch erhebliche Datenlücken in der REACH-Registrierungsdatenbank gibt, die sofort durch eine Aktualisierung der bestehenden REACH-Registrierungsanforderungen behoben werden sollten.

Diese Leitlinien und Methoden können von REACH-Registranten sofort angewendet werden, um die Sicherheit ihrer Stoffe zu gewährleisten, Datenlücken zu schließen und ggf. sicherere Alternativen zu verwenden oder Risikominderungsmaßnahmen (RMM) zu implementieren. Darüber hinaus können die EU-Mitgliedstaaten und die ECHA sie bei der Identifizierung von PMT/vPvM-Stoffen als besonders besorgniserregende Stoffe (SVHC) gemäß Artikel 57f der REACH anwenden.

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List of abbreviations

CLP	Regulation 1272/2008/EC on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006
DNEL	Derived no effect level
D_{OW}	Octanol-water distribution coefficient for all species
EC10	Concentration of a chemical that shows effects for 10% of the test animals
HPLC	High-performance liquid chromatography
$\log K_{oc}$	Soil sorption coefficient normalized to the total organic carbon
LSER	Linear solvation energy relationship
M	Mobility criterion
MW	Molecular weight
P	Persistent criterion
PBT	Persistent, bioaccumulative and toxic
Pro S.P.	A previously developed IT Tool by ECHA for chemical substance data
NOEC	No observed effect concentration
PM	Persistent and mobile
PMT	Persistent, mobile and toxic
QSAR	Quantitative structure activity relationship
REACH	Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)
RMM	Risk management measures
RW	Raw water
SMILES	Simplified molecular-input line-entry system
STOT RE	Specific target organ toxicity - repeat exposure
SVHC	Substances that may have serious and often irreversible effects on human health and the environment can be identified as substances of very high concern (SVHCs) under the REACH regulation.
T	Toxic
TPA	Tonnes per annum
UVCB	Substances of "Unknown or Variable composition, Complex reaction products or Biological material"
vP	Very persistent
vM	Very mobile
vPvB	Very persistent and very bioaccumulative
vPvM	Very persistent and very mobile

Summary

The German Environment Agency (UBA) has developed, justified and proposed criteria for identifying Persistent, Mobile and Toxic (PMT) substances as well as very Persistent and very Mobile (vPvM) substances in the regulatory context of the EU REACH Regulation (EC No 1907/2006) (Neumann and Schliebner, 2019). PMT/vPvM substances are those which have intrinsic substance properties that would pose a hazard to the sources of our drinking water if released into the environment. As part of the EU's Chemical Strategy for Sustainability for a Toxic-Free Environment (European Commission, 2020), the European Commission (EC) has outlined its initiative to adopt PMT and vPvM as two new hazard classes in the EU CLP regulation (EC No 1272/2008). The PMT/vPvM criteria proposed by the EC in 2021 are less stringent than the PMT/vPvM criteria proposed by the UBA in 2019, particularly in relation to the mobility criterion. The M/vM criteria proposed by UBA in 2019 are a minimum, experimentally measured log K_{OC} determined at a pH between 4-9 of < 4.0 for M and log K_{OC} <3.0 for vM. In 2021 the EC proposed a log K_{OC} thresholds for M and vM of <3.0 and <2.0, respectively (European Commission, 2021), which was later published as a Delegated Amendment to the CLP regulation in December, 2022 (European Commission, 2022).

To assist the implementation of the PMT/vPvM criteria, this report presents i) updated guidance and methods for assessing if a substance meets the PMT/vPvM criteria and ii) the application of these guidance and methods to all substances in the REACH registration database as of September 2019 as well as their transformation products

Updated guidance and methods for assessing if a substance meets the PMT/vPvM criteria

Updated guidance and methods for the identification and assessment of PMT/vPvM substances was developed. This guidance be applied for both prospective registration of substances under REACH as well as retrospective assessments for substances already in the REACH registration database. A traffic light colour scheme was developed that accounts for both data quality and the conclusion of the PMT/vPvM assessment. The criteria for persistence are based on media specific simulated biodegradation half-lives, $t_{1/2}$ (days), which are rarely available. The criteria for mobility is based on the log K_{OC} value, which are available for approximately 20% of REACH registered substances. Due to these large data gaps, screening parameters for half-lives (e.g. readily biodegradable tests, QSARs) and K_{OC} (i.e. using K_{OW} and D_{OW} values) were investigated empirically in this report to: i) assess their statistical performance in predicting if a substance meets the P/vP and M/vM criteria based on simulated half-lives and experimental log K_{OC} data, respectively; and, ii) based on this performance, develop a weight-of-evidence for assessing PMT/vPvM substances based on screening parameters.

Applying the updated guidance and methods to the substances in the REACH registration database as of September 2019 as well as their transformation products

22400 substances were in the REACH registration database as of September 2019. For 15474 of these an organic structure could be identified. Upon closer examination, only 12960 organic chemical structures were unique. After considering known transformation reactions, an additional 445 organic chemical structures were identified, bring the total number of unique organic chemical structures to 13405. The PMT/vPvM assessment was applied to all 13405. Only 2.6% (343 of 13405) met the PMT/vPvM criteria proposed by the UBA in 2019 compared to only 1.9% (259 of 13405) that met the less stringent PMT/vPvM criteria proposed by the EC in 2021.

Following Article 14(1) of REACH, a PBT/vPvB assessment needs to be carried out for substances which are produced or imported in volumes > 10 tpa and are not used as an intermediate only (according to Article 14(1) of the REACH regulation). After taking Article 14 into account, only 3893 unique chemical structures could be identified that belong to a substance registered at volumes > 10 tpa. Considering only these 3893 substances, the proportion of PMT/vPvM substances were 4.9% (192 of 3893) and 3.6% (139 of 3893), respectively. The results indicate that the implementation of the PMT/vPvM criteria into REACH regulation would therefore only classify a minor fraction of REACH registered substances as PMT and/or vPvM, indicating the impact on the industrial chemical market would be very limited.

The utilization of this guideline is encouraged by registrants and regulators to identify substances that they produce or monitor. This will help prioritize which substances need the most urgent action for preventing emissions, or for removing from the sources of our drinking water. Doing so will enable the European and International goals related to zero pollution and drinking water safety to be met, thereby protecting future generations.

Zusammenfassung

Das Umweltbundesamt (UBA) hat Kriterien für die Identifizierung persistenter, mobiler und toxischer (PMT) sowie sehr persistenter und sehr mobiler (vPvM) Stoffe im Regelungskontext der REACH-Verordnung (EG Nr. 1907/2006) entwickelt, begründet und vorgeschlagen (Neumann und Schliebner, 2019). PMT/vPvM-Stoffe haben intrinsische Stoffeigenschaften, die eine Gefahr für die Ressourcen unserer Trinkwässer darstellen, wenn sie in die Umwelt freigesetzt würden. Im Rahmen der Chemikalienstrategie der EU für Nachhaltigkeit für eine schadstofffreie Umwelt (Europäische Kommission, 2020) hat die Europäische Kommission ihre Initiative zur Annahme von PMT und vPvM als zwei neue Gefahrenklassen in der EU-CLP-Verordnung (EG Nr. 1272/2008) skizziert. Die von der Kommission 2021 vorgeschlagenen PMT/vPvM-Kriterien sind weniger streng als die vom UBA 2019 vorgeschlagenen PMT/vPvM-Kriterien, insbesondere in Bezug auf das Mobilitätskriterium. Die vom UBA 2019 vorgeschlagenen M/vM-Kriterien sind ein minimaler, experimentell gemessener log KOC bei einem pH-Wert zwischen 4-9 von < 4,0 für M und log KOC < 3,0 für vM. Im Jahr 2021 schlug die Kommission eine log KOC-Schwellenwerte für M und vM von < 3.0 bzw. < 2.0 vor (Europäische Kommission, 2021a), die später im Dezember 2022 als delegierte Änderung der CLP-Verordnung veröffentlicht wurde (Europäische Kommission, 2022).

Um die Implementierung der PMT/vPvM-Kriterien zu unterstützen, werden in diesem Bericht vorgestellt: i) aktualisierte Leitlinien und Methoden zur Bewertung, ob ein Stoff die PMT/vPvM-Kriterien erfüllt und ii) die Anwendung dieser Leitlinien und Methoden auf alle Stoffe in der REACH-Registrierungsdatenbank Stand September 2019 sowie auf ihre Transformationsprodukte.

Aktualisierte Leitlinien und Methoden zur Bewertung, ob ein Stoff die PMT/vPvM-Kriterien erfüllt

Es wurden aktualisierte Leitlinien und Methoden für die Identifizierung und Bewertung von PMT/vPvM-Stoffen entwickelt. Diese Leitlinien gelten sowohl prospektiv für die Registrierung von Stoffen im Rahmen von REACH als auch für eine retrospektive Bewertungen von Stoffen, die

bereits in der REACH-Registrierungsdatenbank enthalten sind. Es wurde ein Ampelfarbenschema entwickelt, das sowohl die Datenqualität als die Schlussfolgerung der PMT/vPvM-Bewertung selbst visualisiert. Die Kriterien für die Persistenz basieren auf medienspezifischen simulierten Halbwertszeiten des biologischen Abbaus, t1/2 (Tage), die nur selten verfügbar sind. Die Mobilitätskriterien basieren auf dem log KOC-Wert, der für etwa 20 % der in der REACH-Verordnung registrierten Stoffe verfügbar ist. Aufgrund dieser großen Datenlücken wurden die Screening-Parameter für Halbwertszeiten (z. B. Test auf leichte biologische Abbaubarkeit und QSARs) und K_{OC} (d. h. K_{OW}- und D_{OW}-Werten) in diesem Bericht empirisch untersucht, um i) ihre statistische Leistung bei der Vorhersage zu bewerten, ob ein Stoff die P/vP- und M/vM-Kriterien auf der Grundlage simulierter Halbwertszeiten bzw. experimenteller Log-KOC-Daten erfüllen würde; und ii) auf der Grundlage dieser Leistung einen *weight-of-evidence* für die Bewertung von PMT/vPvM-Stoffen auf der Grundlage von Screening-Parametern zu entwickeln.

Anwendung der aktualisierten Leitlinien und Methoden auf die Stoffe in der REACH-Registrierungsdatenbank Stand September 2019 sowie auf ihre Transformationsprodukte

Im September 2019 befanden sich 22400 Stoffe in der REACH-Registrierungsdatenbank. Für 15474 davon konnte eine organische Struktur ermittelt werden. Bei näherer Betrachtung waren nur 12960 organische chemische Strukturen einzigartig. Nach Berücksichtigung bekannter Transformationsreaktionen wurden weitere 445 organische chemische Strukturen ermittelt, wodurch sich die Gesamtzahl der einzigartigen organischen chemischen Strukturen auf 13405 erhöht. Die PMT/vPvM-Bewertung wurde auf alle 13405 angewandt. Nur 2,6 % (343 von 13405) erfüllten die vom UBA 2019 vorgeschlagenen PMT/vPvM-Kriterien, gegenüber nur 1,9 % (259 von 13405), die auch die von der Kommission 2021 vorgeschlagenen weniger strengen PMT/vPvM-Kriterien erfüllten.

Gemäß Artikel 14 Absatz 1 der REACH-Verordnung ist für Stoffe, die in Mengen > 10 tpa hergestellt oder eingeführt werden und nicht nur als Zwischenprodukt verwendet werden, eine PBT/vPvB-Bewertung durchzuführen (gemäß Artikel 14 Absatz 1 der REACH-Verordnung). Nach Berücksichtigung von Artikel 14 konnten nur 3893 einzigartige chemische Strukturen ermittelt werden, die zu einem Stoff gehören, der in Mengen > 10 tpa registriert ist. Betrachtet man nur diese 3893 Stoffe, so betrug der Anteil der PMT/vPvM-Stoffe 4,9 % (192 von 3893) bzw. 3,6 % (139 von 3893). Die Ergebnisse deuten darauf hin, dass die Implementierung der PMT/vPvM-Kriterien in die REACH-Verordnung daher nur einen kleinen Teil der REACH-registrierten Stoffe als PMT und/oder vPvM einstufen würde, was darauf hindeutet, dass die Auswirkungen auf den Markt für Industriechemikalien sehr begrenzt wären.

Die Registranten und Regulierungsbehörden werden ermutigt, diese Leitlinie zu nutzen, um Stoffe zu identifizieren, die sie herstellen oder überwachen. Dies wird dazu beitragen, Prioritäten zu setzen, welche Stoffe die dringendsten Maßnahmen zur Vermeidung von Emissionen oder zur Entfernung aus den Ressourcen unserer Trinkwässer benötigen. Dies wird es ermöglichen, die europäischen und internationalen Ziele in Bezug auf das Null-Schadstoff-Ziel und die Trinkwassersicherheit zu erreichen und damit künftige Generationen zu schützen.

This report is part of research project (FKZ 3719 65 408 0) that started in 2019 to address several aims related to the implementation and utilization of the PMT/vPvM criteria to assist REACH registrants, regulators, researchers and the water sector to help develop strategies for managing these hazardous substances. The key results of this project are presented in four reports:

Arp, H.P.H., Hale, S.E. (2023):
REACH: Guidance and Methods for the Identification and Assessment of PMT/vPvM Substances.
UBA TEXTE 19/2023. Neumann, M., Schliebner, I. [ed.], ISSN 1862-4804. German Environment Agency (UBA), Dessau-Roßlau, Germany, 66 pages
https://www.umweltbundesamt.de/publikationen/reach-guidance-methods-for-the-identification

Arp, H.P.H., Hale, S.E., Neumann, M. (2023):
PMT/vPvM assessment of REACH registered Substances Detected in Wastewater Treatment Plant Effluent, Freshwater Resources and Drinking Water.
UBA TEXTE 20/2023. Neumann, M., Schliebner, I. [ed.], ISSN 1862-4804 German Environment Agency (UBA), Dessau-Roßlau, Germany, 259 pages
https://www.umweltbundesamt.de/publikationen/pmtvpvm-assessment-of-reach-registered-substances

Arp, H.P.H., Hale, S.E., Schliebner, I., Neumann, M. (2023):
Prioritised PMT/vPvM substances in the REACH registration database.
UBA TEXTE 21/2023. Neumann, M., Schliebner, I. [ed.], ISSN 1862-4804. German Environment Agency (UBA), Dessau-Roßlau, Germany, 177 pages
https://www.umweltbundesamt.de/publikationen/prioritised-pmtvpvm-substances-in-the-reach

Arp, H.P.H., Hale, S.E., Borchers, U., Valkov V., Wiegand, L., Zahn, D., Neuwald, I., Nödler, K. Scheurer, M. (2023):
A prioritization framework for PMT/vPvM Substances under REACH for registrants, regulators, researchers and the water sector.
UBA TEXTE 22/2023. Neumann, M., Schliebner, I. [ed.], ISSN 1862-4804. German Environment Agency (UBA), Dessau-Roßlau, Germany, 238 pages
https://www.umweltbundesamt.de/publikationen/a-prioritization-framework-for-pmtvpvm-substances

This report (UBA TEXTE 19/2023) is the first in the series, presenting an updated guidance and methods for the identification and assessment of PMT/vPvM substances registered under REACH. The other three reports present: an investigation of the number of substances detected in six water media that are in the REACH registration database and meet the PMT/vPvM criteria (UBA TEXTE 20/2023); the UBA list of prioritized PMT/vPvM substances in the REACH registration database (UBA TEXTE 21/2023); and, a prioritization framework for PMT/vPvM substances under REACH for identifying which PMT/vPvM substances need the most urgent attention (UBA TEXTE 22/2023).

1 Introduction

Safe and clean drinking water is essential for life. The United Nations (UN, Resolution 64/292) and the World Health Organization (WHO, Guidelines for drinking-water quality) consider access to clean drinking water essential to the realisation of human rights and the protection of human health. The European Union's (EU) drinking water directive (98/83/EC, amended 2015/1787) has the objective "*to protect human health from the adverse effects of any contamination of water [...] by ensuring that it is wholesome and clean*". The EU's groundwater directive (2006/118/EC) states, "*groundwater is a valuable natural re-source and as such should be protected from [...] chemical pollution*". Moreover, the EU's water frame-work directive (2000/60/EC) states that "*Member States shall ensure the necessary protection for the bodies of water identified with the aim of avoiding deterioration in their quality in order to reduce the level of purification treatment required in the production of drinking water*". For this is it is critical that drinking water resources are protected from chemical pollution.

Under the EU´s chemical regulation REACH (Regulation (EC) No 1907/2006), industry must demonstrate in their registration dossiers the safe use of substances over their entire life cycle. However, REACH currently lacks criteria for intrinsic substance properties that indicate a potential drinking water resource contaminant. Consequently, there is a regulatory gap between the requirements of the drinking water directive and REACH to fulfil the precautionary protection of the sources of our drinking water. In order to close this gap, the German Environment Agency (UBA) has scientifically, technically and regulatorily developed criteria under REACH for substances considered persistent, mobile and toxic (PMT) and very persistent and very mobile (vPvM). These criteria were proposed in 2019 (Neumann and Schliebner, 2019).

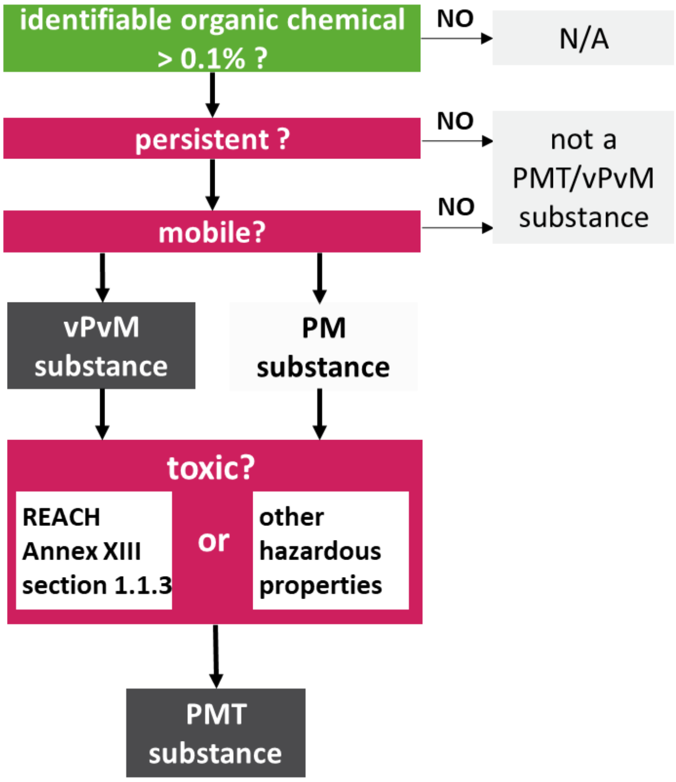
In 2020, the European Commission (EC) presented its aim to adopt the PMT/vPvM criteria in REACH for the identification of SVHCs and in CLP (Classification, Labelling and Packaging, Reg. (EC) 1907/2006) as new hazard categories (European Commission, 2021). This would pave the way for the adoption also in the United Nation's Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and in other regions (Jin et al., 2020). Such regulatory advancements would be welcomed by the water suppliers. Recently. a memorandum by 170 water suppliers in 2020 states that "*for precautionary protection of drinking water, all substances and their degradation and transformation products should be reviewed and assess for the PMT properties [...] in order to prevent the introduction of particularly critical substances into the water cycle*" (ERM-Coalition, 2020). The same sentiment was also reflected in a follow-up memorandum in 2022 aiming to protect groundwater for future generations (ERM-Coalition, 2022).

2 Guidance and Methods for the PMT/vPvM assessment

2.1 Overview of the PMT/vPvM assessment procedure

The PMT/vPvM assessment procedure was proposed by Neumann and Schliebner (2019). Figure 1 shows that the first step of the PMT/vPvM assessment is identical to the PBT/vPvB assessment within REACH. A PBT/vPvB assessment is mandatory for substances manufactured and imported in amounts of 10 or more tpa (Article 14(1) of REACH), unless they are exempted based on Article 14(2), e.g. for constituents present at less than 0.1%, on-site or transported isolated intermediates, or substances used for product and process-oriented research and development. Further, regarding substance composition, the guideline for PBT/vPvB assessments states that "*regardless of whether full substance identification is possible or not for the whole composition, the registrant should make efforts for carrying out a PBT/vPvB assessment for all constituents, impurities and additives present in concentrations above 0.1% (w/w)*" (ECHA, 2017a). For unknown variable composition or biological (UVCB) substances, which may have many constituents <0.1% (w/w), structurally similar constituents should be grouped together if applicable concentrations are above 0.1% (w/w), for instance using representative "proxy substances" for the group.

Figure 1: Overview of the assessment procedure to identify PMT/vPvM substances registered under REACH



Source: Neumann and Schliebner (2019).

After step one, the assessment of persistent (P) or very persistent (vP) is carried out for all applicable substances, as described in Section 2.4. Only substances that meet the P or vP criteria are further assessed for their mobility to see if they fulfil the mobile (M) or very mobile (vM) criteria, as described in Section 2.5. If a substance does not contain any organic constituents that fulfil the criteria for P/vP or M/vM, no further action is required, and the substance is considered not a PMT/vPvM substance.

If a substance fulfils both the criteria for vP and vM, it is classified as vPvM substance. If it fulfils any combination of the following criteria: P and M, vP and M, or P and vM it is considered persistent and mobile (PM substance). For both, PM or vPvM substance, an assessment is carried out for toxic properties (T), as described in Section 2.6. If the T criteria is additionally fulfilled it is classified as PMT substance (any combination of P and M and T, vP and M and T, P and vM and T, or vP and vM and T). Hence, some substances can be classified both vPvM and PMT substances.

2.2 Impact of Data Quality

The PMT/vPvM assessments has to deal with missing information and data as well as with the varying quality of information and data. Data quality ultimately plays a key role in the weight-of-evidence behind individual P, M or T conclusions. In Table 1, a strategy is presented for dealing with missing information and data, or information and data of varying quality; whereby the PMT/vPvM assessment conclusions are ultimately ranked using a traffic light colour scheme. The advantage of a traffic light colour scheme is that it can help to make visual summaries in the form of charts or lists that are clear and easy to disseminate.

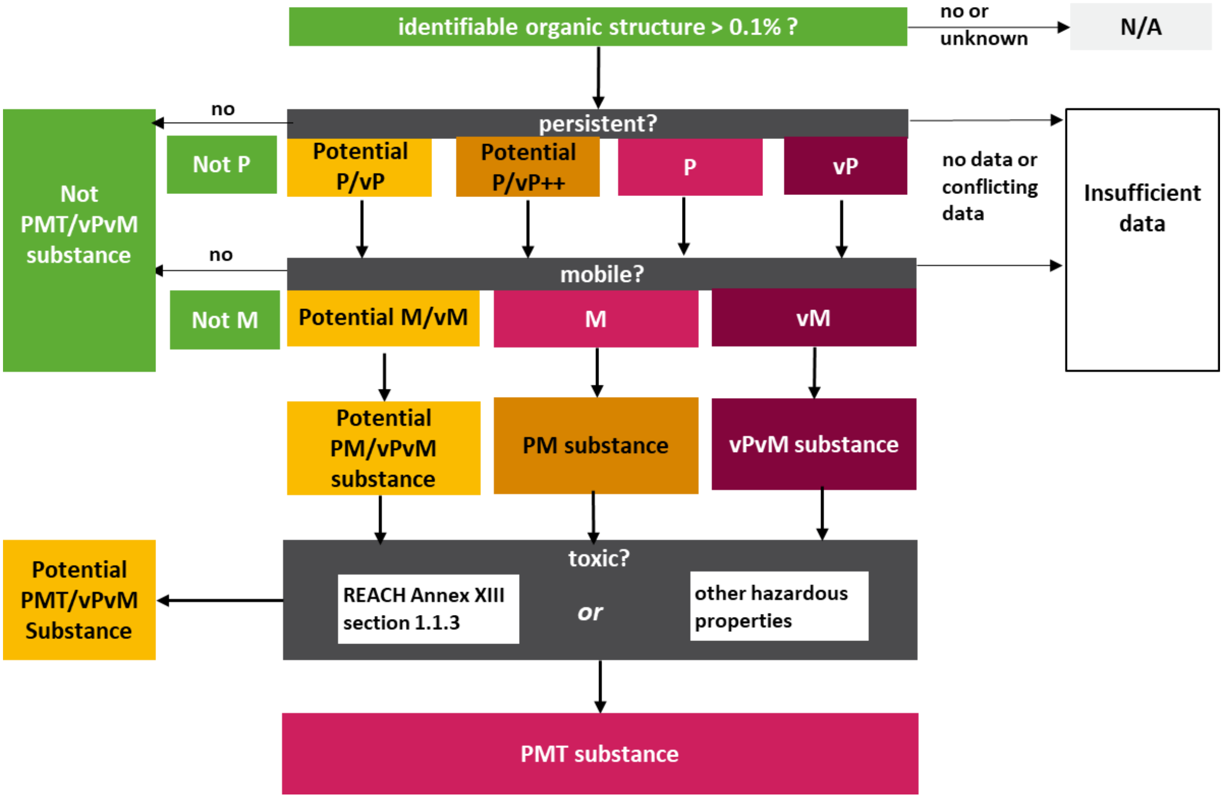
Table 1: Traffic light colour scheme representing whether P, M or T criteria are met and the corresponding level of data quality

Criteria or PMT/vPvM conclusion	Explanation
Insufficient data	Data missing or data quality too poor or inconsistent to make a screening level assessment
vP or vM	High quality data or sufficient weight-of-evidence that the criteria for vP or vM are met
vPvM	High quality data or sufficient weight-of-evidence that the criteria for vP and vM is met
vPvM & PMT	High quality data or sufficient weight-of-evidence that the criteria for vP, vM and T criteria are met
P, M or T	High quality data or sufficient weight-of-evidence that the criteria for P, M or T are met.
PMT	High quality data or sufficient weight-of-evidence that the criteria for P, M and T, or vP, M and T or P, vM and T are met
PM	High quality data or sufficient weight-of-evidence that the criteria for P and M, or vP and M, or P and vM are met, but there are currently no high-quality consensus conclusions that the criteria for T is met.
Potential P/vP++	Sufficient weight-of-evidence that the criteria for P is very likely met, and possibly the criteria for vP is met. This is considered as equivalent to P or in some cases equivalent to vP depending on the weight-of-evidence.
Potential P/vP, Potential M/vM or Potential T	Screening data or low-quality data indicates that the criteria for P/vP, M/vM or T could potentially be met. More high-quality data for sufficient weight-of-evidence is needed to reach a conclusion.
Potential PMT/vPvM	Screening data or low-quality data indicates that the criteria for P/vP and M/vM could potentially be met
Not P, Not M or Not T	High quality data or sufficient weight-of-evidence that the criteria for P, M or T are not met.
Not PMT/vPvM	High quality data or sufficient weight-of-evidence that either the criteria for P and/or M are not met

2.3 Details of the PMT/vPvM assessment procedure

The details of the PMT/vPvM assessment and data quality considerations is presented in Figure 2. Identifiable organic chemicals present in substances > 0.1% are first assessed for persistency. If the substance is assessed as "not P", it is considered "not PMT/vPvM", meaning that mobility is not assessed for. If no data is available, the assessment is concluded as "insufficient data", pending persistency data that may become available in the future. If they meet the P, vP, Potential P/vP++ or Potential P/vP, then they are to be assessed for mobility.

Figure 2: Details of the assessment procedure to identify PMT/vPvM substances registered under REACH



Source: original figure

If a P, vP or Potential P/vP++ substance meets the M or vM criteria in addition, it can either be a persistent and mobile (PM) substance or a vPvM substance (in the case of the Potential P/vP++ conclusion, a weight-of-evidence decision needs to be applied if it should be considered P or vP, see Table 1, before concluding PM or vPvM). If a P, vP, Potential P/vP++ or Potential P/vP substance is considered "not M", it is considered "not PMT/vPvM", or if it is assessed as “Potential M/vM” (meaning the data is not clear if the "Not M", M or M criteria is met) it is considered a "Potential PMT/vPvM" substance. Alternatively, a Potential P/vP substance considered M or vM, would also be a "Potential PMT/vPvM" substances. Finally, if a persistent and mobile substance is considered toxic, it is considered a PMT substance; if a vPvM substances is considered toxic, it is considered a vPvM & PMT substance.

2.4 Persistency

The same criteria for persistent (P) and very persistent (vP) as defined in Annex XIII of REACH for the PBT/vPvB assessment have been proposed as the basis for the PMT/vPvM assessment, both in 2019 by UBA (Neumann and Schliebner, 2019) and in 2021 by EC (European Commission, 2021), with the only the modification of adding a pH range from 4 - 9. These P/vP criteria are reproduced in Box 1a.

Box 1a. P/vP assessment criteria

A substance fulfils the persistent criterion (P) in any of the following situations:

- (a) the degradation half-life in marine water at 9 °C is higher than 60 days;
- (b) the degradation half-life in fresh or estuarine water at 12 °C and pH 4-9 is higher than 40 days;
- (c) the degradation half-life in marine sediment at 9 °C is higher than 180 days;
- (d) the degradation half-life in fresh or estuarine water sediment at 12 °C and pH 4-9 is higher than 120 days;
- (e) the degradation half-life in soil at 12 °C and pH 4-9 is higher than 120 days.

A substance fulfils the "very persistent" criterion (vP) in any of the following situations:

- (a) the degradation half-life in marine (9 °C), fresh or estuarine water (12 °C and pH 4-9) is higher than 60 days;
- (b) the degradation half-life in marine (9 °C) fresh or estuarine water sediment (12 °C and pH 4-9) is higher than 180 days;
- (c) the degradation half-life in soil (12 °C and pH 4-9) is higher than is higher than 180 days.

Source: Neumann and Schliebner (2019), based on REACH Annex XIII

If no degradation half-life data is available, the P/vP assessment must be based on the available screening information. Indication of P and vP properties may be taken from ready and inherent biodegradation tests or QSAR models, as presented in Box 1b.

Box 1b. Indication of P and vP properties

- (a) Results from tests on ready biodegradation in accordance with Section 9.2.1.1 of Annex VII;
- (b) Results from other screening tests (e.g. enhanced ready test, tests on inherent biodegradability);
- (c) Results obtained from biodegradation QSAR models in accordance with Section 1.3 of Annex XI;
- Other information provided that its suitability and reliability can be reasonably demonstrated.

Source: Annex XIII of REACH

Guidance for the assessment of P/vP within the PMT/vPvM assessment is identical to the guideline for the PBT/vPvB assessment (ECHA, 2017a). Persistence is an intrinsic substance property that refers to the degradation rate of a substance in an environmental compartment as simulated in the lab under specified conditions. Test guidelines have been developed to measure single compartment half-lives in water, soil, sediment under defined conditions (darkness, temperature, microbial activity, etc.) such as the OECD test guideline 307, 308 and 309 (ECHA, 2017a; Matthies et al., 2016; McLachlan et al., 2017).

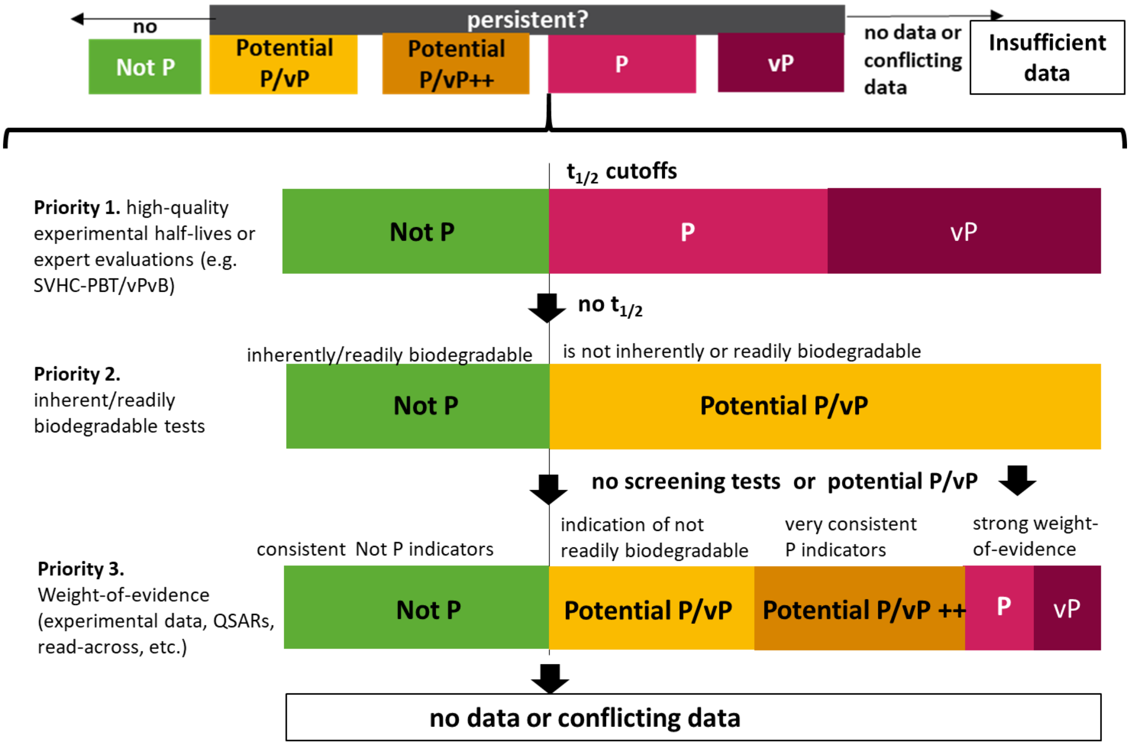
Simulated test systems present a simplification of natural variability in the real world. Some soils can be biodegradation hot spots, others barren (Kodešová et al., 2016). Half-lives are dependent on temperature (Veeh et al., 1996), depth (Veeh et al., 1996), nutrient loads (Kodešová et al., 2016), pH (Kodešová et al., 2016), oxygen levels (Ying et al., 2007), bioavailability and the presence of non-extractible residues (Hughes et al., 2020), as well as other factors. Based on this, the OECD test system should be run with different standard soil types or different standard sediment types. Even though simulated half-lives from standard test systems are not representative for all global environments, they are useful to provide an indication about the intrinsic biodegradation potential and to rank one substance in comparison to the other under controlled conditions (McLachlan et al., 2017). Therefore, the OECD simulation test systems serve as a way of benchmarking the intrinsic hazard of persistence. Further details are given about why the existing Annex XIII P/vP definition are fit-for-purpose for protecting the sources of our drinking water from PMT/vPvM substances are given in the previous version of this guidance Arp and Hale (2019, 2022).

Simulated half-life results from e.g. an OECD test guideline 307, 308 or 309 tests for soils, sediments and water, respectively, are rare, due in part to the cost of performing such studies. In 2013, UNEP reported that only 220 out of 95,000 chemicals used by industry had experimentally determined biodegradation half-lives (UNEP, 2013). To address this, the European Chemicals Agency (ECHA) developed screening information to see if there is an indication persistency, which allow registrants to conclude "Not P" or "Potential P/vP" based on readily or inherently biodegradable testing (ECHA, 2017a). However, such screening information can only be used for the identifying potential persistency, or as part of the "other information" in a weight of evidence approach to conclude P or vP. Other information that can be used as identifiers of P/vP (Box 1b) include read-across methods, QSARs to predict half-lives, or alternatively field measurements (ECHA, 2017a).

Figure 3 presents three tiered priority levels, consistent with REACH Annex XIII (ECHA, 2017a), when carrying out a P/vP assessment. Priority 1 is high-quality simulated half-lives or harmonized P/vP assessments based on the REACH criteria; whereas Priority 2 and 3 use weight-of-evidence information. Priority 2 allows for a conclusion of "Not P" based on the results of readily/inherently biodegradability tests. Priority 3 considers additional weight-of-evidence to carry out an assessment on a case-by-case basis, that includes screening tests, QSARs, read-across methods, experience with drinking water production, and other evidence.

Figure 3: The three, tiered priority levels of conducting a P/vP assessment.

SVHC-PBT = substance of very high concern because of its persistent, bioaccumulative and toxic properties or very persistent, very bioaccumulative properties as defined in the REACH regulation.



Source: original figure, based on earlier designs (Arp and Hale, 2022, 2019)

The type of data used to conduct the P/vP assessment herein are as follows, in the order of priority:

Priority 1)

- established P or vP assessment under Article 57 of REACH or assessment made by the Stockholm Convention;
- experimentally determined simulated half-lives extracted for water, soils and sediments as compared to REACH Annex III criteria for P/vP (see Box 1a).

Priority 2)

- experimental readily biodegradable screening tests (e.g. OECD301A-F, OECD310) or inherent biodegradation screening tests. In cases where all available results concluded "readily/inherently biodegradable" the substance is classified as "Not P"; however, if the number of screening tests reporting "not readily/inherently biodegradable" is equal to or greater than those that did report "readily/inherently biodegradable", a preliminary conclusion of "Potential P/vP" is assigned;

Priority 3)

- conclusions of P or vP from other literature, including a listing of "broad consensus" of meeting the PBT/vPvB criteria from ECHA (ECHA, 2020) to conclude either P or vP;

- if no other data is available, read-across methods and QSARs were utilized for a Priority 3 weight-of-evidence approach should be conducted. Box 2 presents the approach for Priority 3.

Box 2. Priority 3 Weight-of-evidence for P/vP assessments

In cases where there is no readily/inherently biodegradability test data and only data from multiple QSARs are available, then a recommended approach to a Priority 3 P/vP assessment level is:

- a) "Not P" if data from at least three different QSARs based on different calibration datasets and underlying assumptions consistently conclude "Not P"
- b) "Potential P/vP" based on consistent conclusions of P/vP across all QSARs tested, provided these QSASs are based on different calibration datasets or underlying assumptions, OR the substance was detected in drinking water sources, to err on the side of caution;
- c) "Potential P/vP++" based on additional weight-of-evidence on a case-by-case basis (e.g. known difficulty in removal during water treatment, ubiquity in monitoring data, read-across methods) where the rationale is clearly stated;
- d) "no data/low quality data" if the substance is outside the applicability domain of QSARs used, or all QSARs consulted gave a conflicting result of whether a substance is "Not P" or "Potential P/vP".

If a substance is considered "Potential P/vP" based on the result of a Priority 2 readily/inherently biodegradability test, then the following criteria is recommended for a Priority 3 P/vP assessment:

- (e) "Not P" if additional evidence exists on a case-by-case basis to make this conclusion, such as if the substance is rapidly hydrolysable under ambient conditions;
- f) "Potential P/vP++", "P" or "vP" if at least three QSARs gave output and concluded persistence (P or vP), followed by a manual investigation of the literature to make an expert judgement for the assignment of one of these persistency categories.
- g) case-by-case information to conclude "Potential P/vP++", "P" or "vP" based on additional information (e.g. monitoring data, difficulty to remove from drinking water production, read-across, etc.)

Source: Arp and Hale (2019, 2022)

As an example of a priority 3 weight-of-evidence assessment being used to make a conclusion of "Not P", the substance 6-PPD (CAS 793-24-8) is considered not readily biodegradable based on Priority 2 screening tests according to its REACH dossier, but it is readily hydrolysable (Seiwert et al., 2022); therefore, 6-PPD is considered "Not P". As an example of a conclusion a priority 3 weight-of-evidence assessment being used to make a conclusion of "vP", one can consider that there is only half-life data for available for a limited set of PFAS; however, read-across can be used to conclude vP for of the vast majority of "perfluorinated alkyl substances", or P and vP of "polyfluorinated alkyl substances" if they are known to degrade to a stable PFAS (Cousins et al., 2020; Wang et al., 2017). It should also be noted that should transformation products of "Not P" substances receive a PMT or vPvM conclusion, the parent substances should be considered a precursor to a PMT/vPvM substance.

2.5 Mobility

The mobile criterion (M) and very mobile criterion (vM) are unique to the PMT/vPvM assessment. The M/vM criteria proposed in 2019 by UBA are shown in Box 3a, and the less stringent M/vM criteria proposed in 2021 by EC are presented in Box 3b.

Box 3a. M/vM criteria proposed in 2019 by UBA

A substance fulfils the mobile criterion (M) in the following situation:

- (a) the lowest organic carbon-water coefficient log K_{OC} over the pH range of 4-9 is less than 4.0

A substance fulfils the very mobile criterion (vM) in the following situation:

- (b) the lowest organic carbon-water coefficient log K_{OC} over the pH range of 4-9 is less than 3.0

Source: Neumann and Schliebner (2019)

Box 3b. M/vM criteria proposed in 2021 by EC

A substance fulfils the mobile criterion (M) in the following situation:

- (a) the lowest organic carbon-water coefficient log K_{OC} over the pH range of 4-9 is less than 3.0

A substance fulfils the very mobile criterion (vM) in the following situation:

- (b) the lowest organic carbon-water coefficient log K_{OC} over the pH range of 4-9 is less than 2.0

Source: EC (2021)

If no K_{OC} data is available, screening for mobility is recommended. Recommended screening parameters for mobility are the octanol-water partition coefficient (K_{OW}) or the pH-dependant octanol-water coefficient for ionisable substances (D_{OW}), as shown in Box 3c.

Box 3c. Indication of M and vM properties

- (a) For ionisable substances, the lowest pH dependent octanol-water distribution coefficient (D_{OW}) experimentally determined between pH 4-9 in accordance with Section 7.8 of Annex VII of REACH or estimated by QSAR models in accordance with Section 1.3 of Annex XI of REACH.
- (b) For other substances, the octanol-water partition coefficient (K_{OW}) experimentally determined in accordance with Section 7.8 of Annex VII of REACH or estimated by QSAR models in accordance with Section 1.3 of Annex XI of REACH.
- (c) Other information provided that its suitability and reliability can be reasonably demonstrated.

Source: Neumann and Schliebner (2019)

Threshold values of D_{OW} and K_{OW} to be used as mobility screening parameters are not presented in Box 3c. This is in agreement with the lack of a criterion for the screening assessment for B and vB properties in Annex XIII of REACH. A log K_{OW} value of greater than 4.5 to test for the potential for bioaccumulation is not defined within Annex XIII of REACH but was only introduced in the ECHA guidance document for PBT/vPvB assessments (ECHA, 2017a). For mobility, the screening information for the mobility assessment is (Neumann and Schliebner, 2019):

> *the lowest pH-dependant octanol-water distribution coefficient log D_{OW} over the pH range of 4-9 is less than 4.5.*

The D_{OW} in the pH range 4-9 can be derived from K_{OW} if the dissociation constant (pKa) is known, such as for monoprotic acids and bases through the following relationships:

$D_{OW} = (1/(1+10pH - pKa))\ K_{OW}$ (for monoprotic acids) (M1)

$D_{OW} = (1 - 1/(1+10pH - pKa))\ K_{OW}$ (for monoprotic bases) (M2)

For neutral and non-ionisable substances over a specified pH range the D_{OW} has the same value as the octanol-water partition coefficient (K_{OW}).

2.5.1 Justification of the M/vM assessment criteria and screening criteria

As the M/vM assessment criteria and screening criterion are unique to the PMT/vPvM assessment, some additional explanation on the suitability and background to the use of log K_{OC} values for the M/vM criteria and the log D_{OW} (or log K_{OW}) is provided.

In Annex II section 12.4 of REACH, mobility in soil is defined as:

"*the potential of the substance or the components of a mixture, if released to the environment, to move under natural forces to the groundwater or to a distance from the site of release. The potential for mobility in soil shall be given where available. Information on mobility in soil can be determined from relevant mobility data such as adsorption studies or leaching studies, known or predicted distribution to environmental compartments, or surface tension. For example, K_{oc} values can be predicted from octanol/water partition coefficients (K_{ow}). Leaching and mobility can be predicted from models. This information shall be given where available and appropriate, for each individual substance in the mixture which is required to be listed in Section 3 of the safety data sheet. Where experimental data is available, that data shall, in general, take precedence over models and predictions*".

Hereby, REACH itself points to the use of the organic carbon-water coefficient, K_{OC}, as a central intrinsic substance property to describe mobility, alongside K_{OW}. The use of this parameter is firmly rooted in scientific literature with a long history. Mobility in the subsurface is the potential of a substance to be transported long distances with porewater flow. In a local environment, mobility depends on the persistence of the substance within the soil, the sorption capacity of the substance to the surrounding soils and sediments and the hydraulic conditions (e.g. flow rate, rainfall) (Hale et al., 2020a). Sorption capacity is generally quantified using the equilibrium distribution coefficient, K_D, which is the equilibrium concentration of a substance in soil, sediment or sludge phase (C_{solid}, $\mu g/kg_{solid}$) to the that of the (pore)water phase (C_{water}, $\mu g/L_{water}$), see equation M3. Often for organic substances, the K_D is normalized to the mass fraction of "organic carbon", f_{OC} (kg_{OC}/kg_{solid}), typically defined as all carbon that is not present as carbonate (Schumacher, 2002), see equation M4.

$$K_D = C_{solid} / C_{water} \qquad \text{(M3)}$$

$$K_{OC} = K_D / f_{OC} \qquad \text{(M4)}$$

Standardized methods to determine equilibrium K_{OC} values (l/kg_{OC}) at defined conditions have been developed. These include batch tests where a mixture of solids and water are spiked with a substance and mixed until equilibrium is reached (e.g. OECD 106),(OECD, 2000), high-performance liquid chromatograph (HPLC) columns that have been correlated with a K_{OC} value for *neutral* organic substances (e.g. OECD 121)(OECD, 2001), as well as several methods developed by the USEPA (EPA OPPTS methods 835.1110, 835.1220, 796.2750). The K_{OC} has been favoured historically for comparing mobility data and conducting exposure assessments for neutral, organic substances (ECHA, 2016), because the organic carbon phase is widely considered the dominating sorption component of soils, sediments and sludges (Bronner and Goss, 2011a, 2011b). This normalization allows laboratory determined K_{OC} values using defined conditions to be also considered an intrinsic, laboratory-based substance parameter, though with some natural variation in values to account for the differences in sorption owing to the presence of diverse types of organic carbon.

The use of the K_{OC} as part of a persistence and mobility assessment can be traced back to the "Groundwater Ubiquity Score" or GUS, developed by Gustafson (1989). The GUS was an early and influential approach to identify persistent and mobile substances based only on soil-half lives, $t_{1/2,soil}$, and K_{OC} (M2) and was used to assessed only the hazard to groundwater.

$$GUS = \log t_{1/2,soil} (4- \log K_{OC}) \qquad \text{(M5)}$$

When applying this equation, substances with a GUS < 1.8 were considered as being a "non-leacher" to groundwater, and those with a GUS > 2.8 were considered a "leacher" that can contaminant groundwater (

Figure 4). This type of conceptualization of persistency and mobility has been used in various forms. In Europe, an important use is the guidance on the Biocidal Products Regulation (EU 528/2012) that uses thresholds of $t_{1/2,soil} > 21$ days and log $K_{OC} < 2.7$ L/kg_{OC} for whether or not groundwater impacts need to be assessed (ECHA, 2017b). This corresponds to a GUS of 1.7 (or just across the border of being a "non-leacher"). Similarly, the United Nation's Food and Agricultural Organization uses soil half-lives and log K_{OC} values to characterize the degree of degradability and mobility in soil (FAO, 2000).

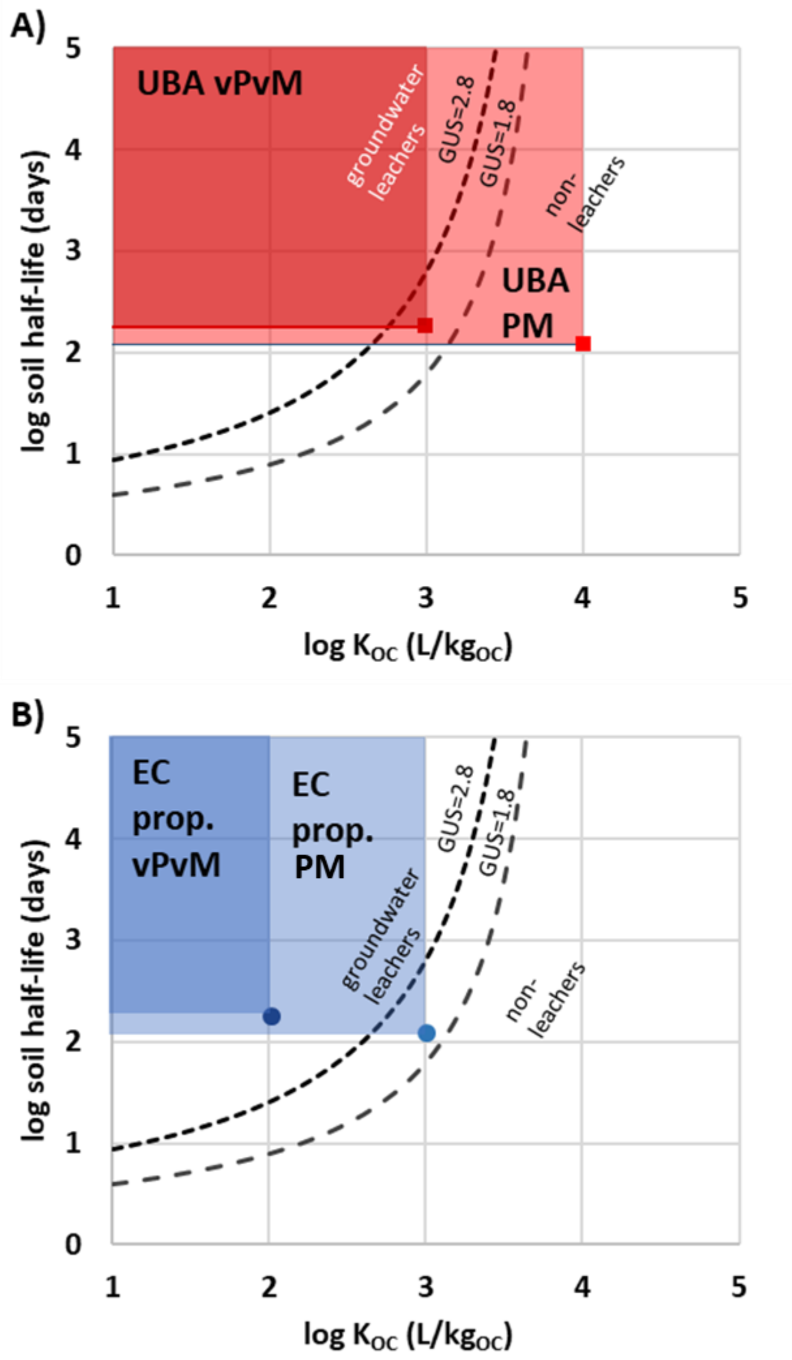
The main similarity between the PMT/vPvM assessment and the GUS is that both use a combination of half-lives and log K_{OC} as criteria; the main differences are that 1) the PMT/vPvM criteria considers persistency in other environmental compartments than just soil; 2) toxicity is not considered in the GUS criteria; and 3) the PMT/vPvM criteria proposed by UBA and by the

EC uses fixed half-lives and log K_{OC} values, unlike GUS which uses these parameters as variables in a threshold-function (equation M5 and

Figure 4).

Figure 4: Overview GUS-Plots of soil half-life vs. log K_{OC}

The GUS-Plots present different criteria for persistent and mobile substances, including the GUS-index of <1.8 for non-leachers in groundwater, > 2.8 for leachers in groundwater, considering persistency and mobility criteria A) proposed in 2019 by UBA and B) the proposed in 2021 by EC



Source: Arp & Hale (2022)

The 2019 PMT criteria proposed by UBA would include toxic substances that are "non-leachers" to groundwater, according to the GUS (

Figure 4). However, these toxic "non-leachers", with a log K_{OC} between 3.0 and 4.0, have been found to be present in drinking water and groundwater, as presented in Figure 5.

Figure 5: Distribution of experimental log K_{OC} values substances detected in drinking water and groundwater

Data is presented for A) all 209 detected substances that are registered under REACH and, and B) the 88 of these substances which were assessed to be P/vP or Potential P/vP++. In both panels, the 2019 M and vM criteria proposed by UBA of log K_{OC} 4.0 and 3.0, respectively, are presented, as well as the 2021 M and vM criteria proposed by EC of log K_{OC} 3.0 and 2.0, respectively. Dark red indicates vM, red indicates M and green indicates Not M. The striped green/red pattern indicates the shift from log K_{OC} 4.0 to 3.0, which is the shift from the M criteria proposed in 2019 by UBA to the less stringent M criteria proposed in 2021 by the EC. The striped dark red/red pattern indicates the shift from log K_{OC} 3.0 to 2.0, which is the shift from the 2019 vM criteria proposed by UBA to the 2021 vM criteria proposed by EC.

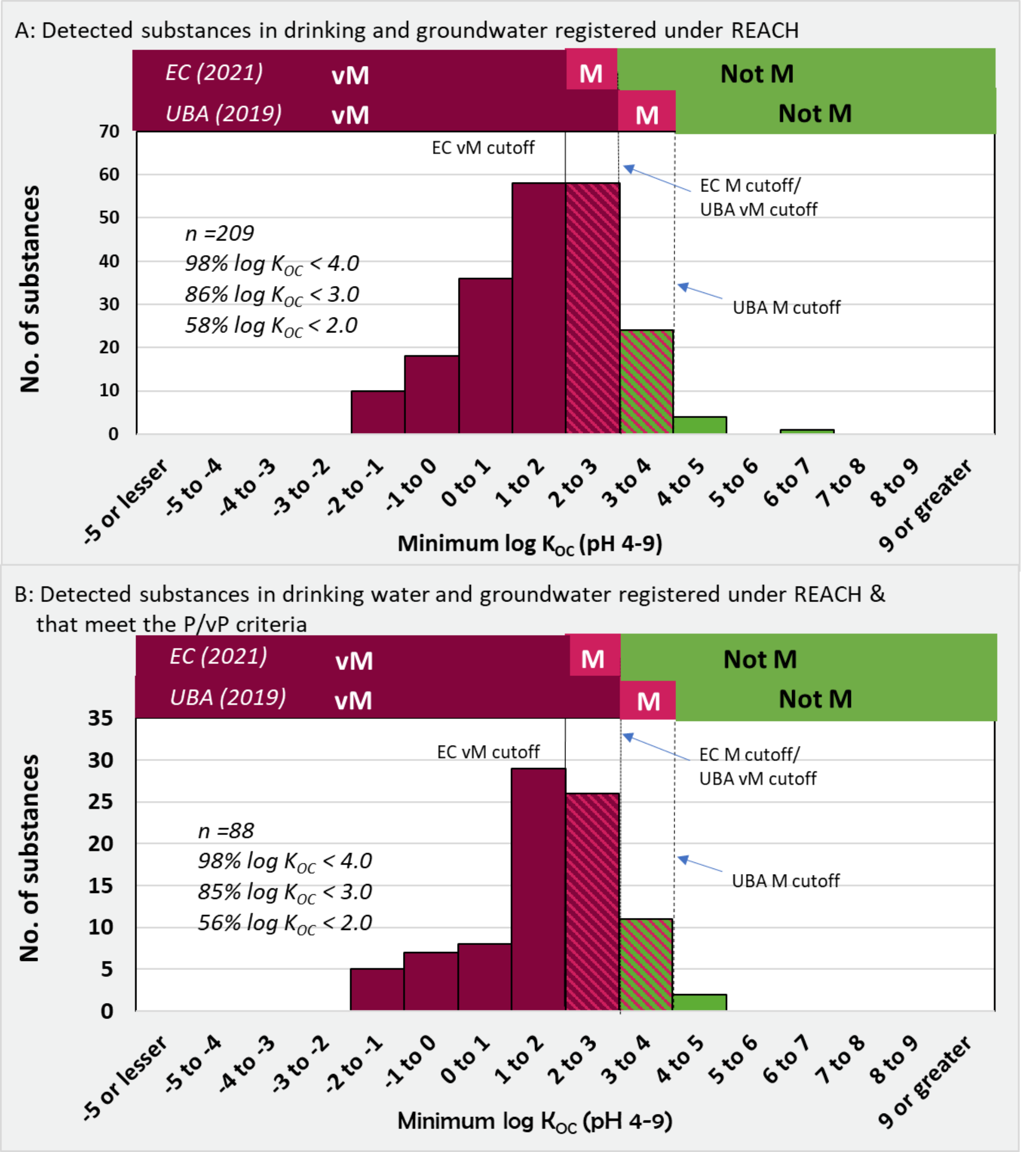


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Figure 5 shows the outcome of a literature review, conducted in a parallel report to this one, that first sought to compile a large list of detected substances in groundwater and drinking water (Arp et al., 2023a). This larger list was then filtered for only substances that were registered under REACH and had an experimentally determined log K_{OC} value. This resulted in the 209 REACH registered substances with an experimentally determined log K_{OC} value that are plotted in Figure 5A. Of these REACH registered substances that are detected in drinking water and groundwater, 98% (204 out of 209) have a log $K_{OC} < 4.0$ while 86% (180 out of 209) have a log $K_{OC} < 3.0$ and 58% (122 out of 209) have a log $K_{OC} < 2.0$. The distribution is similar in Figure 5B, when just considering the 88 of these 209 substances that also met the criteria for P, vP or Potential P/vP++. Of them, 98% (86 out of 88) have a log $K_{OC} < 4.0$, 85% (75 out of 88) have a log $K_{OC} < 3.0$ and 56% (49 out of 88) have a log $K_{OC} < 2$.

This indicates two things:

> 1) that the 2019 M criterion of log $K_{OC} < 4.0$ proposed by UBA is supported by this empirical data set, as it captures 98% of substances detected in drinking water and ground water, including the persistent substances. In other words, the vast majority P or vP substances that have been detected in drinking water or groundwater water would be considered a "PM substance" or vPvM substance (though whether they would be considered a PMT substances would depend on the toxicity assessment);
>
> 2) that the less stringent criteria proposed 2021 by EC only considers 85% of the P or vP substances detected in drinking water and ground water to be either a "PM substance" or a vPvM substance. In other word, there is circa 13% of P or vP substances that have been detected in drinking water or groundwater that would not be considered to pose a PMT/vPvM hazard. The EC criteria is therefore less protective.

Consequently, the empirical data from (Arp et al., 2023a) presented in Figure 5 indicate that the PMT/vPvM criteria are fit-for-purpose and support the scientifically, technically and regulatorily justification in order to protect against bank filtration breakthrough and groundwater transport of persistent, mobile and toxic substances (Arp and Hale, 2019).

2.5.2 Indication of Mobility Properties

Experimental K_{OC} data for the mobility assessment was available for approximately one-fifth of the 13405 unique chemical structures in the REACH registration database. This means there is a need for screening parameters for the majority of REACH registered substances to evaluate if a log K_{OC} value should be measured.

Some more commonly available parameters for REACH registered substances are the D_{OW} for ionizing substances and the K_{OW} for neutral substances. These parameters do not account for ionic interactions between organic compounds and soil, which can substantially lower the mobility of ionic species (Droge and Goss, 2013a, 2013b; Henneberger and Goss, 2019), as well as being influenced by pH, counterions in the porewater, and heterogeneity of the soil and minerals present (Droge and Goss, 2013a, 2013c, 2013b; Henneberger and Goss, 2019; Kah et al., 2017; Tülp et al., 2009). The D_{OW} does account for the solubility of the charged and neutral species at a specific pH, but not the pH dependence of the ionic interactions of the soil (Sigmund et al., 2022). Nevertheless, D_{OW} and K_{OW} are suitable screening parameters for prioritizing which charged or ionizable substances are potentially mobile (Arp and Hale, 2022, 2019; Sigmund et al., 2022). The goal of the screening is to identify candidates that are suspected to be mobile substances. The availability of K_{OC} data and K_{OW}/D_{OW} for the REACH registered organic substances, based on data sources presented in Annex A, are presented in

Figure 6.

Figure 6: **Distribution of best available sorption coefficients for all unique chemical structures in the REACH registration database.**

The minimum experimental log K_{OC} value (n=2845) is considered as the best , followed by the minimum experimental log K_{OW}/log D_{OW} value (n=3250), with the estimated log K_{OW}/log D_{OW} value (n=7308) of the lowest priority. Also presented is the 2019 M and vM criteria proposed by UBA of log K_{OC} 4.0 and 3.0 respectively, as well as the 2021 M and vM criteria proposed by EC of log K_{OC} 3.0 and 2.0 respectively. Experimental log K_{OC} is given in different colours based on their relation to these thresholds. Dark red indicates vM, red indicates M and green indicates Not M. The striped green/red pattern indicates the shift from log K_{OC} 4.0 to 3.0, which is the shift from the 2019 M criteria proposed by UBA to the 2021 M criteria proposed by EC. The striped dark red/red pattern indicates the shift from log K_{OC} 3.0 to 2.0, which is the shift from the 2019 vM criteria proposed by UBA to the 2021 vM criteria proposed by EC.

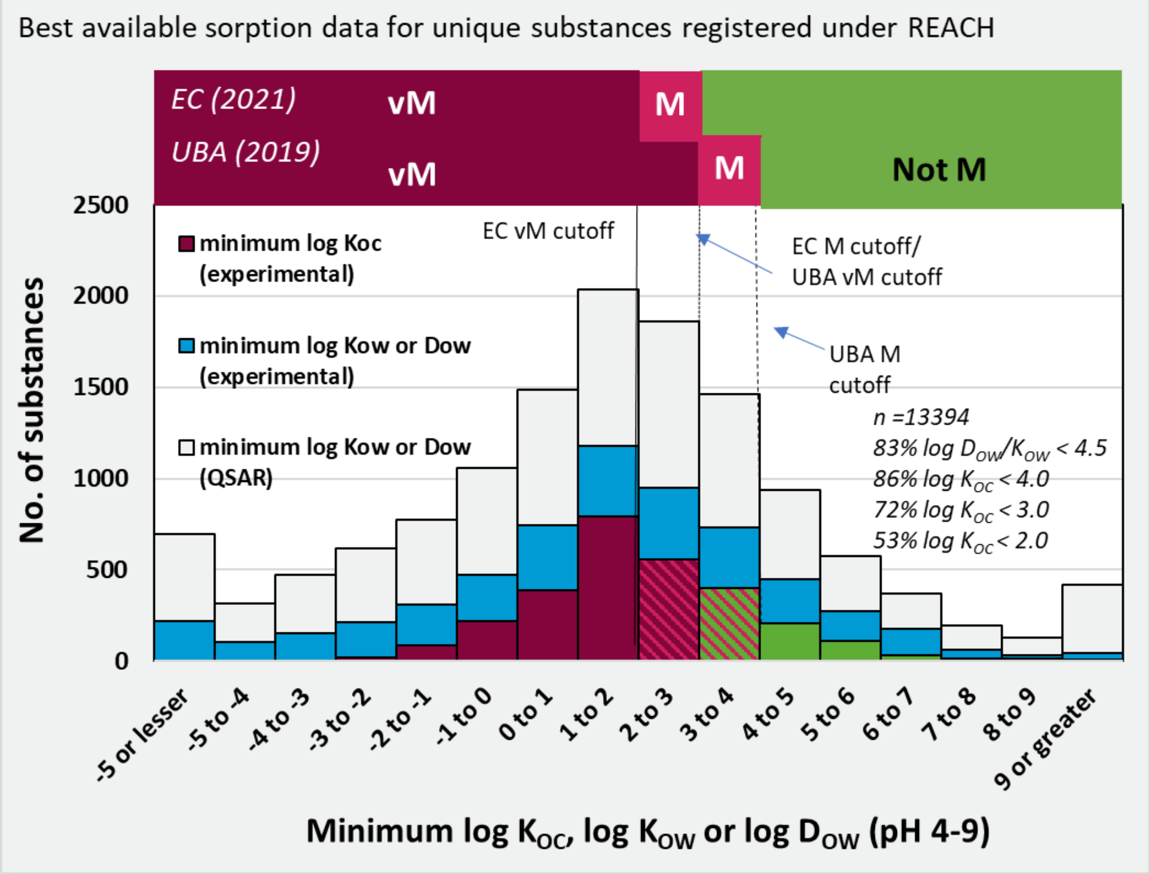

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Figure 6 shows a histogram distribution of the best available sorption coefficients for all identified unique chemical structures in the REACH registration database. The minimum experimental log K_{OC} is considered the best available data (n=2845), followed by the minimum experimental log K_{OW}/log D_{OW} (n=3250) and with the estimated log K_{OW}/log D_{OW} (n=7301) of the lowest priority. No mobility descriptor could be estimated for 9 substances (mainly organometallics, for which none of the QSARs gave output). Several interesting trends can be seen from the histograms in

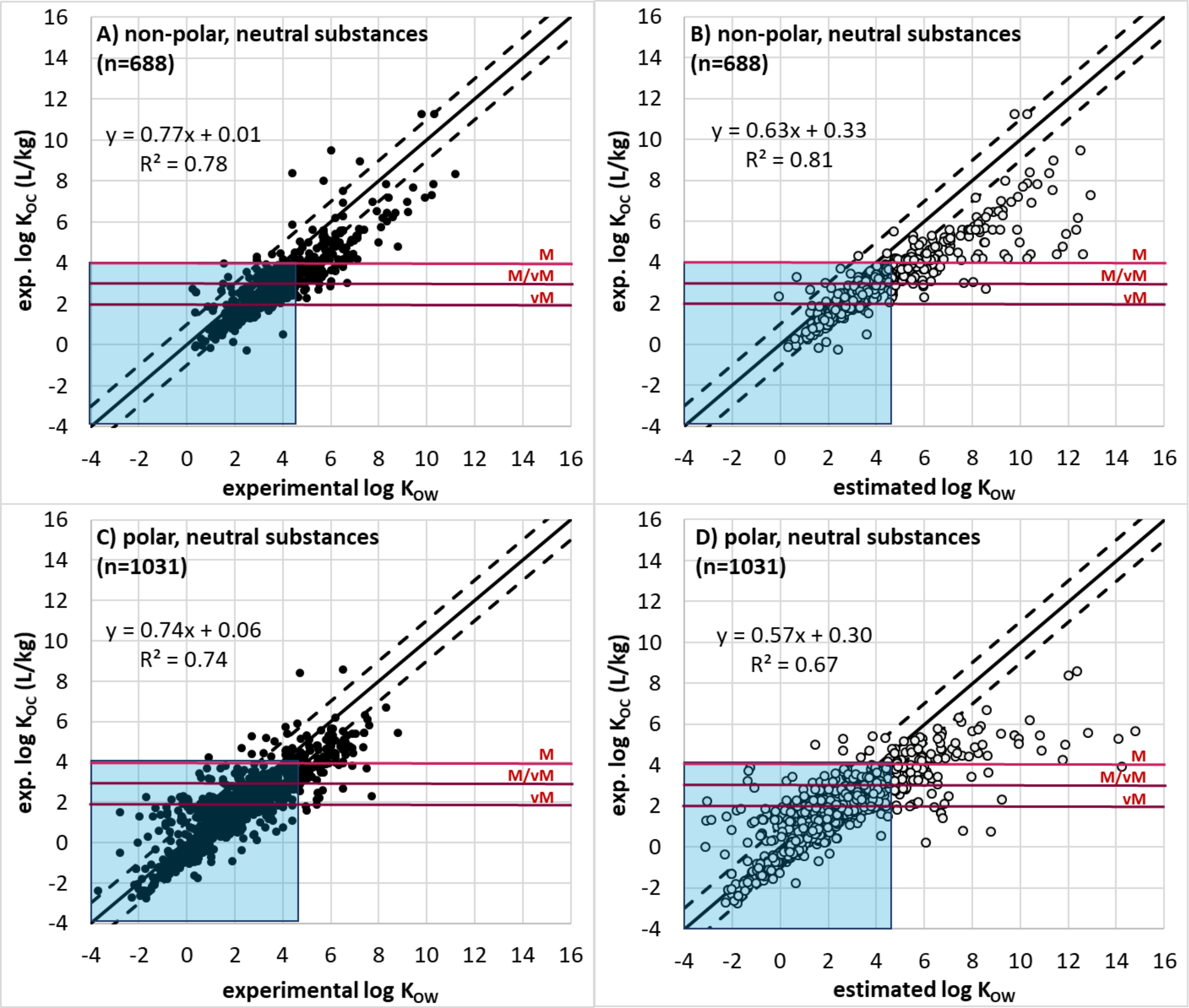
Figure 6, such as 1) the peak frequency of both log K_{OC} and log K_{OW}/log D_{OW} is between log 1.0 to 2.0 log units, implying that this is the most common range of these sorption descriptors for organic substances registered under REACH; 2) there is a larger portion of substances in the

REACH registered database with a log K_{OC} > 4.0 (14 %, 384 out of 2845 substances) than the REACH registered substances detected in drinking water and groundwater with log K_{OC} > 4.0 (2%, or 5 out of 209, all in groundwater, see Figure 5); 3) the number of substances with a log K_{OW}/log D_{OW} < 4.5 (83%, 8316 out of 10551) is similar to those with a log K_{OC} < 4.0 (86%, 2461 out of 2845).

To understand whether K_{OW}/D_{OW} are suitable as screening parameters, a correlation analysis was conducted for substances that had experimental log K_{OC}, experimental K_{OW}, and estimated K_{OW}/D_{OW} parameters available. Experimental log K_{OC} data was then plotted against log K_{OW} for neutral non-polar substances (n=689), neutral polar substances (n=1032), substances that are anionic or ionize to an anion (n=487), substances that are cationic or ionize to a cation (n=607), and zwitterions/amphoteric substances, as defined by their structure (n=71). These plots are presented in Figure 7 for neutral substance and Figure 8 for ionic/ionizable substances, with regression statistics presented in Table 2.

Figure 7: Experimental log K_{OC} – log K_{OW} plots for neutral substances

The panels present a comparison of experimental log K_{OC} data and a) experimental log K_{OW} values for non-polar substances, b) estimated log K_{OW} values for non-polar substances, c) experimental log K_{OW} values for polar substances, and d) estimated log K_{OW} values for polar substances. Here polar substances are considered those that have a mass fraction of oxygen and nitrogen of 12% or greater, of the molecular mass. The solid line indicates the 1:1 line, with the two dotted lines showing deviations of a factor 10. Shaded blue areas indicate the area with a log K_{OC} < 4.0 and log K_{OW} < 4.5, to visually illustrate the proportion of substances meeting both the K_{OC} criteria and K_{OW} screening criteria proposed in 2019 by UBA. Also presented in red lines are the 2021 log K_{OC} criteria proposed by EC, with thresholds at <4.0, <3.0 and 2.0.



Source: Arp & Hale (2022)

2.5.2.1 Neutral substances

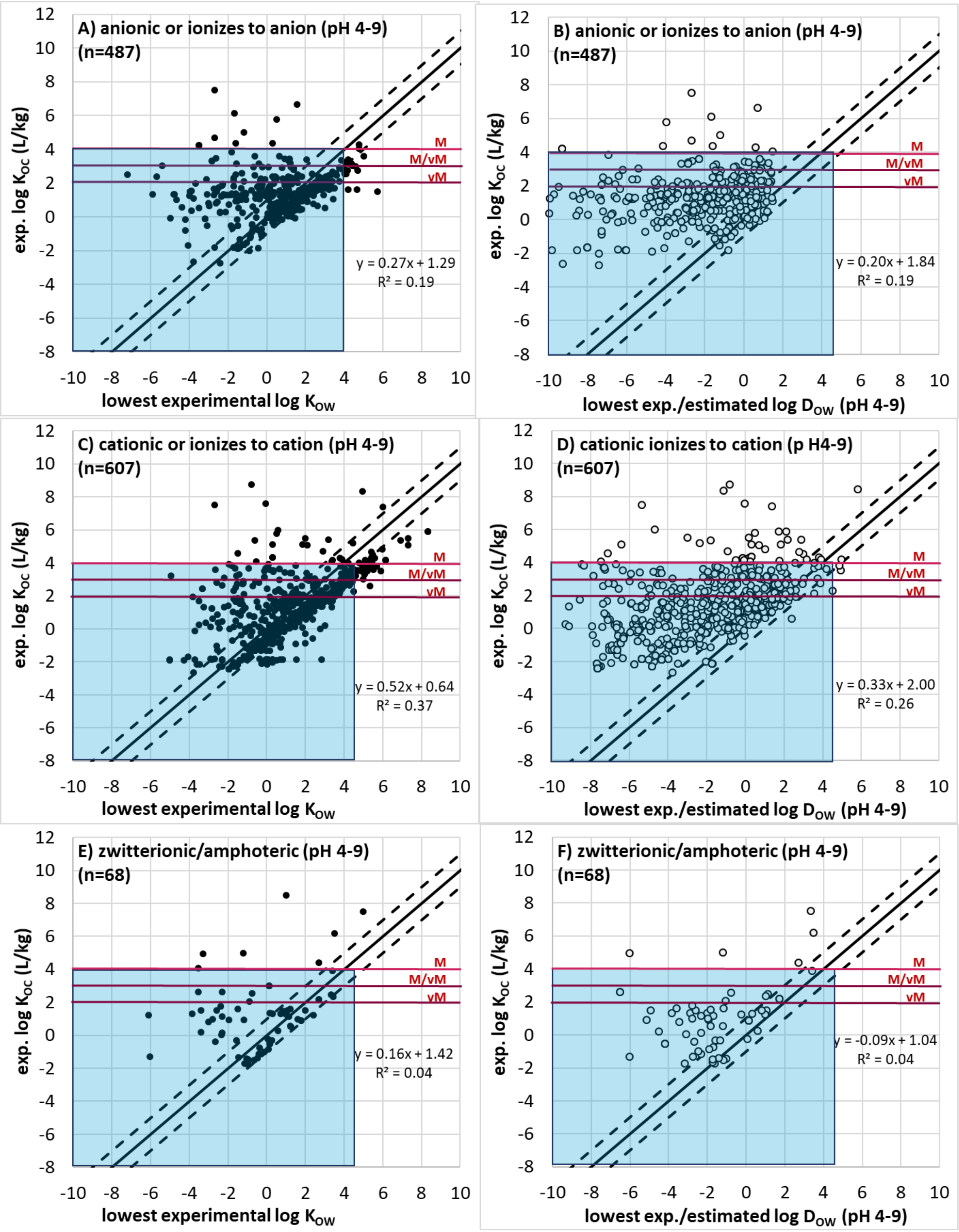
The log K_{OC}-log K_{OW} correlation for neutral non-polar substances in Figure 7a is as good as expected based on similar plots reported in the literature (Arp et al., 2009; Bronner and Goss, 2011a). The regression equation for the experimental values was log K_{OC} = 0.77 log K_{OW} ± 0.01 (r^2=0.78, root mean square error (rmse) = 0.73), indicating the log K_{OC} value was in most cases slightly smaller than the log K_{OW} (Schwarzenbach et al., 2016). These types of correlations for neutral non-polar substances have been popular since the 1980s (Karickhoff et al., 1979), though they are generally made for a narrow group of substance classes (e.g. alkanes, PAHs, PCBs, etc.)(Schwarzenbach et al., 2016), and very rarely for many substances, unless to establish linear free energy relationships (LFERs), QSARs or similar (Bronner and Goss, 2011a). The correlation in Figure 7a would not be suitable for LFERs or QSARs, as the individual data points were not checked for their quality, but just obtained from database using the specified search criteria and data filters. This may explain the high rmse (0.73) and visible outliers.

The correlation with estimated log K_{OW} values had slightly better statistics for neutral, non-polar substances, with log K_{OC} = 0.63 log K_{OW} + 0.33 (r^2=0.81, rmse= 0.68). The slight improvements in the correlation statistics may be due to estimated K_{OW} values already including the same K_{OC} values in their calibration statistics, and fewer outliers caused by badly reported experimental data (e.g. unit errors). In both Figure 7a and Figure 7b, the data gets more scattered and deviating towards very large log K_{OW} values (> 6.0) (Chessells et al., 1991). This is anticipated as K_{OW} for such substances are hard to measure accurately, and estimation methods would therefore be more prone to extrapolation bias owing to a lack of calibration with such data.

Comparing the log K_{OC}-log K_{OW} relationships for non-polar and neutral, polar substances (Figure 7a and c), the general range of log K_{OW} data shifts from values of "0 to 13" log units to "-3 to 9" log units, as expected due to increased preference for water. As a note, "polarity" is often used synonymously with solubility, but this need not be the case. Very large molecules that are not very soluble (e.g. with a log K_{OW} of 9), can be still be considered polar due to the sufficient presence of polar functional groups (consistent with the definition of polarity applied here). The correlation statistics for polar substances are worse than for the non-polar substances, (log K_{OC} = 0.74 log K_{OW} + 0.06 (r^2=0.74, rmse= 0.88)), as the r^2 value is slightly lower and the rmse is slightly higher. This is partially explained by polar interactions with organic matter and octanol being somewhat different, and also variable across diverse soil types (Schwarzenbach et al., 2016). The correlation statistics obtained when using estimated log K_{OW} data for polar substances (Figure 7d) were slightly worse at log K_{OC} = 0.57 log K_{OW} ± 0.30 (r^2=0.67, rmse 0.99); this is caused by extremely high estimated log K_{OW} values (from 9.0-14.0) that correspond with experimental log K_{OW} values that are much lower (from 2.0-8.0).

Figure 8: Experimental log K_{OC} – log K_{OW} / log D_{OW} plots for ionic and ionizable substances

The panels a), c) and e) present comparisons of experimental log K_{OC} values with the experimental log K_{OW} values of the neutral species for ionizable anionic, ionizable cationic and zwitterionic/amphoteric substances, respectively, and panels d), e) and f) showing comparisons with the lowest log D_{OW} between pH 4-9, for ionizable anionic, ionizable cationic and zwitterionic/amphoteric substances, respectively. The solid line indicates the 1:1 line, with the two dotted lines showing deviations of a factor 10. Shaded blue areas indicate the area with a log K_{OC} < 4.0 and log K_{OW} < 4.5, to visually illustrate the proportion of substances meeting both the K_{OC} criteria and K_{OW} screening criteria proposed in 2019 by UBA. Also presented in red lines are the 2021 log K_{OC} criteria proposed by EC, with thresholds at <4.0, <3.0 and 2.0.



Source: Arp & Hale (2022)

2.5.2.2 Charged and Ionizable Substances

Comparing Figure 7 for neutral substances and Figure 8 for charged and ionizable substances, the difference in log K_{OC}-log K_{OW}/D_{OW} correlations is striking. The ionizable substance correlations are poor, with r^2 ranging from 0.04 to 0.37 and rmse values ranging from 1.36 to 2.11. However, the data is not randomly distributed despite these poor correlation statistics. General clustering patterns are evident. When just considering the log K_{OC}-log K_{OW} correlation for the ionizable substances (Figure 8 a, c and e), nearly half of the data is clustered between the 1:1 line and 1.5 orders of magnitude below. The relative percentage of substances that are ionizable anionic, ionizable cationic and zwitterionic are 50 %, 56 % and 40 %, respectively. This area is also where most of the substances clustered for the neutral non-polar substances (77%) and neutral polar substances (68%,). However, when considering the log K_{OC}-log D_{OW} (minimum between pH 4-9) correlations (Figure 8 b, d and f), the majority of the remaining data is above the 1:1 line (i.e. log K_{OC}>log D_{OW}) for ionizable anionic substances (87%), ionizable cationic substances (93%) and zwitterions (92%), in contrast to neutral non-polar substances (9%) and neutral polar substances (13%). The obvious mechanistic explanation for this is that they only account for an increase in porewater solubility, and not for the attractive ionic interactions with the soil. For acids with a pKa < 4 or conjugated acids with a pKa > 9, D_{OW} can be more than 5 orders of magnitude lower than the neutral form K_{OW} within this pH range (based on equation M1 and M2). Therefore, in general, log K_{OC} values are greater than log D_{OW} values due to this pH influence. The correlations for anions and cations were not that different, despite soil cationic exchange interactions being generally larger than anion exchange interactions (Bergaya et al., 2013).

Table 2: Comparison of experimental log K_{OC} values with experimental and estimated log K_{OW} values, as well as minimum log D_{OW} values (pH 4-9) for neutral and ionizable substances.

Shown are log-log regression statistics (r^2 and rmse = root mean square error) and the statistical performance of using log K_{OW} or log $D_{OW} < 4.5$ as a screening parameter for the UBA Mobility criteria of log $K_{OC} < 4.0$. A performance of 100% implies the screening parameter agreed with the conclusion based on log K_{OC} in all cases. Overall efficiency refers to the percentage of when the screening criteria agree predicted M and Not M correctly. Overall efficiency = [(%M substances predicted correctly) (n of M substances) +(%"Not M" substances predicted correctly)·(n of "Not M" substances)]/(total n)

Chemical category		M	Not M	Overall	Linear Regression	r^2	rmse
		substances	substances	Efficiency			
		log $K_{OC}<4$ &log $K_{OW}/D_{OW}<4.5$	log $K_{OC}\geq4$ &log $K_{OW}/D_{OW}\geq4.5$				
Neutral non-polar	exp. log K_{OW}	88%	91%	89%	log K_{OC} = (0.77±0.02) log K_{OW} + (0.01±0.06)	0.78	0.73
(n=689 with 82% log $K_{OC} \leq 4.0$)	est. log K_{OW}	85%	98%	87%	log K_{OC} = (0.63±0.01) log K_{OW} + (0.33±0.05)	0.81	0.68
Neutral polar	exp. log K_{OW}	92%	79%	91%	log K_{OC} = (0.74±0.01) log K_{OW} + (0.06±0.04)	0.74	0.88
(n=1032 with 92% log $K_{OC} \leq 4.0$)	est. log K_{OW}	91%	90%	91%	log K_{OC} = (0.57±0.01) log K_{OW} + (0.30±0.04)	0.67	0.99
Anionic or ionizes to anion	exp. log K_{OW}	98%	57%	95%	log K_{OC} = (0.27±0.03) log K_{OW} + (1.29±0.07)	0.19	1.36
(n=487 with 93% log $K_{OC} \leq 4.0$)	est. log K_{OW}	100%	29%	95%	log K_{OC} = (0.20±0.02) log K_{OW} + (1.84±0.07)	0.19	1.36
Cationic or ionizes to cation	exp. log K_{OW}	96%	51%	93%	log K_{OC} = (0.53±0.03) log K_{OW} + (0.64±0.07)	0.37	1.59
(n=607 with 93% log $K_{OC} \leq 4.0$)	est. log K_{OW}	100%	7%	93%	log K_{OC} = (0.34±0.02) log K_{OW} + (2.00±0.09)	0.26	1.74
Zwitterionic/amphoteric	exp. log K_{OW}	100%	14%	91%	log K_{OC} = (0.22±0.09) log K_{OW} + (1.31±0.25)	0.07	2.04
(n=68 with 91% log $K_{OC} \leq 4.0$)	est. log K_{OW}	100%	0%	80%	log K_{OC} = (-0.04±0.06) log K_{OW} + (1.08±0.30)	0.01	2.11

Source: Arp & Hale (2022)

Both Figure 7 and Figure 8 show the substances that meet both the mobility criteria of a log K_{OC} < 4.0 and also meet the screening criteria of log K_{OW}/ log D_{OW} < 4.5 in the blue square. As is evident, many substances do cluster in this area, but not all. A comparison of the frequency for which substances with a log K_{OW} / log D_{OW} < 4.5 have a log K_{OC} < 4.0 is presented in Table 2 for estimated and experimental values. This occurs for 85% to 88% of the neutral non-polar substances, respectively; for 91% and 92% of the neutral polar substances, respectively; for 98% and 100% of the (ionizable) anionic substances, respectively; for 96 and 100% of the (ionizable) cationic substances, respectively; and for 100% of the zwitterionic/amphoteric substances. Overall the screening criteria is not suitable for identifying "Not Mobile" ionic substances, as many of these had a log K_{OW}/D_{OW} < 4.5 due to extra ionic interactions with organic carbon. The sensitivity in correctly predicting "Not Mobile" using estimated and experimental values was 98 and 91% of the neutral non-polar substances, respectively and was 90 and 79% of the neutral polar substances, respectively. However, this decreased to 29 and 57% of the (ionizable) anionic substances, respectively; to 7 and 51% of the (ionizable) cationic substances, respectively; and to 0 and 15% of zwitterionic substances, respectively.

The overall efficiency in predicting "M" or "Not M" with this screening criteria was quite high, ranging from 85%-95% for all ionizable substances, despite the poor sensitivity for predicting "Not Mobile", as most of ionic substances had both a log K_{OC} < 4.0 and log K_{OW} / log D_{OW} < 4.5. Most ionizable substances with measured log K_{OC} values fulfil both the log Koc < 4.0 and log K_{OW} / log D_{OW} < 4.5 criteria.

Based on this good overall efficiency, the screening criteria of log K_{OW}/log D_{OW} is < 4.5 is considered suitable for concluding "Potentially M/vM", based on the log K_{OC} < 4.0 threshold for Mobility, but not for "Not M".

2.5.3 Guidance for the M/vM assessment

2.5.3.1 Measurement and Selection of log K_{OC} values

The natural variation of K_{OC} can be quite large in the case of charged and ionizable compounds. For this the variation of K_{OC} is not just dependent on the organic carbon content, but also the concentration of contamination (non-linear sorption) and fluctuations in pH that affect the ionizability of soil and the analyte (Tülp et al., 2009). In addition to this, the K_{OC} data themselves can be biased by the ion-exchange interactions of minerals (Droge and Goss, 2013b), competition effects with counterions (Droge and Goss, 2013b), the presence of strong sorbents like black carbon and tars (Arp et al., 2009), weathering effects that create non-exchangeable residues (Loeffler et al., 2020), sorption hysteresis (Sander et al., 2005), enrichment of surfactants on the air-porewater interface (Kim et al., 1997; Lyu et al., 2018), coagulation with humic matter (Markiewicz et al., 2013), sorption site and pore-blocking by organic matter (Mitchell and Simpson, 2013), heterogeneity in types of organic carbon present (Huang et al., 2003) and other factors. All these complex effects are extremely important for risk assessment at the local scale yet are also challenging to fully account for due to their complexity. However, for a generic ranking or benchmarking, the hazard of mobility in all (globally occurring) soil types, can be characterised by measuring K_{OC} values for various soil/sediment types, using a standardized test procedure (e.g. OECD 106 or equivalent). The basic set up of these test procedures is that soil, sediment or sludge is added to a closed container with water at defined ionic strength (e.g. 0.001 $CaCl_2$), with or without a disinfectant to prevent biodegradation, and shaken in the dark to prevent photolysis (Arp et al., 2014). After equilibrium is reached, the solid and water phase concentrations are determined, and the K_D is calculated (equation M3), which is then normalized to the fraction of organic carbon in the sample (equation M4). These tests can be done over a range of porewater conditions (e.g. pH). Challenges to porewater concentration measurements (e.g. low solubility, matrix effects, sorption to DOC), can often be aided by the use of equilibrium passive sampling devices (Jonker et al., 2020). Once available, a statistical distribution of K_{OC} from diverse soil can be made to conclude on the most appropriate K_{OC} for the mobility assessment in Box 3a or 3b. Generally, the most appropriate value would be the minimum K_{OC}, unless there was reason to suspect it was an outlier and not representative.

2.5.3.2 Weight-of-evidence screening categories

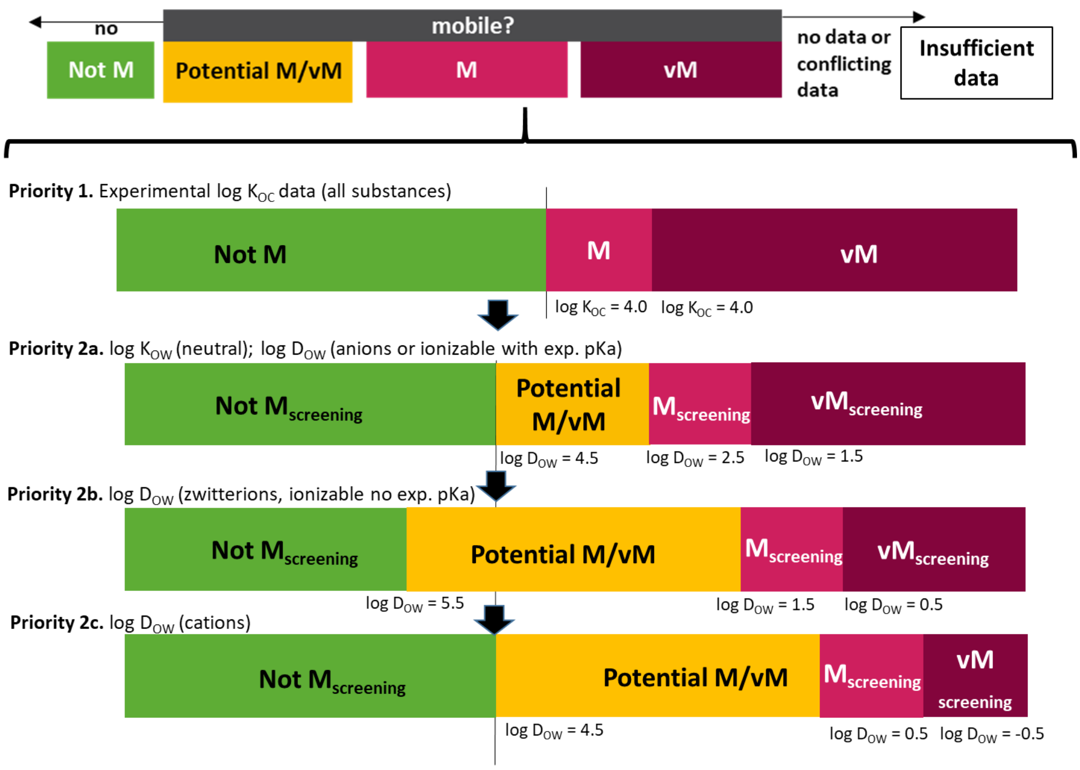
If no K_{OC} data is available, the screening parameter for mobility of a log K_{OW}/log D_{OW} values (pH 4-9) <4.5 can be used to see if the substance is Potential M/vM (Box 3c). Additionally, based on the correlations presented in Figure 7 and Figure 8 for neutral, ionizable and ionic substances, this screening parameter can also be used as weight-of-evidence assessment to conclude the following screening categories: "Not $M_{screening}$", "Potential M/vM", "$M_{screening}$" or "$vM_{screening}$". This is presented in Figure 9A using these screening categories and the M/vM criteria proposed in 2019 by UBA , and in Figure 9B for the 2021 criteria proposed by EC. In Figure 9, Priority 1 represents the actual criteria to be applied to all substance classes (Box 3a an 3b). Priority 2 is the screening level criteria. Priority 2a applies to neutral substances (between a pH 4-9), anions, and ionizable substances that have an experimental pK_a available. Here Potential M/vM corresponds to the log K_{OW}/log D_{OW} range of 4.5 to 2.5, $M_{screening}$ corresponds to the range between 2.5 to 1.5, and $vM_{screening}$ corresponds to everything < 1.5 for "M/vM". Priority 2b is applied to zwitterions and ionizable substances with an estimated pK_a, as these are associated with the most uncertain log K_{OW}/log D_{OW} values (e.g. the rmse is 2 orders of magnitude for zwitterions (see Table 2) and the uncertainty around predicted pK_a values (see Annex A2)); these are considered "Potential M/vM" between 5.5 and 1.5, $M_{screening}$ from 1.5 to 0.5, and $vM_{screening}$ < 0.5. Finally, Priority 2c is used for cations to account for the stronger binding potential to soils; here "Potential M/vM" corresponds to the range between 4.5 and 1.5, $M_{screening}$ from 0.5 to -0.5, and $vM_{screening}$ < -0.5.

Based on the data distribution in Table 2, these screening conclusions can be considered as conservative, as they are more likely to make "false positive" assessments of M/vM then "false negative" predictions of "Not M".

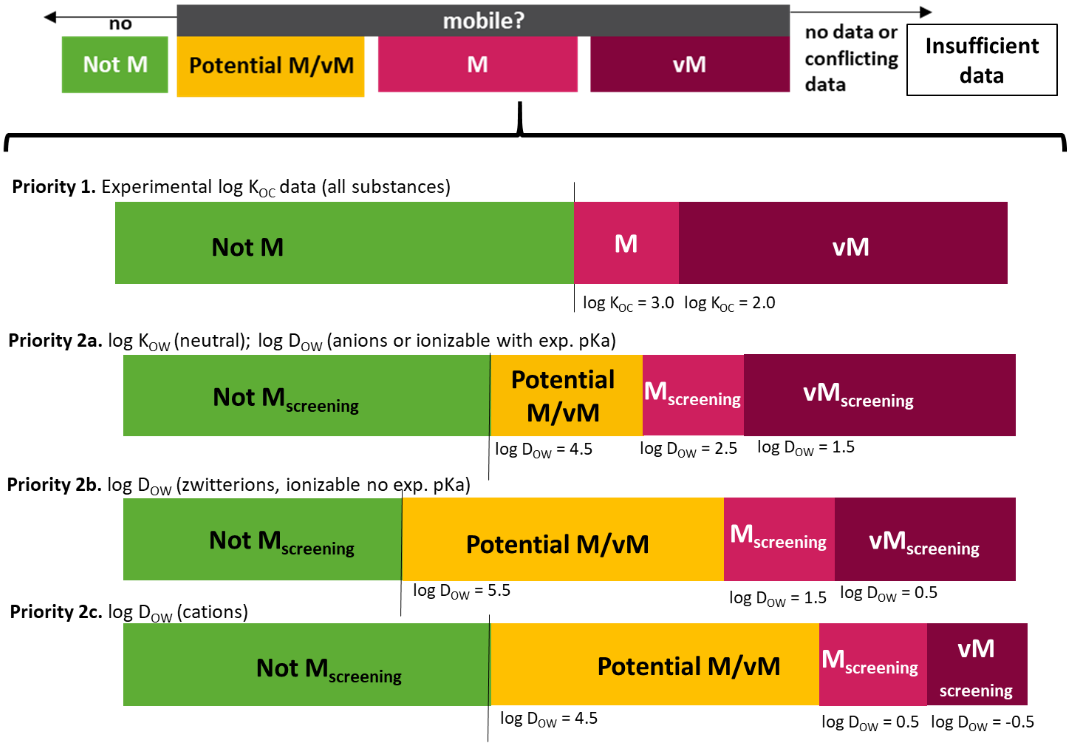
Figure 9: Screening for mobility using log D_{OW} or log K_{OW} values for the M/vM assessment in the absence of high-quality log K_{OC} data

The M/vM criteria is based on a) that proposed in 2019 by UBA (Box 3a), and b) that proposed in 2021 by EC (Box 3b).

A –Screening for mobility based on the 2019 M/vM criteria proposed by UBA



B – Screening for mobility based on the 2021 M/vM criteria proposed by EC



Source: modified from Arp & Hale (2019, 2022)

2.6 Toxicity

The criteria for Toxicity (T) in the PMT/vPvM assessment is based on those of Annex XIII for the PBT/vPvM assessment and additional criteria specific for drinking water exposure (Neumann and Schliebner, 2019) and is presented in Box 4.

Box 4. T criteria

A substance fulfils the toxicity criterion (T) in the following situation:

- ► (a) the long-term no-observed effect concentration (NOEC) or EC10 for marine or freshwater organ is less than 0.01 mg/l;
- ► (b) the substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B, or 2) according to Regulation EC No 1272/2008;
- ► (c) there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification: specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to Regulation EC No 1272/2008;

The preceding situations are those described in Annex XIII, 1.1.3 of REACH. Beyond these situations, there might be cases where it is necessary to identify persistent and mobile (PM) substances with other properties posing a risk to human health and the environment. In such cases an equivalent level of concern to the T-criteria set out in Annex XIII, 1.1.3 of REACH, should be demonstrated. Aspects to be considered are comparable to the SVHC identification for respiratory sensitizers and include:

- Type and severity of possible health effects,
- Irreversibility of health effects,
- Delay of health effects,
- Is derivation of a 'safe concentration' possible?
- Effects on quality of life and societal concern,
- others

Evidence (so called indicators) for significant risk to human health and the environment for persistent and mobile (PM) substances in arises in any of the following situations:

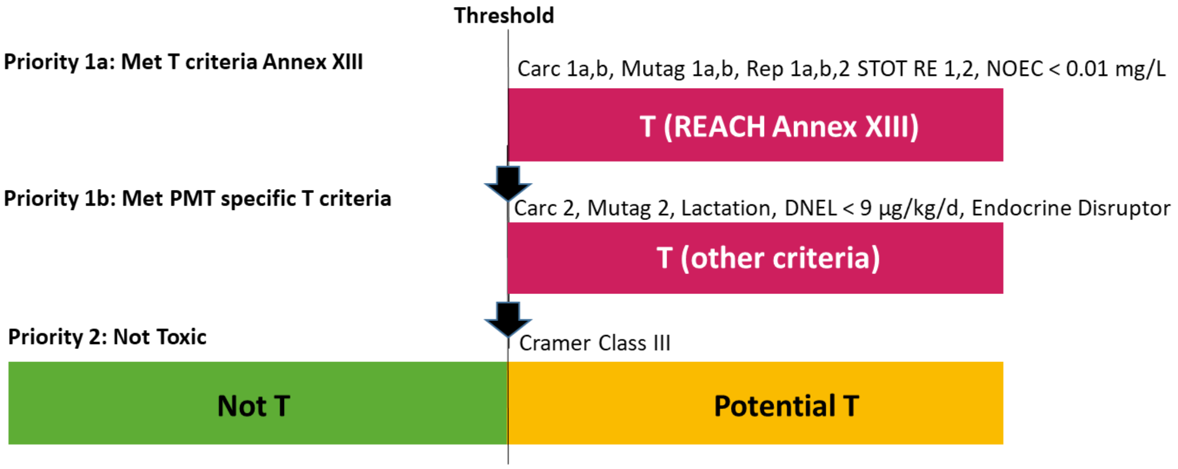
- ► (d) the substance meets the criteria for classification as carcinogenic (category 2), or germ cell mutagenic (category 2) according to the CLP Regulation EC No 1272/2008;
- ► (e) the substance meets the criteria for classification as additional category for "effects on or via lactation", according to Regulation EC No 1272/2008;
- ► (f) the Derived-No-Adverse-Effect-Level (DNEL) is ≤ 9 µg/kg/d (oral, long term, general population), as derived according to Annex I of REACH;
- ► (g) the substance acts as an endocrine disruptor in humans and/or wildlife species according to the WHO/IPCS definition of an endocrine disruptor.

Source: Neumann and Schliebner (2019)

The overall guidance for the T assessment is presented in Figure 10. This figure shows that if a PM or vPvM substance fulfils the T criteria according to Annex XIII of REACH (situations a-c in

Box 4; **Priority 1a** in Figure 10), it would be considered PMT. If a substance does not meet the T criteria based on Annex XIII, the substance is assessed for situations relevant to persistent and mobile substances in drinking water (i.e. situations d – g in Box 4; **Priority 1b** in Figure 10). For this assessment, only high-quality consensus conclusions that the criteria for T should be considered; therefore, for emerging substances, this is not always available. If the substance does not meet any of the Priority 1a or Priority 1b T criteria based on a high-quality consensus conclusion, the chemical structure of the substance should be screened using the Cramer classification scheme, which is used to make a "Threshold of Toxicological Concern" estimation (Kalberlah et al., 2014). Within this classification, Class I and Class II Cramer classes are considered "Not T", but a Class III definition implies *"...chemical structures that permit no strong initial impression of safety and may even suggest a significant toxicity"* (Cramer et al., 1976). As part of **Priority 2**, Class III structures are considered "Potential T", and Yellow according to the traffic light colour scheme for data quality (Table 1).

Figure 10: Schematic representation of the approach used to evaluate T



Source: Arp & Hale (2019)

3 PMT/vPvM assessment of REACH registered substances

3.1 REACH registered substances

The list of all registered substances in the REACH registration database was downloaded on September 19'th 2019 (ECHA, 2019). At this time, it contained a total of 22400 registered substance. This includes substances that are exclusively used as intermediates. When presenting the PMT/vPvM assessment a distinction is made between the results for all registered substances (i.e. those with registered volumes > 1 tpa) and for only those with registered volumes > 10 tpa.

3.2 Transformation pathways

Transformation products were also considered in the PMT/vPvM assessment. To identify the transformation products of a REACH registered substance, lists of experimentally demonstrated transformation pathways were utilized from the EAWAG-BBD database (EAWAG, 2016), the EAWAG-soil database (Latino et al., 2017; Wicker et al., 2016) and the SwissPest19 database (Kiefer et al., 2019a, 2019b; Reemtsma et al., 2013). These databases mainly included pharmaceutical substances; nevertheless, there were matches with 1066 registered substances in the REACH registration database.

3.3 Identifying unique chemical structures

To identify the number of unique chemical structures from the list of 22400 registered substances, including the 1066 registered substances with experimental transformation pathways available, the following procedure was used.

Simplified Molecular Input Line Entry System (SMILES) codes from the following sources, in order of priority. First, available and quality-controlled SMILES for substances in the REACH registration database EC-numbers from an earlier study was used (Arp et al., 2017). For the remaining substances, chemical structure information was obtained, in order of priority, from the QSAR Toolbox structure database (https://qsar-toolbox.org/, accessed October 1, 2020), the IUCLID database (i.e. what REACH registrants provided, https://iuclid6.echa.europa.eu/de/reach-study-results, downloaded prior to this study in April 2017), and if information was still missing, the ChemAxon "Name to Structure" converter, was used to convert CAS numbers and common names to structural information (https://www.chemaxon.com/, accessed September 22, 2019). Structures from QSAR toolbox, IUCLID and ChemAxon "Name to Structure" were then processed using the Open Babel software (O'Boyle et al., 2011) available online (http://openbabel.org/wiki/Main_Page), to convert all structural information into SMILES codes into the same dative format, as well as or International Chemical Identifier Key codes (InChIKey). REACH substances that either contained no carbon atoms (1002 substances), or where no structure information was provided/available (6668 substances) were excluded.

To automatically flag inconsistently reported structures or incorrect structures across databases, a topographical analysis was used to flag the following: 1) differences in number of elements (i.e. the number of carbons, oxygens, etc. should match across the different SMILES database for a given CAS number), and 2) differences in net the charge of the structure (net charge of all positive and minus charges should be zero). In cases of mismatch of elements or net-charge, the structures were manually checked to see if one of the provided/predicted structures was clearly wrong (i.e. text entries instead of SMILES codes). In some cases where this was not clear, manual comparisons were carried out with the website PubChem (https://pubchem.ncbi.nlm.nih.gov/) to choose the best structure. Structures were classified as pseudo-organic (just one carbon atom), organic (more than one carbon atom), organoboranes (organic with at least one boron), organosilicon (organic with at least one silicon) or organometallic (organic structure with one other atom other than H, B, N, O, S, P, Si or a halogen). Collectively these are referred to as "unique chemical structures" and were included in the PMT/vPvM substance assessment. Other molecules with no structure, inorganic, or carbonaceous solids (e.g. activated carbon, charcoals) and carbides were excluded from further consideration. Tautomerism and stereoisomerism were not explicitly checked for.

3.4 Number of unique chemical structures

Not all 22400 registered substances had chemical structure information available, and of the structures that were available contain several duplicates. After a thorough search, at least one unique chemical structure was identified for 15474 of the 22400 registered substances. Of these there were 12960 unique chemical structures that could be identified, 998 of which occurred in multiple REACH substances. The most commonly reoccurring organic substances were acetate (in 61 substances), carbonate (in 54 substances) and toluene sulfonic acid (in 38 substances).

Considering the 1066 substances in the REACH registration database with known transformation pathways, collectively these led to 617 unique transformation products. Of these, 172 were already on the REACH registered database, and 445 were not. The most common, re-occurring transformation products were oxidized benzene rings (catechol, hydroquinone, hydroxybenzoic acid) or small aliphatic chains (formaldehyde, acetaldehyde, etc.).

The REACH registration database contained several substances that were salts or mixtures, i.e. multi-constituent substances and UVCBs. In cases of well-defined multi-constituent substances, where it was explicitly stated what chemicals were present, a prefix to the EC number would be associated with each of the unique chemical structures. This prefix has the form "(sx)-", where "s" indicated "salt/mixture" and "x" was a number to indicate the order based on molecular weight (i.e. s1-indicates the structure with the largest MW in the substance, s2 the second largest MW, etc.). In cases were the mixture was not well defined, a system of structural flags was used to note that, regardless of the presence of a "(sx)-" prefix, the structure is uncertain. These structural flags are:

- ***charge balance*** **-** in cases where the positive and negative charges on the structure or mixture did not cancel out due to e.g. counterions not being provided (285 structures);
- ***reaction product*** - in cases when the parent substances to a reaction was reported, but not the actual reaction products (83 unique chemical structures across 329 substance entries);
- ***petro*** - in cases where the substances were distillates of petroleum products according to their name (48 unique, proxy structures identified across 212 substance entries);
- ***residues*** - in cases where the word "residue" was in the name, excluding petroleum distillates, which occurred for 22 unique substances;
- ***mixture*** - for substances that were loosely defined mixtures, where the name contained words like "derivatives", "branched", "isomers", "ethoxylated", "and", "of", or plural forms of chemical names (e.g. ethers, alcohols) (207 unique proxy structures across 2522 substance entries);

- ***extracts*** in cases where a substance had the word "extract" in its name (5 unique structures).

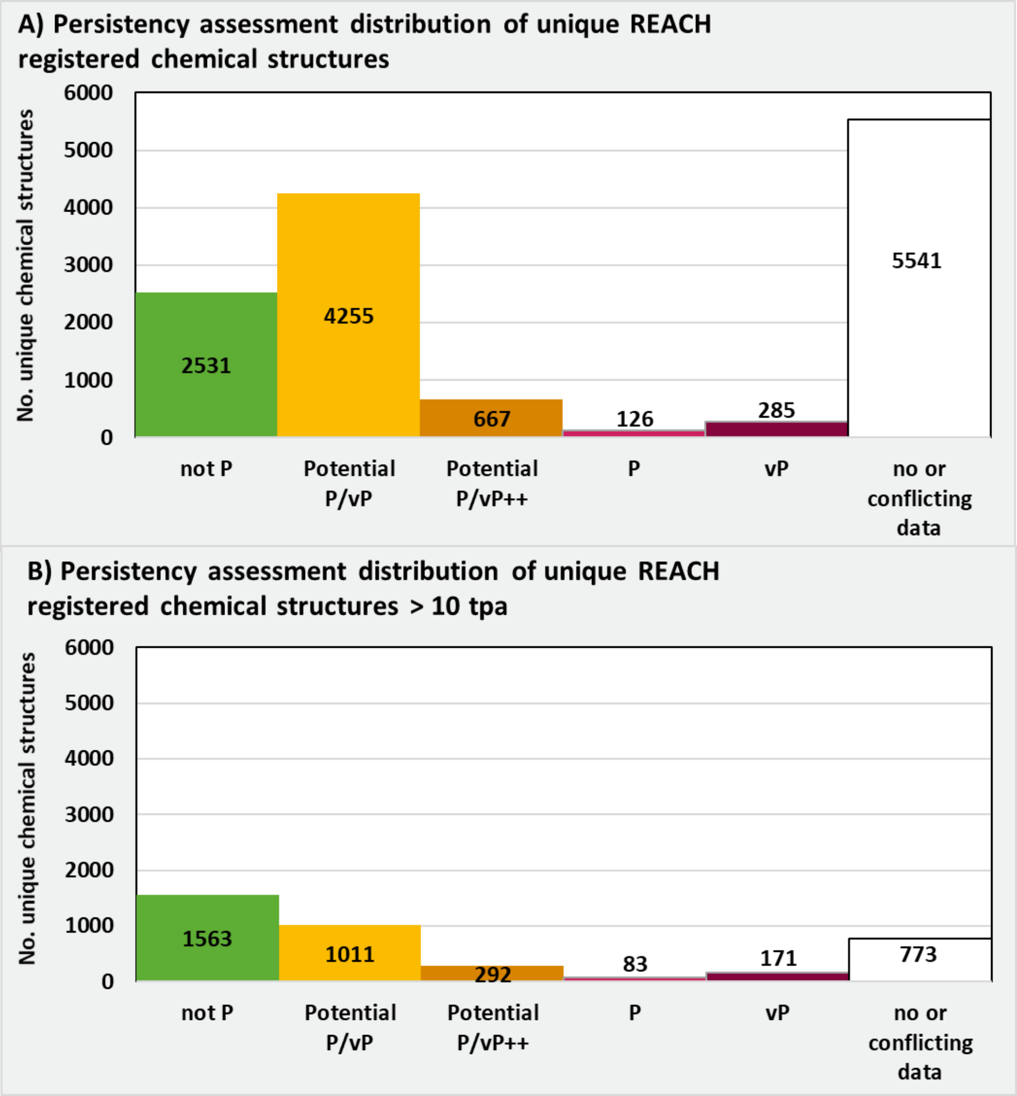
For the rest of this report, we will mainly refer to this list of 13405 unique chemical structures in the REACH registration database as of September 2019 and their known transformation products, as well as the smaller to a list of 3893 unique chemical structures that were present in the REACH registration database with registered volumes > 10 tpa.

3.5 P/vP assessment

The P/vP assessment procedure was applied to the unique chemical structures that could be identified amongst substances in the REACH registration database and their known transformation products. The data sources and how they were used as part of this is presented in Annex A. The final distribution of P/vP assessments is presented in Figure 11.

Figure 11: Overview of persistency conclusions

Unique chemical structures that are A) all REACH registered substances and their transformation products (n=13405), B) REACH registered substances with registered volumes > 10 tpa (n=3893)



Source: original figure based on Arp & Hale (2022)

As evident from Figure 11 A), there were 41% (5541 out of 13405) of unique chemical structures where there was no or conflicting information and a PMT/vPvM conclusion of "insufficient data" was made. However, for substances with registered volumes > 10 tpa (Figure 11 B), there is more data available, and the PMT/vPvM conclusion of "insufficient data" was only made for 20% (773 out of 3893) of the unique chemical structures. This is attributed to the fact that a PBT/vPvB assessment is required for substances with registered volumes > 10 tpa based on Article 14 of REACH. A substantial percentage of substances in each group were given the uncertain conclusion of being "Potential P/vP". This comprised 32% (4255 out of 13405) and 26% (1011 out of 3893) of the unique chemical structures belonging to all REACH registered substances and to only those with registered volumes > 10 tpa, respectively. Considering the "Potential P/vP" and "No or conflicting data" categories together, there is evidently an extremely large data gap related to the assessment of persistency of REACH registered substances. This has also been highlighted in previous studies (Arp et al., 2017; Strempel et al., 2012; Zheng et al., 2019).

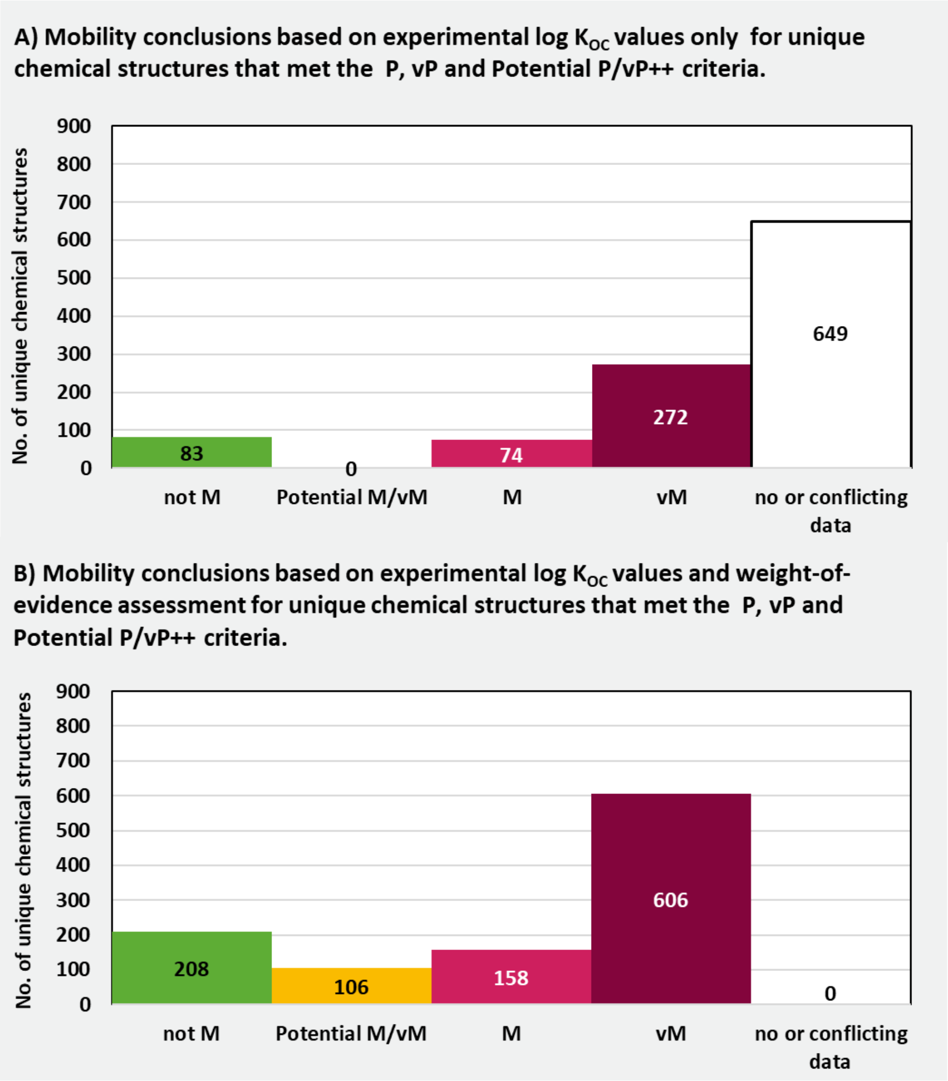
Conclusions of "Not P" were reached for 19% (2531 out of 13405) and 40% (1563 out of 3893) of the unique chemical structures belonging to all REACH registered substances and to only those with registered volumes > 10 tpa, respectively. There were only 3.1% (411 out of 13405) unique chemical structures assessed to meet the P/vP when all REACH registered substances were considered, and 6.5% (n=254 out of 13405) when only those with registered volumes > 10 tpa were considered. Of the 411 substances considered P or vP, the primary reasons for this conclusion were either i) substances that are on either the Candidate list for SVHC because they fulfil the PBT/vPvB criteria, the Stockholm Convention list of Persistent Organic Pollutants, or is a broad consensus to meet the PBT/vPvB criteria (33 substances) among registrants of these substances in REACH; ii) simulated half-lives exceeding the half-live criteria (72 substances); iii) read-across based on the presence of a PFAS moiety (47 substances), iv) weight-of-evidence decisions either in this study, the literature or REACH registration dossiers (259 substances).

3.6 M/vM assessment

As part of the PMT/vPvM assessment workflow (Figure 2), only persistent or very persistent substances need to be evaluated for mobility. Figure 12 presents the outcome of mobility assessments for all the 1078 P, vP and Potential P/vP++ unique chemical structures assessed in this study. Results are shown when only Priority 1 log K_{OC} data is used (Section 2.5) and when the Priority 2 screening assessment in Figure 9A is considered. The data sources and how they were used as part of this assessment is presented in Annex A2. As is evident, there were 649 of the 1078 persistent unique chemical structures where no log K_{OC} was available. However, this data gap could be filled when the weight-of-evidence assessment outlined in Figure 9 was used. In this case there were no persistent substances for which a mobility assessment could not be made. The conclusions following the use of the screening method were mostly vM (56%, 606 out of 1078), followed by Not M (19%, 208 out of 1068), M (15%, 158 out of 1068) and potential M/vM (10%, 106 out of 1068). Consequently, using the log K_{OW}/log D_{OW} screening thresholds presented here increases the substances considered persistent and mobile from 346 to 764.

Figure 12: Mobility conclusions for unique chemical structures in the REACH registration database that met the P, vP and Potential P/vP++ criteria

Panel A) utilizes only experimental log K_{OC} data, and B) additionally a weight-of-evidence mobility conclusion, utilizing log K_{OW}/D_{OW} data (Figure 9a).



Source: original figure

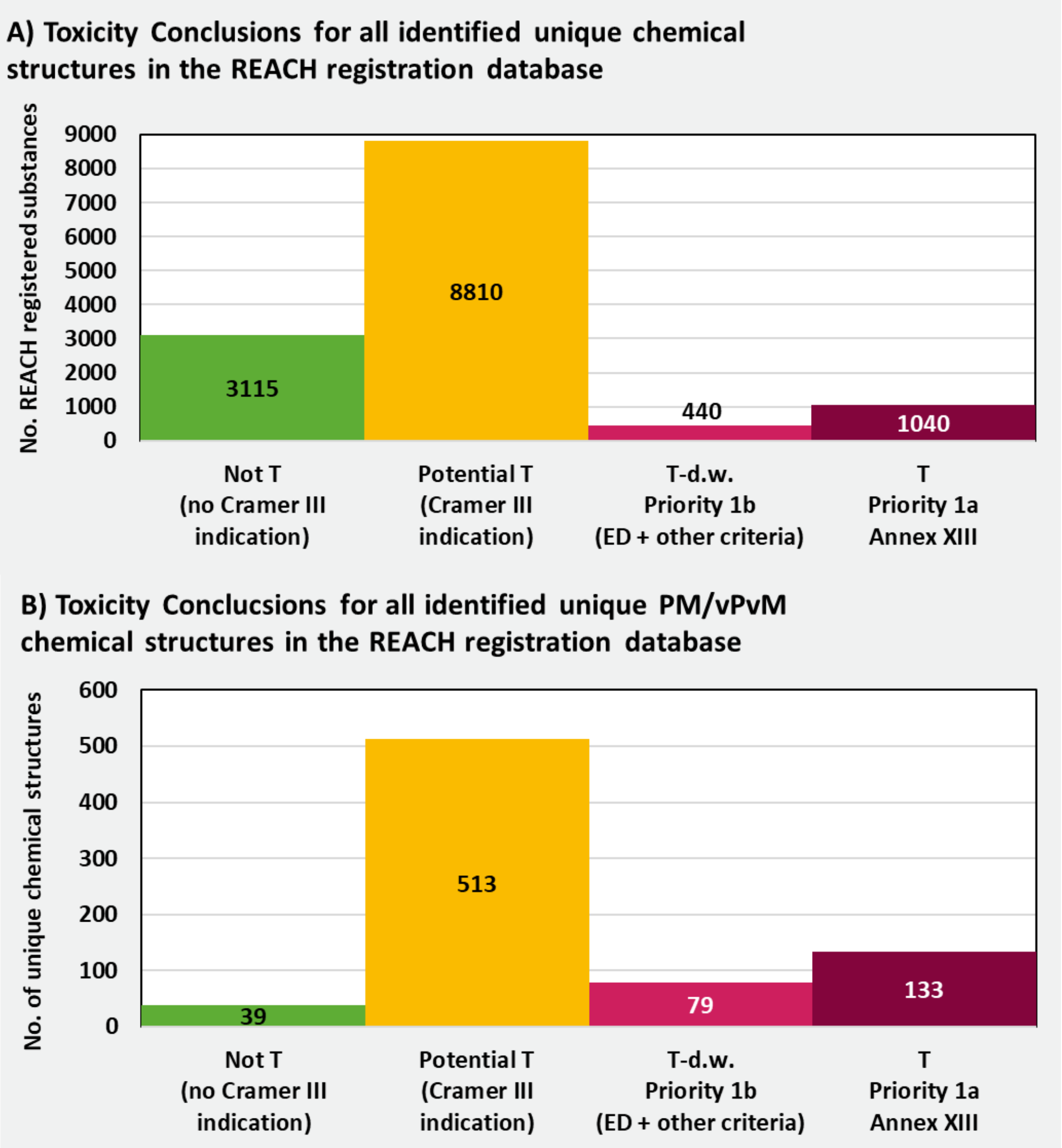
3.7 T assessment

The compilation of toxicity conclusions for all 13405 identified unique chemical structures in the REACH registration database is presented in Figure 13A. The data sources and how they were used for the T assessment is presented in Annex A3. Based on the REACH Annex XIII criteria that considers toxicity to aquatic organisms and diverse human health endpoints, 1040 of these substances are considered toxic (Priority 1a in Figure 10). Considering also the additional criteria proposed in 2019 by UBA, there are an additional 440 substances that are considered to meet the T criteria (Box 4; Priority 1b in Figure 10). Figure 13B presents toxicity conclusions for only the 764 chemical structures considered already as PM or vPvM. Of these, 133 of them are considered toxic according REACH Annex XIII (Priority 1a) and an additional 79 are considered toxic when using the additional Priority 1b toxic criteria. Note that for this assessment only high-quality consensus conclusions that the criteria for T are considered. Only a minority of PM and vPvM substances meet the T criterion based on high-quality consensus conclusions (212 out of 764, or 28%).

Of the substances that are not considered to fulfil the T criterion, most of them have structures that meet the Cramer Class III criterion, implying their structures permit no strong indication of safety and that they are "Not T" (Cramer et al., 1976). For all substances in the REACH registration database, 66% of them met the Cramer Class III criterion though without a toxic endpoint identified, and for those substances considered to be persistent and mobile, this applied to 67% of them.

Figure 13: Distribution of toxicity conclusions

A) all identified unique chemical structures in the REACH registration database or transformation products thereof as of September 2019, and B) all identified persistent and mobile (PM) or very persistent and very mobile (vPvM) chemical structures registered under REACH. T-d.w. (additional considerations specific for drinking water exposure) refers to additional toxicity criteria than those in REACH Annex XIII (Box 4; **Priority 1b** in Figure 10)



Source: Original Figure

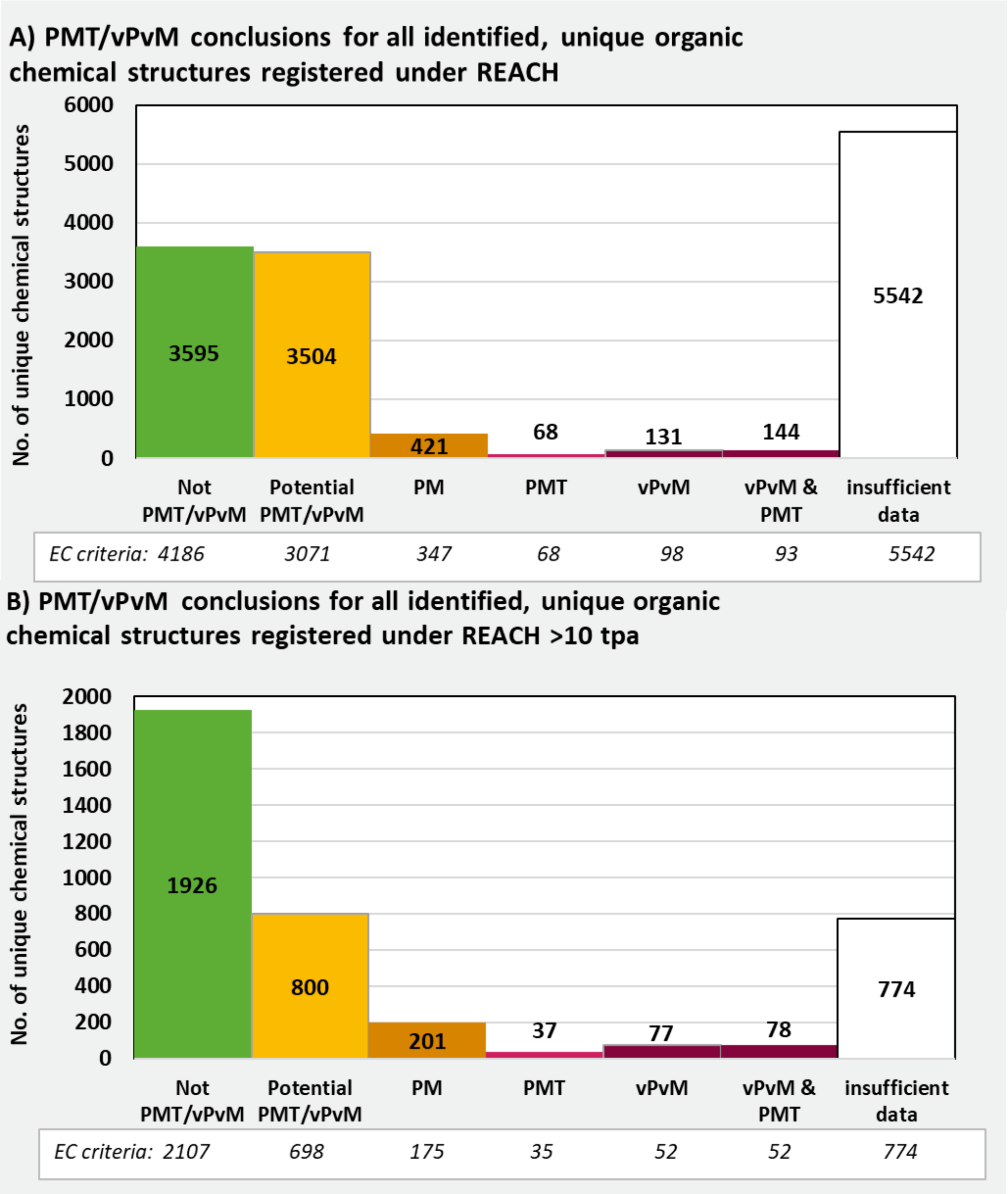
4 Outcome of the PMT/vPvM Assessment

4.1 Distribution of the PMT/vPvM Conclusions

In Chapter 3, the assessment of P, M and then T were presented. In this chapter the overall outcome of the PMT/vPvM assessment is presented. Figure 14 and Table 3 present the overall distribution of PMT/vPvM conclusions using the 2019 PMT/vPvM criteria proposed by UBA for all unique chemical structures amongst substances in the REACH registration database (as of September 2019) or transformation products thereof and, those with registered volumes > 10 tpa. Further, the results using the 2021 PMT/vPvM criteria proposed by EC (2021) are indicated.

Figure 14: Distribution of the PMT/vPvM conclusions

A) all identified unique chemical structures in the REACH registration database or transformation products thereof as of September 2019, and B) only those 3893 with registered volumes > 10 tpa.



Source: Original Figure

As evident in Figure 14, there was insufficient data to carry out a PMT/vPvM assessment for 41% (5542 of 13405) of all identified unique chemical structures in the REACH registration database (Figure 14a), and 30% (774 of 3893) for those with registration volumes > 10 tpa (Figure 14b). If the weight-of-evidence assessments were not included (Priority 3 for persistence in Figure 3 and Priority 2 for mobility in Figure 9), the % of substances with insufficient data to perform an assessment would increase substantially. As also presented in Figure 14, 23% (3504 out of 13405) of all identified chemical structures received the ambiguous conclusion "Potential PMT/vPvM" substance, as well as 16% (800 out of 3893) for those belonging to substances with registration volumes > 10 tpa. The substantial number of conclusions being either " insufficient data" or "Potential PMT/vPvM" shows a substantial data gap for simulated environmental half-lives and K_{OC} data that needs to be addressed. There is more data available for substances with registration volumes > 10 tpa, indicating that chemical regulation and reporting requirements can help close this data gap. For substances with registration volumes > 10 tpa, persistency testing (and screening) is mandatory under REACH Article 14. Therefore, it can be expected that including the PMT/vPvM criteria hazard category in the CLP regulation will help close this data gap even further.

Many persistent and mobile substances are not considered as PMT substances, as they did not fulfil the toxicity criteria based on available data. As shown in Figure 14a, only 68 of the 489 persistent and mobile substances are considered PMT substances and 144 of the 276 vPvM substances would be considered "vPvM & PMT". Even though a majority of substances registered under REACH have a log K_{OC} < 4 or 3 (see

Figure 6), only a few percent of these ultimately are considered PMT or vPvM, because the relative rarity of meeting both the P and T criteria, or vP criteria, respectively.

In total there were 343 out of 13405 identified unique chemical structures in the REACH registration database that met the PMT/vPvM criteria which corresponds to 2.6 % of all identified unique chemical structures in the REACH registration database. Just considering the identified unique chemical structures with registration volumes > 10 tpa, there are 192 out of 3893 that met the PMT/vPvM criteria, corresponding to 1.4% of all identified unique chemical structures in the REACH registration database.

Box 5. Number of PMT/vPvM Substances in the REACH Registration Database

Following the 2019 PMT/vPvM criteria proposed by UBA, there are:

- 343 unique chemical structures that met the PMT/vPvM criteria (belonging to 474 registered substances). This corresponds to 2.6% of all unique chemical structures that were identified in the REACH registration database that.

Following the 2021 PMT/vPvM criteria proposed by EC, there are:

- 259 unique chemical structures in the REACH registration database that met the PMT/vPvM criteria (belonging to 360 registered substances). This corresponds to 1.9% of all unique chemical structures that were identified in the REACH registration database that.

4.2 Thresholds and Sensitivity Analysis

The number of substances that are assessed as PMT/vPvM substances within any given inventory are dependent on: 1) the thresholds of P, M and T that are defined, and 2) the data quality requirements for assessing those thresholds. It is straightforward to conceptualize what the effect of adjusting the P/vP threshold would be. For instance, increasing threshold half-live values to a larger number of days would reduce the number of P/vP substances (and increase the number of "Not P" substances). Not allowing for weight-of-evidence conclusions would expand the number of "Potential P/vP" and "insufficient data" conclusions, while decreasing the number of "Not P" and P/vP conclusions. If one were to introduce an alternative persistency threshold than media specific half-lives, like the emission scenario dependant multimedia parameter P_{ov} (Redman et al., 2021), this would either severely restrict the number of substances that could be evaluated for persistency if intense data requirements are needed, or have an unknown impact if low data quality modelling threshold values are introduced as weight-of-evidence. If the Priority 2 readily/inherent biodegradability screening tests were used as the threshold for persistence as part of the workflow in Figure 3, then the "Potential PMT/vPvM" substances would all become either PM, PMT or vPvM, which would encompass approximately a third of the substances in the REACH registration database. Therefore, the way in which the P/vP criteria are parameterized has a substantial impact on the number of PMT/vPvM substances.

Similarly, the sensitivity of adjusting log K_{OC} thresholds directly impacts the number of persistent substances meeting the M/vM criteria. A sensitivity analysis of this can be made by comparing the differences in the number of PMT/vPvM substances when using the 2019 criteria proposed by UBA (Neumann and Schliebner, 2019) with the 2021 criteria proposed by the EC (European Commission, 2021). The different log K_{OC} criterion (Box 3a and 3b) influences the screening value assessments (Figure 9). The sensitivity of using either of these two PMT/vPvM criteria is presented in Table 3. As expected, if instead of the using the log K_{OC} 4.0/3.0 as criteria for M/vM as proposed in 2019 by UBA, the criteria of log K_{OC} of 3.0/2.0 as proposed in 2021 by the EC is adopted, this will increase the number of "Not PMT/vPvM" substances. Indeed, as presented in there is an increase in Table 3 the "Not PMT/vPvM" substances from 27 % to 31% for all REACH registered substances and from 49 % to 54 % for only those with registration volumes > 10 tpa. Similarly, the total number of PMT, vPvM and "vPvM & PMT" substances decreases from 2.6 % to 1.9% (all REACH registered substances) and from 4.9 % to 3.6% (> 10 tpa). Further, the number of "Potential PMT/vPvM" substances also decreases from 26 % to 23 % (all REACH registered substances) and from 21 % to 18 % (> 10 tpa). The only conclusions where sensitivity to the log K_{OC} thresholds are not obvious are PM and PMT substances, as the number of these substances can increase and decrease. The increase is due to vPvM and vPvM & PMT substances becoming PM and PMT substances, respectively. The decrease is due to PM and PMT substances becoming either Not PMT or Potential PMT/vPvM substances. Therefore, the number of PMT substances was both 68 using the 2019 PMT/vPvM criteria proposed by UBA or the 2021 criteria proposed by EC, but their identities were different.

Table 3: Total numbers of PMT/vPvM conclusions for all substances in the REACH registered database as of September 2019.

The distribution of PMT/vPvM conclusions is presented based on all unique chemical structures registered under REACH as of September 2019 (left column) and based on only those with registration volumes > 10 tpa (right column) based on publicly available information. Compared are the PMT/vPvM criteria proposed 2019 by UBA versus the less stringent PMT/vPvM criteria proposed 2021 by EC.

PMT/vPvM conclusion based on PMT/vPvM criteria proposed in	**REACH substances with registration volumes > 1 tpa** 2019 by UBA vs. 2021 by EC	**REACH substances with registration volumes > 10 tpa** 2019 by UBA vs. 2021 by EC
Total number of substances in the REACH registration database as of September 2019	22400	7782
Total number of unique chemical structures assessed	13405	3893
no PMT/vPvM conclusion or no data	5542	774
Not PMT/vPvM	3595 vs. 4186	1926 vs. 2107
Potential PMT/vPvM	3504 vs. 3071	800 vs. 698
PM (incl. PvM and vPM)	421 vs. 347	201 vs. 175
PMT/vPvM	343 (2.6%) vs. 259 (1.9%)	192 (4.9%) vs. 139 (3.6%)
PMT	68 vs. 68	37 vs. 35
vPvM	131 vs. 98	77 vs. 52
vPvM and PMT	144 vs. 93	78 vs. 52

5 Recommendations

Identifying PMT/vPvM substances is the first step needed towards protecting drinking water resources from them. The second step is the implementation of risk mitigation measures (RMM), to ensure that emissions of PMT/vPvM substances are minimized and controlled. Below, recommendations to both REACH registrants and regulatory authorities are provided to achieve such aims.

5.1 REACH registrants

The safe use of chemicals across their full life cycle is a key component of REACH. Through REACH, it becomes the responsibility of the registrants to characterize the intrinsic hazard of the substances. Registrants can use the 2019 PMT/vPvM criteria proposed by UBA and the 2021 PMT/vPvM criteria proposed by EC already now to perform a PMT/vPvM assessments in the context of their chemical safety report (CSR). This will allow the identification of PMT/vPvM substances during REACH registration, or already during product development.

Registrants should follow a similar assessment procedure for PMT/vPvM substances, as for PBT/vPvB substances and substances meeting the hazard classes in Article 14(4) of REACH. This assessment procedure is comprised of the following steps as outlined in Annex I section 4.0.2 of REACH:

- Step 1: Comparison with the Criteria
- Step 2: Emission Characterization

For PMT/vPvM substances, "Step 1: Comparison with the Criteria", the criteria in this report can be used. For substances registered under REACH as of September 2019, registrants can already identify if any of the 343 unique chemical structures that met the PMT/vPvM criteria (belonging to 474 registered substances) are within their portfolio (Arp et al., 2023b). Registrants should also be aware that there was insufficient data to make a PMT/vPvM assessment for 41% (5542 out of 13405) unique chemical structures in the REACH registration database. Therefore, registrants are encouraged to ascertain if high quality persistency information is available for substances that are not readily or inherently biodegradable in their portfolio, such as through simulated half-life tests, or other information if the suitability and reliability can be reasonably demonstrated. An example advance in this is regard is a recent, simpler and low-cost method for benchmarking simulated half-lives in freshwater, following the OECD 309 guideline, that substituted (expensive) 14C-labeled compounds with non-radiolabelled aniline (Hofman-Caris and Claßen, 2020). Similarly, if log K_{OC} data is not available for the mobility assessment, it is strongly recommended to obtain this data, in particular for substances that are not readily or inherently biodegradable or if they have registration volumes > 10 tpa. The best data for addressing the mobility criteria is to conduct K_{OC} tests on soils, such as with OECD 106, over a range of relevant pH conditions (i.e. 4 to 9). For addressing ionic and ionizable substances, registrants are encouraged consider how their data relates to the state-of-the art understanding of sorption for these substances (Sigmund et al., 2022). For substances that are persistent and mobile, registrants should be aware that there is currently a limited understanding of the toxicity of these substances. Existing toxicity bioassays were mainly developed for substances that bioaccumulate, and largely ignored this chronic exposure route of substances that are less prone to bioaccumulate, such as persistent and mobile substances. Therefore, for registrants with persistent and mobile substances in their portfolio that are not considered toxic, it is recommended to follow current research on the toxicity assessments of such substances, as robust toxicity assessment frameworks are currently being developed.

If a registrant has a PMT/vPvM substance in their portfolio, "Step 2: Emission Characterization" can essentially follow a similar procedure as already in place for PBT/vPvB substances. Details of how this characterization can be carried out are given in sections R.11.3.4 and R.11.4.1.4 of the REACH PBT guidance document (ECHA, 2017a). The key step is the exposure assessment following Annex I, Section 5 of REACH, which includes recommendations for risk management measures (RMM) to minimize emissions. Analogously to other hazardous substances under REACH, regulatory measures for PMT/vPvM substances may only need to be considered by authorities if registrants and downstream users do not put the necessary RMM into place.

It is strongly recommended that PMT/vPvM properties should be communicated during the scope of registration and throughout the supply chain the same way as PBT/vPvB properties are, i.e. via the Chemical Safety Report and/or the Safety Data Sheet. This should also include recommendations for the minimization of emissions during the supported use. Such proactive actions would assist industry in fulfilling their obligation under REACH to guarantee safe use of their registered substances.

5.2 European Commission, ECHA and Member States

The recent action by the European Commission to include PMT/vPvM substances in the CLP and REACH regulations (European Commission, 2020) is a needed step forward. The European Commission and member states should strive to implement these criteria as quickly as possible, in particular in the CLP regulation, to instigate a harmonized classification by member states and industry.

As evident from Table 3 and discussed in section 4.2, transitioning from the 2019 PMT/vPvM criteria proposed by UBA to the 2021 criteria proposed by EC is associated with a decrease in the number of substances that are classified as being PMT/vPvM substances from 343 to 259, or a decrease of 25%. This is only because of the change in the mobility criteria. The less stringent criteria will therefore miss several of the persistent substances with a log K_{OC} between 3.0 and 4.0 and several of the very persistent substances with a log K_{OC} between 2.0 and 3.0 that have been detected in drinking water (Arp et al., 2023a). The impact on the cost-benefit asymmetries from this are needed to assess whether this change in the PMT/vPvM criteria are in the best interest of European society. However, regardless of the outcome of such an assessment, should the 2021 PMT/vPvM criteria proposed by the EC be the easiest to implement in the short term within CLP and REACH, it is recommended to use these criteria. Readjusting the mobility criteria to be more protective can be discussed in future revisions.

As part of the upcoming revisions of REACH, there are many possibilities to implement the PMT/vPvM criteria and to establish a PMT/vPvM assessment. One option is that Annex I calls for the assessment of PMT/vPvM within the registration dossiers and e.g. the determination of K_{OC} could be required at a low tonnage level below registration volumes of 10 tpa. Article 14(4) could also include PMT/vPvM substances and ask for an exposure assessment and a risk characterization. The revised REACH regulation should include PMT/vPvM substances as substances of very high concern (SVHC) following Article 57. Consequently, Article 57 and Annex XIII could be expanded in order to include the PMT/vPvM criteria. Further, Article 68(2) could be amended to allow fast-track restriction for PMT/vPvM substances for consumer uses.

ECHA's upcoming CLP and REACH guidance documents should be amended to incorporate a PMT/vPvM assessment. This current report could be used by ECHA as an initial point of origin when developing and publishing an ECHA guideline for the PMT/vPvM assessment under REACH and under CLP.

Member states can already now start identifying PMT/vPvM substances, and prepare proposals for future amendments to the CLP regulation. This can already also be implemented in REACH, as the hazard caused by PBT/vPvB substances is comparable to the hazard caused by PMT/vPvM substance under Article 57 (f) because of the "*scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern*" (Hale et al., 2020b).

Following implementation of the PMT and vPvM hazard classes in the CLP regulation, introducing the same hazard classes also in the United Nation's Globally Harmonized System of Classification and Labelling of Chemicals (GHS) should be pursued as an immediate follow-up. This would ensure a level playing field amongst European chemical manufacturers with the international market, facilitate compliance, and help enable the realization of the Sustainable Development Goals related to ensuring drinking water safety for future generations.

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7 List of Annexes

- Annex A. Data sources used in the PMT/vPvM assessment

A Data Sources Used in the PMT/vPvM assessment.

The databases, literature sources and QSAR tools for the P, M and T assessments that are used in Chapter 3 are presented here in Annex A. The purpose of this annex is mainly to present the data sources used in Chapter 3 for transparency, and to briefly discuss the data quality issues of these sources and how these quality considerations were integrated into the traffic light colour scheme. The assessment in Chapter 3 could have been made using additional or alternative data sources. More information about these data sources and an evaluation of their quality has been presented in a recent study (Arp and Hale, 2022).

A.1 Persistence

The data sources and procedures used to conduct the P/vP assessment herein (Arp et al., 2017; Arp and Hale, 2019; ECHA, 2017a; Huang et al., 2021) were as follows, in the order of priority:

1) established P or vP classifications under Article 57 of REACH or by the Stockholm Convention;

2) simulated half-lives extracted from eChemPortal for water, soils and sediments (at reliability levels 1, 2 & 4, www.echemportal.org, accessed May 28, 2020). These values were compared to REACH Annex III criteria for P/vP (i.e. >40/>60 days for freshwater; >120/>180 days for freshwater sediment and soil) and if a half-life threshold for P or vP was exceeded the substance from this database would receive that classification herein;

3) weight-of-evidence persistency conclusions from Berger et al. (Berger et al., 2018) or a listing of "broad consensus" of a substances meeting the PBT/vPvB criteria on the ECHA website's "advances search for chemicals" (https://echa.europa.eu/advanced-search-for-chemicals, accessed May 31, 2020) to conclude either P or vP;

4) experimental readily biodegradable screening tests (e.g. OECD301A-F, OECD310) or inherent biodegradation screening tests as extracted from eChemPortal. If all available results concluded "readily/inherently biodegradable" the substances was classified as "Not P" herein. However, if the number of screening tests reporting "not readily/inherently biodegradable" was equal to or greater than those that did report "readily/inherently biodegradable", a preliminary conclusion of "Potential P/vP" was assigned;

5) if no other data was available, read-across methods and QSARs were utilized for a weight-of-evidence approach as elaborated below.

Various QSAR methods were considered and compared for the P/vP assessment. QSARToolbox software (https://qsartoolbox.org/, version 4.4, accessed 28-30 May, 2020) was used to run EPISuite's BIOWIN biodegradability QSARS 1 through 6 and the QSARToolbox "P predictor". Additional tools were the open source software OPERA (https://github.com/NIEHS/OPERA, accessed August 16, 2021) used for half-life predictions; as well as an Iterative Fragment Selection (IFS) QSAR approach that was previously developed to rank likelihood of persistence (Arp et al., 2017). The BIOWIN data was processed in two ways. The first was to use the approach in the ECHA PBT/vPvB guideline (ECHA, 2017a), which is to conclude "Potential P/vP" if the BIOWIN 2 (non-linear model) or BIOWIN 6 (MITI non-linear prediction) result is < 0.5 and the BIOWIN 3 (ultimate biodegradation time) result is ≤ 2.25. The other method was to convert BIOWIN output to estimated half-lives in freshwater using the regression models presented in Arnot et al. (2005), where the geometric average of all models plus one geometric standard deviation was used to derive an estimated half-life, to err on the side of caution (Arp et al., 2017). The half-life derived by this method is referred to here as the "$t_{1/2}$-QSAR". The persistency database produced by ECHA in 2014, and called Pro S.P. (Arp and Hale, 2019) which provided persistency conclusions (though little traceability) was also consulted.

An approach to see if substances that obtained Priority 2 "Potential P/vP" assessment based on readily or inherently biodegradability tests could be assessed as P, vP or "Potential P/vP++" based on Priority 3 weight-of-evidence from QSARs was recently developed by the authors (Arp and Hale, 2022). The conclusion was that, based on the possible underprediction of $t_{1/2}$-QSAR by a factor 10 error, if the $t_{1/2}$-QSAR conclusion was greater than 400 and 600 days, respectively, , than the substances could be considered P or vP, respectively, as part of a weight-of-evidence assessment, provided that other QSARs gave a consistent conclusion of persistency, and a manual inspection of the data and literature gave no indication the substance was hydrolysable or otherwise not persistent.

A.2 Mobility

Experimental K_{OC} and K_{OW} data were acquired from two sources. The first was eChemPortal (extracted May 28, 2020), where only experimental or read-across data at reliability levels 1, 2 and 4 were used. The data was manually curated by removing extremely high values (e.g. > 10 log units), due to the suspicion the data was reported incorrectly (e.g. K_{OC} values reported as log K_{OC} values). The second was the UFZ-LSER database (Ulrich et al., 2017) (accessed September 23rd, 2020), which provides K_{OC} and K_{OW} data based on the output of poly-parameter free energy relationships (PP-LFER) for neutral substances. These UFZ-LSER outputs are considered of experimental quality if all the PP-LFER descriptors are experimentally determined (Bronner and Goss, 2011a; Endo and Goss, 2014). For K_{OC} data, the PP-LFER of Bronner and Goss (Bronner and Goss, 2011a) was selected, and for K_{OW} it was from Abraham and Acree Jr (2010).

If multiple log K_{OC} values from several studies were given, then depending on data availability either the minimum log K_{OC} data (unless it is an outlier), the minimum log K_{OC} from a reported range, or the average log K_{OC} minus one standard deviation was used for the mobility assessment, to err on the side of caution. A similar consideration was made for experimental values of log K_{OW}. Many data were reported with the operators <, <=, ca., > and >=. Some of this data had to be excluded as including such operators led to ambiguous mobility conclusions (e.g. a log K_{OC} > 1 could be M, vM or not M). There were frequently occurring log K_{OC} entries in eChemPortal of > 5.63 or <1.25, which clearly indicate not M or vM, respectively. Such entries arelikely based on the limits of a log K_{OC} testing methodology (such as analytical detection limits in the water or soil phase). No discrimination was made in the obtained K_{OC} data for pH, temperature or experimental protocol, due to the rarity of such data in the eChemPortal database.

In cases where K_{OC} data was not available, a screening approach was tested using K_{OW} and D_{OW} data for its reliability in correctly predating M/vM conclusions based on higher quality K_{OC} data. This screening approach was introduced in previous work by UBA, using fewer data than the current study, and states that a minimum log K_{OW} or minimum log D_{OW} < 4.5 could be used as the basis for screening for mobility (Arp and Hale, 2019; Neumann and Schliebner, 2019). Estimated K_{OC} values were not considered for the development of a screening or weight-of-evidence approach, despite estimated K_{OC} values being available on eChemPortal and the UFZ-LSER database (using estimated PP-LFER descriptors). The reason for this was to be consistent with the PMT/vPvM criteria proposed in 2019 by UBA and 2021 by EC to only use the minimum of experimentally measured K_{OC} data for this assessment. An additional reason is that the such estimation methods are often calibrated based on K_{OW} data. For this development, estimated K_{OW} for neutral species were obtained from two sources: the UFZ-LSER database (by using estimated PP-LFER descriptors instead of the experimental ones), and ChemAxon (accessed September 22, 2019). Minimum D_{OW} values between a pH of 4 to 9 were calculated from the dataset of best available K_{OW} (neutral species) and pK_a values as follows for all identified acids and bases:

$$D_{OW} = (1/(1+10^{pH - pKa}))K_{OW} \text{ (for monoprotic acids: } AH \text{ -> } A^- + H^+) \quad \text{(A1)}$$

$$D_{OW} = (1 - 1/(1+10^{pH - pKa}))K_{OW} \text{ (for monoprotic bases: } BH^+ + OH^- \text{ -> } B + H_2O) \quad \text{(A2)}$$

Though equation A1 and A2 are explicitly for monoprotic acids and bases, they were applied to multiprotic acids as well for simplicity, using the pK_a of the most acidic proton (equation A1) or of the most acidic conjugate acid (equation A2). The minimum D_{OW} was calculated for acids at pH 9, and for conjugated acids at pH 4. For amphoteric molecules and zwitterions, which have complex dependency on pH, the minimum of the eChemPortal data, UFZ-LSER data, or Chemaxon D_{OW} predictions between a pH 4 and 9 were used as the D_{OW} value for further analysis. By comparing log K_{OC} values with log K_{OW} and log D_{OW} values for organic compounds that were neutral non-polar, neutral polar, ionizable and anionic, ionizable and cationic, and zwitterionic (see Section 2.5.2), the suitability of the log K_{OW} and log D_{OW} screening parameter of < 4.5 was tested, and further weight-of-evidence thresholds based on this data for M, vM, Potential M/vM and Not M were derived.

A.2.1 QSAR prediction of pK_a values

Table A1 compares experimental pK_a data (Arp et al., 2017; Kaljurand et al., 2013) to estimations from Chemaxon, specifically considering the most acidic proton of the substance or conjugate acid. In general, pK_a predictions match the best for substances with a single acidic proton (either acids or conjugate acids), with a match of 0.1 ± 1.1 log units (n=166). The worst agreement was for the pK_a of amphoteric substances, with an agreement of 0.9 ± 3.2 (n =265), which is attributable to the inherent complexity of their pH dependant ionization behaviour and indicates speciation predictions are the most uncertain for these substances.

Table A1. Comparison of experimental pK_a values of most acidic proton and those predicted by ChemAxon.

Ionization class	$\Delta pK_a = pK_a$ (experimental) – pKa (Chemaxon)	n
all ionizable substances	0.5 ± 2.6	521
just one proton (acid or conjugate acid)	0.1 ± 1.1	166
acids (mono and multiprotic)	0.3 ± 1.9	89
bases (mono and multiprotic)	0.0 ± 1.2	167
amphoteric substances	0.9 ± 3.2	265

A.2.2 Polarity and ionizability characterization

All substances were classified as being *neutral non-polar*, *neutral polar*, *ionizable anionic*, *ionizable cationic* and *amphoteric/zwitterionic* based on the best available SMILES notation and pK_a values. As a first point of reference, the presence of a net "+" or "-" charge(s) in the SMILES code of each identified chemical structure when expressed in a non-dative notation (e.g. expressing a nitro group as -N(=O)=O rather than dative bond notation of [N+]([O-])=O), was complied. A net "+" would indicate a cation or a substance that can ionize to a cation; a net "-" would indicate an anion or substance that can ionize to an anion; the presence of both a "+" and "-" would indicate a zwitterion or an amphoteric substance that could ionize to a zwitterion. The best available pK_a data was taken from the following data sources, in order of priority: experimental pK_a data from the peer-reviewed literature (Arp et al., 2017; Kaljurand et al., 2013), experimental pK_a data values reported on the eChemPortal database available from ECHA and the OECD (https://www.echemportal.org/echemportal/ , at reliability levels 1, 2 and 4, accessed May 28, 2020); and finally, if no experimental data was available, estimated pK_a values using ChemAxon software (https://www.chemaxon.com/, Sept. 22, 2019).

The classification of amphiprotic/zwitterionic was given if the SMILES (in non-dative form) contained both a positive and negative charge (as mentioned above), or alternatively if the structure had both an acidic proton with a $pK_a < 9.3$ (i.e. for $A\text{-}H \rightarrow A^- + H^+$) *and* a conjugate acidic proton with a $pK_a > 3.7$ (i.e. for $BH^+ + OH^- \rightarrow B + H2O$), and therefore would be amphiprotic for the ambient pH range of 4-9. Ionizable anionic or ionizable cationic were used to indicate the substance would either be ionic, or transition to an ionic form, within the pH range of 4-9. If the most acidic proton had a $pK_a < 9.3$ or the strongest conjugate base had a $pK_a > 3.7$, the substances would be classified as transitions to anion (pH 4-9) or transitions to cation (pH 4-9), respectively. As a quality control check, substances that were ionizable anionic and basic or ionizable cationic and acidic were flagged, as this is uncommon. In all cases where this occurred, it was verified to be correct, as these substances would transition from ions to zwitterions depending on pH. As an example, most instances of acidic cations were substance that had a permanently charged cationic group (e.g. a quaternary amine) in addition to an acidic moiety (e.g. a carboxylic acid) elsewhere on the molecule, which allowed them to transition from a cation to a zwitterion with increasing pH. The remaining substances were classified as neutral non-polar and neutral polar (within the pH range of 4-9), where a polar classification was given if the weight percentage of nitrogen and oxygen in the molecule was greater than 12% (Bronner and Goss, 2011a, 2011b).

A.3 Toxicity

The toxicity (T) assessment here used the criteria for toxicity based on Annex VIII of REACH. In summary these are: i) a long term no observable effect concentration (NOEC) or effect concentration at 10% (EC10) for marine or freshwater organisms is <0.01 mg/L; ii) carcinogenic categories 1A or 1B; iii) germ cell mutagenic categories 1A or 1B; iv) toxic for reproduction categories 1A, 1B or 2; and v) specific target organ toxicity after repeated exposure (STOT RE) categories 1 and 2. Additional categories (Box 4) were also included due to the additional considerations of long term exposure to the general population. The additional categories are carcinogenic category 2, cell mutagenic category 2, effects on lactation, a Derived-No-Adverse-Effect-Level (DNEL) for general population (oral, long term) <= 9 µg/kg/day, and endocrine disrupting properties (Neumann and Schliebner, 2019). NOEC/EC10 data was obtained from the EnviroTox database version 1 (https://envirotoxdatabase.org/, accessed September 7'th 2020). Data for the hazard categories, including Endocrine Disruption, were acquired from the ECHA website's advanced search for chemicals (https://echa.europa.eu/advanced-search-for-chemicals, accessed May 31'st 2020 for harmonized classifications, and June 18'th 2020 for minority opinions). DNEL data was obtained from the IUCLID 6 database (https://iuclid6.echa.europa.eu/de/reach-study-results, last accessed January, 2018). Additional endocrine disruption data was obtained from the CHEMSec SINList of endocrine disrupters (https://sinlist.chemsec.org/, accessed May 30'th, 2020). Further a list of suspected endocrine disruptors was obtained from the 2014 Pro S.P.(Arp and Hale, 2019) list mentioned above. If none of the listed toxicity criteria were met, a Cramer Class assessment was conducted using QSAR Toolbox (conducted May 29. 2020), with Cramer Class III being considered "Potential T". In case a Cramer Class III did not occur, the substance was assumed to be "Not T".