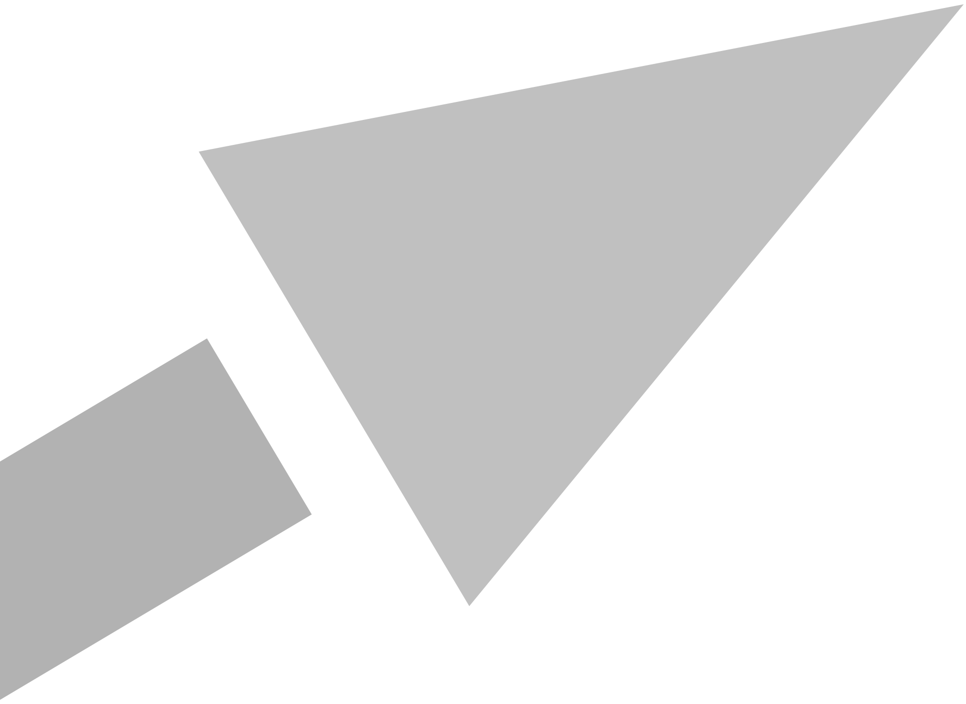
# Persistent chemicals and water resources protection

Technical Report No. 139

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS



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## Technical Report No. 139

Brussels, May 2021

ISSN-2079-1526-139 (online)

## ECETOC Technical Report No. 139

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## *Contents*

# SUMMARY

In order to protect European Union (EU) drinking water resources from chemical contamination, the German Environmental Agency (UBA) has proposed criteria for identifying persistent, mobile and toxic (PMT) substances and very persistent and very mobile (vPvM) substances under the EU REACH Regulation ((Registration, Evaluation, Authorisation and Restriction of Chemicals; (EC) No 1907/2006) (Neumann and Schliebner, 2019).

This report evaluates the scientific basis of the property-based PMT/vPvM criteria, discusses the theoretical concepts which dictate why chemicals may migrate into groundwater and examines the chemical monitoring data in the natural environment. The report is the outcome of an ECETOC Task Force which was established to review the available scientific tools, knowledge and explore options to protect the sources of our drinking water. The Task Force has developed the UBA proposal into a tiered approach and has identified a number of research topics that would improve the reliability of the tools when used for assessing chemical risks for humans via drinking water.

The review of existing EU legislation concludes that several water policies in the EU, such as the Water Framework Directive, the Groundwater Directive and the Drinking Water Directive, aim for the protection of surface, ground, bathing and drinking water. These regulations also include the protection of aquatic ecology and habitats. A better harmonisation between different water policy legislations, especially between the Water Framework Directive and Drinking Water Directive, would be beneficial to ensure drinking water quality. EU chemical regulations for plant protection products, biocides, medicinal products and for industrial chemicals (i.e., registered under REACH) already cover, to a certain extent, groundwater exposure and/or risks to humans via consumption of drinking water, as part of the required risk assessment. These existing chemical regulations could provide opportunities to improve the risk assessment for humans via drinking water. In a monitoring data analysis summarised by Neumann and Schliebner (2019), REACH registered substances comprised 46% of the total drinking water contaminants detected and 40% of the 187 total groundwater contaminants detected. This may highlight a need for a more harmonised regulatory approach.

A joint consideration of degradation rates and ability to cross natural barriers (sediment, soil) is desirable to make a scientifically sound prediction of whether a chemical can reach drinking water sources or not. In addition, an assessment of the quantity of the chemical emitted to the environment should be made, taking into account the compartment to which a substance is initially introduced or predicted to reside. Furthermore, an evaluation of the M metrics concludes that the organic carbon normalised adsorption coefficient ($K_{oc}$) as a measure for mobility may be used on a screening level but should not be used for a definitive regulatory identification purpose. The $K_{oc}$ is too simplistic and does not consider the complex sorption behaviour chemicals can undergo in soils and sediments. Alternative approaches to the simplistic mobility criterion of $K_{oc}$, such as leaching indices, screening models and more sophisticated process-oriented leaching or groundwater models with appropriate scenarios should be considered in a tiered assessment.

Ionic or ionisable substances make up a significant proportion of registered substances in the EU. A statistical evaluation from 2010 showed that approximately half of the substances registered under the REACH regulation are ionisable and similar findings have been published for pharmaceuticals. For hydrophilic and ionisable chemicals, the $K_{oc}$ model is unreliable, particularly (but not exclusively) for soils with low OC contents.

Research is therefore needed to develop suitable descriptors which take into account interactions between these types of chemicals and the complex soil/sediment matrices.

A review of the various tools to predict chemical concentrations in water, developed for industrial chemicals (i.e., those registered under the REACH Regulation), biocides and plant protection products has been carried out.

A tiered approach has been developed by the Task Force. An initial Tier 0 screening level risk assessment, using tools such as the GUS (groundwater ubiquity score) index, SCI-GROW (Screening Concentration In GROund Water) and GWWL (EU Groundwater Watch List), develops the UBA proposal further to include combined degradation and mobility along with an exposure element. In higher tiers, where more refined data are required, a more sophisticated modelling approach is recommended. Tier 1: Use the EUSES (European Union System for the Evaluation of Substances) tool as a conservative approach. The tier 1 assessment may also provide information on the relevant route of exposure to be considered at higher tiers. Tiers 2 and 3: Use the FOCUS Groundwater (FOCUS GW) model to predict the transport from soil to groundwater.

However, this proposal has limitations since the transport of contaminants via bank filtration systems is addressed with a conservative approach in EUSES and is not addressed in the higher tier models. However, a European chemical industry council (Cefic) Long-range Research Initiative (LRI) project (ECO 54)[1], anticipated to start in 2021, includes in its scope the development of a model to refine screening level exposure estimates in drinking water sources by considering the fate of surface water contaminants in river bank filtration.

This report includes an analysis of several monitoring datasets against the proposed P and M criteria. A river-bank filtration analysis revealed that the ratio between chemical concentration in river and groundwater does not correlate with the n-octanol/water distribution coefficient (log $D_{ow}$ (pH 7)) for log $D_{ow}$ values <5.0. Furthermore, the frequency of non-detects was approximately the same across the log $D_{ow}$ scale. Analysis of further datasets for European groundwater and surface water was carried out, comparing concentrations against the common reporting limit for groundwater contaminants (0.1 µg/L), to characterise any trends with respect to M criteria, log $K_{oc}$ or log $D_{ow}$ (pH 7), and biodegradation. This analysis shows that ready biodegradation and log $D_{ow}$ / log $K_{oc}$ are not appropriate predictive criteria for surface water and groundwater contamination. It is suggested that tonnages, emissions, exposure patterns and routes are likely to be other major factors affecting the observed concentration of substances in groundwater.

An evaluation of existing frameworks revealed that they establish a reasonable approach to metabolites, which seems applicable for metabolites within a PMT concept. The identification and quantification of metabolites from REACH-registered substances is limited to OECD (Organisation for Economic Co-operation and Development) 307, 308 and 309 test guidelines using environmentally relevant concentrations. Expected metabolite concentrations based on measured environmental concentrations (MECs) and predicted environmental concentrations (PECs) would be in the range of 0.01 to 10 ng/L, and thus are likely to be below

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[1] LRI ECO 54: DEVELOPING A TIERED MODELING FRAMEWORK IN SUPPORT OF RISK ASSESSMENT OF CHEMICAL SUBSTANCES ASSOCIATED WITH MOBILITY CONCERNS https://cefic-lri.org/projects/eco-54-developing-a-tiered-modeling-framework-in-support-of-risk-assessment-of-chemical-substances-associated-with-mobility-concerns/

any reasonable and reliable analytical detection. In contrast to hydrophobic (lipophilic) substances, hydrophilic substances present a technical challenge since existing analytical methods are only to a limited extent amenable to these substances. Research will be required to develop tools to concentrate, separate and detect such low metabolite concentrations.

The presence of naturally occurring metabolites has been considered since they may interfere with concentrations released from man-made products and thus requires a more detailed analysis on a case-by-case basis. The impact of non-extractable residues (NER) formation on the PMT/vPvM concept was examined. NER formation is complex and may depend on the functional groups in the metabolite molecule and composition of the environmental matrix. Nonetheless, formation of NER is a significant process which limits translocation of chemical substances through soils and sediments. The 0.1 µg/L threshold for drinking water and the measured concentrations in groundwater were considered to provide a worst-case assessment which accounted for NER formation.

The proposed PMT/vPvM hazard criteria include additional criteria, beyond those already established by the PBT (persistent, bioaccumulative, toxic)/vPvB (very persistent, very bioaccumulative) assessment under the REACH Regulation ((EC) No 1907/2006), for the toxicity (T) criteria. An evaluation of the additional T criteria concluded that the existing criteria for T, as set out in Annex XIII, 1.1.3 of REACH, already fulfils the protection goal to ensure a high level of human and environmental safety. There is no scientific justification or evidence that any additional criteria over and above those set out in Annex XIII will increase protection specifically related to drinking water. Furthermore, it is proposed that any T criteria should focus on human health aspects in order to align with the protection goal of safe drinking water for humans.

# 1. INTRODUCTION

Water is a precious resource and without it, life on Earth would simply not be possible. In Europe, drinking water quality is amongst the highest level in the world (WHO, 2019; Yale Center for Environmental Law & Policy[2]).

Annual usage of freshwater within Europe (Member- and non-Member States) is approximately 140 million $m^3$ (EC, 2020a) with groundwater and surface water abstraction representing 20 and 80% of the total, respectively. These figures are open to some interpretation due to inconsistencies in annual reporting from individual countries. It is estimated that the total volume of freshwater supplied, as potable drinking water, in the EU is around 40 million $m^3$ per annum. The contribution of drinking water originating from groundwater and surface water sources is approximately equivalent, although there are broad differences between Member States (EurEau, 2017). Greater than 80% of potable water in Austria, Denmark, Hungary, Switzerland and Slovakia is sourced from groundwater, whereas Ireland, Italy, Slovenia and Norway rely on surface water for more than 80% of their drinking water requirements. The remaining (approx. 100 billion $m^3$ per annum) abstraction of freshwater is predominantly consumed for energy production (cooling water) which is entirely sourced from surface water, with agriculture using both groundwater and surface water sources for irrigation (EC, 2020a).

Whereas the quality of water has always been considered as a matter of high priority, recent awareness has been building over the availability of freshwater. Clearly, the continued supply of good quality freshwater, fit for consumption and in sufficient quantities is of major importance and concern for each and every one of us. The protection of hydrological systems and maintaining them to high environmental standards is a major priority.

Waste water treatment plants (WWTPs), and their performance, are key in the purification of influent waters prior to emission of effluent water in to the environment. Approximately 90% of households are connected to a wastewater collection and treatment system and industrial chemical plants either have their own wastewater treatment facility or are connected to a municipal plant.

Besides the treatment of water, WWTPs generate significant quantities of biosolids. The disposal of sewage sludge depends upon national policy requirements and differs markedly from one country to another. According to EUROSTAT figures (statistical office of the European Union; EC, 2020a), in 2016, of the 5.5 million tonnes of biosolids sent for disposal, approximately 40% were incinerated and about 30% applied to agricultural land. The remaining 30% of sewage sludge underwent landfill disposal and composting. The Netherlands and Switzerland do not perform any applications of biosolids to agricultural land, whereas the majority of sewage sludge production in Ireland is applied as a natural fertiliser to farmland. Application of sewage sludge to agricultural land can result in terrestrial contamination, especially when poorly degradable substances may be released from the sludge once the biosolids itself has been degraded. This exposure route

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[2] https://epi.yale.edu/epi-indicator-report/H2O

is, therefore, considered as an important scenario in our evaluation for terrestrial to groundwater leaching potential.

Furthermore, some substances are introduced directly to the environment, e.g., via plant protection products.

In order to protect EU drinking water resources from chemical contamination, the German Environmental Agency (UBA) proposed criteria for identifying persistent, mobile and toxic (PMT) substances and very persistent and very mobile (vPvM) substances under the EU REACH Regulation ((EC) No 1907/2006; EC, 2006b) (Neumann and Schliebner, 2019). Such substances are considered to pose a hazard to the sources of our drinking water. This is based on the assumption that the combination of persistence (P/vP) and mobility (M/vM) determine the ability of substances to reach drinking water sources and, when combined with toxicity (T), pose a potential risk to human health and the environment. The implication is that REACH substances could be screened for their PMT/vPvM properties to identify those that might pose a hazard in drinking water. Such substances may be subsequently subjected to further assessment or regulatory measures such as identification as a substance of very high concern (SVHC) or restriction.

ECETOC established a Task Force in January 2019 to review the available scientific tools, knowledge and explore options to protect the sources of our drinking water. This review included an evaluation of the proposed PMT/vPvM criteria, a discussion of the theoretical concept behind observations in the natural environment and consideration as to whether higher-tier approaches (e.g., exposure or risk-based approaches) would be appropriate for the protection goal of safe drinking water resources.

This report sets out the findings of this Task Force. First a review of existing legislations related to the quality of water resources is made to put the issue in to context (Chapter 2). The proposed P/vP and M/vM criteria are then evaluated in terms of relevance (Chapter 3). Chapter 4 considers the findings of the previous chapters and investigates options for applying tiered approaches to protecting the sources of our drinking water. Chapter 5 takes this evaluation further by looking at the P and M criteria in terms of available monitoring data and how the application of these cut-offs is actually reflected in practice within the complexity of the natural environment, i.e., do these threshold cut-offs capture the overall picture, or only part of it? Chapter 6 considers how and when to consider relevant metabolites in the PMT/vPvM concept in the context of protection of water sources via risk assessment. The appropriateness of the UBA proposed additional toxicity triggers are discussed in Chapter 7. Where appropriate, knowledge gaps and research needs are identified within each individual chapter. In Chapter 8 the Task Force draws conclusions and makes recommendations for further actions.

# 2. CURRENT LEGISLATION PERTAINING TO QUALITY OF WATER SOURCES

## 2.1 Summary

A combination of European environmental legislation and a long tradition of drinking water management in many European Member States, means that most people living in the EU enjoy good access to high quality drinking water, especially compared to some other regions in the world. Since the 1980s, the EU has applied rules that require stringent water safety checks. This means that urban wastewater is collected and treated, industrial emissions are in principle safely managed, the use of chemicals is approved under strict conditions and a holistic approach is taken to managing water bodies across borders.

A review of existing EU legislation related to the quality of water resources was undertaken to ascertain how these frameworks currently address the protection of drinking water and groundwater, the latter being a major source of public drinking water supplies in many regions. The legislation can be divided into two groups:

i) water directives such as the Water Framework Directive, the Groundwater Directive, the Drinking Water Directive and the Urban Waste Water Treatment Directive that aim to protect all water bodies including surface, ground, bathing and drinking water, and

ii) chemical regulations that aim for the safe use of chemicals. The Sewage Sludge Directive is also relevant as it regulates the use of sewage sludge as a fertiliser to prevent the quality of the soil and of the surface water and groundwater being impaired. These EU frameworks provide both reactive and prospective measures to protect water resources.

The water directives are designed to control and monitor legacy pollutants and substances currently in use. They offer a holistic approach with a) an integrated framework for the management of surface water, groundwater and drinking water at a European level and b) the identification of priority substances from a wide range of chemical types (e.g., industrial chemicals, plant protection products, biocides, veterinary and human medicines). They are living directives and the list of priority substances and watch lists are intended to be updated on a regular basis. There are programmes in place to review and improve the approaches used as science advances. Further, a revision to the Drinking Water Directive has recently been proposed in order to upgrade drinking water standards in line with the latest World Health Organisation (WHO) recommendations (EC, 2018a). The Urban Waste Water Treatment Directive and Sewage Sludge Directive are also subject to potential revision to take into account new technical advances in treatment techniques for waste and emerging pollutants and to exploit the potential that the waste water treatment sector can contribute to the circular economy agenda (EC, 2020c). EU Chemical regulations already cover, to a certain extent, groundwater and/or risks to humans via consumption of drinking water as part of the required risk assessment. These existing chemical regulations could provide opportunities to improve the risk assessment for humans via drinking water. Such a risk-based approach would be in keeping with the frameworks for setting drinking water standards. The WHO guideline values represent the concentration of a chemical constituent that does not result in any significant risk to human health over a lifetime of consumption.

Outside of the EU, other nations have addressed the supply of safe drinking water, for example legal limits for contaminants have been set by the US EPA in the US Safe Drinking Water Act (SDWA) to reflect a level that protects human health and that water suppliers can achieve using best available technology.

## 2.2 Introduction

This chapter provides a review of existing legislation related to the quality of water resources. The focus is on EU regulations but reference to national implementation or comparisons with equivalent regulations in other parts of the world are included where appropriate. It covers water policies designed to protect water resources, such as the Water Framework Directive, the Groundwater Directive, the Drinking Water Directive and Urban Waste Water Treatment Directive, with particular emphasis on the control and monitoring of chemical contaminants. The Sewage Sludge Directive has also been included since the reuse of sludge for agricultural purposes is a potential exposure pathway for chemicals to soil and groundwater, as well as surface water.

Chemical regulations and their respective environmental risk assessment procedures have also been reviewed, paying special attention to any risk evaluation for human health via drinking water and/or the protection of groundwater, which is the most sensitive and the largest body of freshwater in the European Union and a main source of public drinking water supplies in many regions. The EU chemical regulations reviewed include plant protection products, biocides, medicinal products (human and veterinary) and REACH.

As a reservoir for Europe, Switzerland has vast water resources. Its hydrological network is shared between the basins of five European rivers: the Rhine, the Rhone, the Po, the Danube and the Adige. Switzerland’s hydrological network feeds the North Sea, the Mediterranean Sea, the Adriatic Sea and the Black Sea. Even though Switzerland is not a member of the European Union, a review of its water protection legislation was considered within the scope for this chapter.

The WHO guidelines for drinking water quality (GDWQ) have also been included. Although not a legislative framework, the standards recommended by the WHO are used as the basis for drinking water standard setting world-wide, including the EU Drinking Water Directive, for calculating maximum tolerable concentrations and for the identification of priority substances.

## 2.3 Water policies

### 2.3.1 EU Water Framework Directive

The EU Water Framework Directive (WFD) 2000/60/EC (EC, 2000) was introduced in the year 2000 to succeed and replace traditional management practices that previously acted in isolation. One of the innovations of the Directive was that it provided a framework for integrated management of groundwater and surface water for the first time at a European level. It committed European Union Member States to reach ‘good status’ objectives for all water bodies by 2015. Member States that took advantage of an extension beyond 2015 are required to achieve all WFD environmental objectives by the end of the second and third six-year management cycles, which extend from 2015 to 2021 and 2021 to 2027, respectively (Voulvoulis *et al.*, 2017). The major aim of the WFD is to reach good water quality status (including chemical quality) by 2027 at the latest.

The framework for delivering the Directive is through River Basin Management Planning. Each Member State is required to establish river basin management plans (RBMP), which are overseen by a competent authority. Each river basin district is split into small management units, Water Bodies. The surface water bodies may be rivers, lakes, estuary or coastal. The progress towards delivery of the objectives is reported on by the relevant competent authorities at the end of each six-year River Basin Planning cycle.

The key water protection objectives at European level are general protection of the aquatic ecology, specific protection of unique and valuable habitats, protection of drinking water resources, and protection of bathing water. All these objectives must be integrated for each river basin. It is clear that the last three protection objectives – special habitats, drinking water areas and bathing water – apply only to specific bodies of water, i.e., those supporting special wetlands, those identified for drinking water abstraction, and those generally used as bathing areas, respectively. In contrast, ecological protection should apply to all waters: the central requirement of the treaty is that the environment be protected to a high level in its entirety.

The WFD monitoring program aims at collecting data for a status assessment and at controlling the efficiency of water protection measures applied. The water quality status is expressed in terms of five classes (high, good, moderate, poor or bad). There are two elements ‘ecological status’ and ‘chemical status’. Good ecological status is defined in Annex V of the Water Framework Directive and is made up of three groups of quality elements: biological, and two supporting ones, hydromorphological and physico-chemical. The ‘ecologic status’ is not discussed further here since the topic of this report concerns persistent chemicals and water resource protection. More pertinent is the approach to good ‘chemical status’. This is defined in terms of compliance with European environmental quality standards (EQS) for priority substances (PS). EQS values for annual average (AA) or maximum allowable concentrations (MAC) have been derived to protect against long-term exposure or short-term peak concentrations, respectively, and are listed in Annex I of Directive 2008/105/EC (EC, 2008a) on EQS in the field of water policy. The EQS are the environmental threshold concentrations in water, sediment or biota that should not be exceeded in order to protect human health and the environment.

According to article 16 (2) of the WFD, priority substances (PS) are substances identified as posing a significant risk to or via the aquatic environment at EU level. As it stands, the list of PSs in Annex I of Directive 2013/39/EU (as regards priority substances in the field of water policy; replacing former Annex 10 of the WFD; EC, 2013a) contains a total of 45 PSs or PS groups, with 21 classified as priority hazardous substances (PHS) i.e. the PSs that are persistent, toxic and liable to bioaccumulate, or that give rise to an equivalent level of concern (Carvalho *et al.*, 2016a). Member States should take measures to progressively reduce the pollution from PSs and to cease or phase-out discharges, emissions and losses of PHSs (Directive 2000/60/EC).

Under Article 16 (4) of the WFD, later amended by Directive 2013/39/EU, the Commission is required to review the list of substances designated as PS and PHS every six years. Each review comprises an assessment of existing PS and PHS, and also a review of candidate substances for consideration as new PS. The latest review is detailed in the European Commission Joint Research Centre (JRC) report ‘Monitoring-based Exercise: Second Review of the Priority Substances List under the Water Framework Directive’ (Carvalho *et al.*, 2016a). The prioritisation approach in general followed the approach used in the first review using both monitoring- and modelling-based exercises to provide a rank of the substances based on their estimated risk at EU level, by comparing environmental concentrations (measured or estimated) with the substance's PNEC (predicted no-effect concentration) or Environmental Quality Standard (EQS). However, monitoring data-rich substances were evaluated in the monitoring-based exercise, by a new approach that considers the inherent variability of measurements in the monitoring dataset and evaluates the spatial, temporal and extent of PNEC or EQS exceedances (termed 'STE approach'). The spatial frequency of exceedance contains a country factor that is particularly relevant since prioritised substances under the WFD should be selected amongst those that pose the highest risk at the European level, while substances whose risk may be limited to defined countries or water bodies may be regulated by other means, such as under 'river-basin specific pollutants' (RBSPs). In contrast, the first review of 2009 only considered the number of countries monitoring the substance as a criterion for the selection of a manageable list, i.e., only substances monitored by four countries or more were submitted to the prioritisation process.

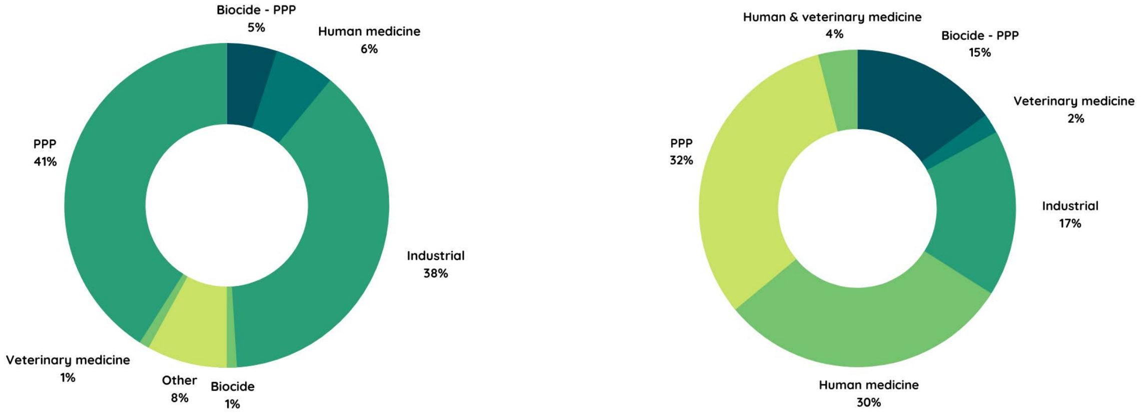

***Figure 2.1: Pie charts showing the distribution of the substances which went through the monitoring exercise (left hand side, 326 substances) and modelling exercise (right hand side, 53 substances) for the selection of the list of potential candidate priority substances in the latest review [Source: Adapted, with permission, from Carvalho et al., 2016b].***

The highest ranked substances identified by the two prioritisation exercises are further scrutinised and discussed as potential candidates for addition to the surface water watch list (WL) and/or for EQS derivation. The surface water watch list (WL) under the WFD is a mechanism for obtaining high-quality Union-wide monitoring data on potential water pollutants for the purpose of determining the risk they pose and thus whether the EQS should be set for them at EU level. According to the EQS Directive (2008/105/EC; article 8b), this list should be updated every 2 years. The first and second watch list has recently been reviewed and recommendations made for the second watch list (Loos *et al.*, 2018).

EQSs should protect freshwater and marine ecosystems from possible adverse effects of chemicals as well as human health via drinking water or ingestion of food originating from aquatic environments. As part of the JRC review process (Carvalho *et al.*, 2016a), quality standards for water abstracted for drinking water ($QS_{dw,\,hh}$) were preferably derived from WHO or EU drinking water standards. When no value was available, a precautionary value of 0.1 µg/L was used for pesticides, according to the Drinking Water Directive (98/83/EC; EC, 1998), unless existing evidence supported the derivation of a new $QS_{dw,\,hh}$ for effects on human health from drinking water following the Technical Guidance for Deriving Environment Quality Standards (TGD-EQS) (EC, 2018b).

The European Commission (EC) acknowledges the need to review the approach to the current listing of PSs under the WFD and to the current assessment of the chemical status, and to consider eventually a wider range of chemical substances that could be covered in future monitoring programmes (Napierska *et al.*, 2018). Some of the substances in the current list of PSs and in the watch list (WL) are considered in groups (e.g., brominated diphenylethers, neonicotinoid insecticides), but the overall approach to chemical pollution is otherwise based on the regulation of single substances (e.g., plant protection product active substances, REACH-registered substances etc.). The Commission also acknowledges the need to consider the potential toxic effects of mixtures of chemicals and the risks from the vast number of chemical substances present in the environment, including their metabolites and transformation products (Napierska *et al.*, 2018). The challenge is to find a way to capture a more holistic picture of the chemical status of water bodies to reflect the cumulative or combined risk. One approach proposed is a battery of bioassays that could be used to assess the chemical status of water environments more holistically (rather than with a limited but ever-growing list of individual EQS), and to try to overcome analytical difficulties and reduce monitoring costs (Napierska *et al.*, 2018). Future development needs of the WFD have recently been published and include recommendations to enhance WFD monitoring and assessment systems, improve programmes of measures and further integrate with other sectorial policies, in particular agriculture (Carvalho *et al.*, 2019a).

### 2.3.2 EU Ground Water Directive

The Groundwater Directive (GWD) 2006/118/EC (EC, 2006a) has been developed in response to the requirements of Article 17 of the Water Framework Directive. Groundwater is the most sensitive and the largest body of freshwater in the EU and is the main source of public drinking water supplies in many regions. The main objective of the GWD is to protect groundwater from deterioration and chemical pollution. Groundwater used for the abstraction of drinking water or intended for such future use must be protected in such a way that deterioration in the quality of such bodies of water is avoided in order to reduce the level of purification treatment required in the production of drinking water. In order to protect the environment as a whole, and human health in particular, detrimental concentrations of harmful pollutants in groundwater must be avoided, prevented or reduced.

There are different pieces of legislation linked to the Water Framework Directive and the Groundwater Directive, which seek to prevent or limit pollutants reaching groundwater. These are listed below:

- The Nitrates Directive (91/676/EEC; EC 1991a) aims to reduce and prevent water pollution caused by nitrates from agricultural sources.
- The Urban Waste Water Treatment Directive (91/271/EEC; EC 1991b) aims to protect the environment from the adverse effects of discharges of urban wastewater and wastewater from certain industrial sectors.
- The Plant Protection Products Regulation (EC 1107/2009 (EC, 2009), formerly Directive 91/414/EEC) concerns the authorisation, placing on the market, use and control within the European Union of active substances and their commercial plant protection products. Regarding groundwater, authorisation is only granted if plant protection products have no harmful effect on human health or on groundwater and do not have undesirable effects on the environment, particularly on the

contamination of water, including drinking water and groundwater (see Section 2.4.1 for more details).

- The Biocidal Products Regulation (EC 528/2012 (EC, 2012), formerly Directive 98/8/EC) deals with the authorisation and the placing on the market of biocidal products. Like the Plant Protection Products Regulation, the authorisation of biocidal products may only be granted if the products have no harmful effect on human health or groundwater and do not have undesirable effects on the environment, particularly on the contamination of water such as drinking and groundwater (see Section 2.4.2 for more details).
- The Integrated Pollution Prevention and Control (IPPC) Directive (2008/1/EC (EC, 2008b), formerly Directive 96/61/EC) lays down measures designed to prevent or reduce air, water or soil pollution. It establishes provisions for issuing permits for existing and new installations of industrial activities with a high pollution potential (e.g., the energy sector, production and processing of metals, the mineral and chemical industries, waste management facilities, food production) and non-industrial activities such as livestock farming. The permits include requirements to ensure the protection of soil and groundwater and set emission limits for pollutants. The Industrial Emissions Directive 2010/75/EU (EC, 2010a) replaced the IPPC Directive as of 7 January 2014.
- The Landfill Directive (1999/31/EC; EC, 1999) seeks to prevent or reduce the negative effects of landfill waste on the environment, including groundwater. Like the IPPC Directive, the directive establishes provisions for issuing permits based on a range of conditions including impact assessment studies. For each site the groundwater, geological, and hydrogeological conditions in the area must be identified.

The GWD establishes EU-wide groundwater quality standards for two types of pollutants, nitrates (50 mg/L) and pesticides (0.1 µg/L in pesticides[3] (a total of 0.5 µg/L for the sum of all individual pesticides detected), including their relevant metabolites, degradation and reaction products). Regarding other pollutants, the establishment of numerical values at Community level has not been considered a viable option, due to the high natural variability of substances in groundwater (depending upon hydrogeological conditions, background levels, pollutant pathways, and interactions with different environmental compartments). Consequently, the GWD requests Member States to establish their own groundwater quality standards (EC, 2010b). Guidelines for establishing these threshold values are provided in Annex II of the GWD. Member States need to take into account at least the list of pollutants/indicators in Annex II Part B. Threshold values should be determined based on the extent of interactions between groundwater and associated aquatic and dependent terrestrial ecosystems, the interference with actual or potential legitimate uses or functions of groundwater and the hydro-geological characteristics including information on background levels and water balance. Depending on which basis they are set, there are different types of threshold values for e.g., protecting drinking water use, protecting aquatic and/or terrestrial ecosystems and handling saltwater intrusion. The guidelines for the determination of threshold values also take account of the origins of the pollutants, their possible natural occurrence, their toxicology and dispersion tendency, their persistence and their bioaccumulation potential.

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[3] 'Pesticides' means plant protection products and biocidal products as defined in Article 2 of Directive 91/414/EEC and in Article 2 of Directive 98/8/EC, respectively (EC, 2006a)

Under this directive the Member States are required to publish a list of substances that they consider to be hazardous on the basis of their intrinsic properties. Hazardous substances must be prevented from entering groundwater. Member State agencies are responsible for monitoring, assessing and managing risks to groundwater resources. Article 8 of the WFD requires the establishment of programmes of monitoring for groundwater. The primary focus is to provide information that can be used to assess the environmental status of the groundwater bodies. The monitoring programmes must include monitoring networks to assess groundwater quality, groundwater levels and flows, and appropriate monitoring to support the achievement of the protected area objectives e.g., for use as drinking water. Monitoring point source activities should assess the effectiveness of programmes of measures (POM) introduced to prevent or limit the inputs of pollutants and/or deterioration of the status of groundwater. Laboratory limits of quantification for the hazardous pollutants are established and, as mentioned previously, threshold values set. These are the concentrations in groundwater below which the danger of deterioration in the quality of the receiving groundwater is avoided.

The development of a prioritised watch list for groundwater by the European Commission’s Common Implementation Strategy Working Group Groundwater (CIS WG GW) is discussed in Section 3.4.1.

### 2.3.3 EU Drinking Water Directive

The objective of the Drinking Water Directive (DWD) (98/83/EC) (EC, 1998) is to protect human health from adverse effects of any contamination of water intended for human consumption. It applies to all distribution systems serving more than 50 people or supplying more than ten cubic meters per day, drinking water from tankers, drinking water in bottles and containers, and water used in food processing. The directive lays down the essential quality standards at EU level. A total of forty-eight microbial, chemical and indicator parameters must be monitored and tested regularly. In general, WHO guidelines for drinking water and the opinion of the European Commission’s Scientific Advisory Committee are used as the scientific basis for the quality standards in the drinking water. When translating the DWD into their own national legislation, Member States can include additional requirements e.g., regulate additional substances that are relevant within their territory or set higher standards. Drinking water quality has to be reported to the European Commission every three years. The Commission assesses the results of water quality monitoring against the standards in the Drinking Water Directive and after each reporting cycle produces a synthesis report, which summarises the quality of drinking water and its improvement at a European level.

The European Commission performed a regulatory fitness and performance (REFIT) evaluation of the DWD in response to the European Citizens' Initiative 'Right2Water' (EC, 2016). It concluded that the 20-year-old directive was fit for purpose, well implemented with overall compliance rates with the parametric values at 99% in all Member States, but that it needed updating. It was considered that the quality standards set in Annex I of the DWD might not be appropriate anymore since they had not been revised since 1998. It recommended that special attention be paid to the relevance of microbiological parameters, where ‘new’ pathogens not considered in the current DWD might present real challenges. The review also identified that an important missing link between the DWD and the WFD was that the former does not refer to the protection of water resources to be used for the abstraction of drinking water. Furthermore, the review publication by Brack *et al.* (2017) highlights that Article 7 of the WFD states that drinking water should be able to be produced with a reduced level of purification treatment required and that drinking water concerns are inadequately reflected by current prioritisation of chemicals within the WFD. The DWD defines chemical parameters for some compounds, such as pesticides and their transformation products (0.1 µg/L), which are not included in the WFD.

On 1 February 2018, the European Commission adopted a proposal for a revised DWD (EC, 2018a)**.** The main elements of the proposal are:

- Upgrade drinking water safety standards in line with latest recommendations of the World Health Organisation (WHO), including the addition of new and emerging substances and pathogens, such as *Legionella* and chlorate;
- Introduce the WHO's holistic risk-based approach to monitoring water quality, involving risk assessments from abstraction through to the point of supply ('source to tap');
- An obligation for Member States to improve access for all people and to ensure that consumers can access information about the quality of drinking water, thus encouraging use of tap water instead of bottled water;
- Contribute to the transition to a circular economy by helping EU countries manage drinking water in a resource-efficient and sustainable manner so as to reduce energy use and unnecessary water loss;
- Empower authorities to better deal with risks to water supply and engage with polluters.

The European Parliament proposed amendments to this Commission proposal at its plenary on 23 October 2018. The Parliament maintained most of the parameters set by the Commission, which are in some cases stricter than those recommended by the WHO. The maximum limit for certain pollutants, such as lead as well as per- and polyfluoroalkyl substances (PFAS), would be tightened and new caps introduced for the endocrine disruptors Bisphenol A and 17-β-estradiol. Levels of microplastics would be monitored. Member States should encourage provision of tap water in restaurants for free or a low service fee. By the end of 2022, Member States would be required to adopt national targets to reduce water leakage levels of water suppliers (Dantin & Hansen, 2019). Parliament concluded its first reading at the second plenary in March 2019 and in September 2019 the Committee on Environment, Public Health and Food Safety (ENVI) decided to open inter-institutional negotiations. Trialogue negotiations between the two EU co-legislators – EU Parliament and EU Council – as well as the European Commission were still ongoing (CEEP, 2019) at the time of writing this ECETOC report.[4]

### 2.3.4 EU Urban Waste Water Treatment Directive and Sewage Sludge Directive

The Urban Waste Water Treatment Directive (UWWTD) (91/271/EEC) is a pollution-focused directive that aims to protect the environment and human health from point sources of pollution. The main action required by Member States of the UWWTD is collection and secondary treatment of waste water in urban agglomerations of at least 2000 population equivalents. It also covers the treatment and discharge of waste water from certain industrial sectors. Member States are required to designate sensitive areas, which includes surface waters that

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[4] The European Parliament formally adopted the revised drinking water directive on the 20 December 2020.

serve as catchment areas for drinking water and apply more stringent treatment. The UWWTD has recently been evaluated (EC, 2019) and the report concludes that inappropriately treated or untreated urban waste water is still one of the main reasons why EU waters fail to achieve at least good status under the Water Framework Directive. The report also suggests that more attention should be given to both existing and emerging sources of pollutants. The European Commission will now carry out an impact assessment to assess options to revise the Directive and thus address the shortcomings identified in the evaluation (EC, 2020c).

The UWWTD is also important for the implementation of the Sewage Sludge Directive (SSD) (86/278/EEC; EC, 1986), which deals with the reuse of sludge for agricultural purposes. The SSD prohibits the use of untreated sludge on agricultural land and requires that sludge should be used in such a way that account is taken of the nutrient requirements of plants and that the quality of the soil and of the surface and groundwater is not impaired. The progressive implementation of the UWWTD in all Member States is increasing the quantities of sewage sludge requiring disposal (EC, 2020c). The sludge destinations vary significantly between Member States (e.g., used in agriculture, incinerated or put in landfills). Most countries report a large share of re-use in agriculture but the share varies significantly between countries (0 – 100%). This exposure route has been considered as an important scenario in our evaluation of potential for terrestrial to groundwater leaching (see Chapter 4).

The present SSD directive sets limit values for only seven heavy metals: cadmium, copper, nickel, lead, zinc, mercury and chromium in soil as well as in sludge itself. The Commission dedicated a monitoring project (‘FATE-SEES’ on sewage sludges and effluents for emerging substances) to gather information about the presence of emerging pollutants in sewage sludge (JRC, 2012). The pan-European snapshot evaluated the concentration of 114 analytes, including minor and trace elements, polyaromatic hydrocarbons (PAHs), perfluoroalkyl substances (PFASs), pesticides, benzotriazoles, personal care products, sweeteners and pharmaceuticals. One of the main conclusions was ‘The monitored concentrations do not justify the introduction of new limit values for the considered parameters’.

In 2014, the Sewage Sludge Directive (SSD) was evaluated as part of an ‘Ex-post evaluation of certain waste stream directives’ (EC, 2014a). It was concluded that SSD has been effective in achieving its initial objectives, by increasing the amount of sludge used in agriculture and by contributing to reducing environmental harm by ensuring that heavy metals in soil and sludge do not exceed the limits set by the Directive. Positive factors contributing to progress include stricter limit values set by Member States while negative factors holding back progress include negative perceptions of sludge amongst stakeholders/public. Other benefits were seen to include the use of sludge in agriculture as a cheaper disposal option compared to landfill and incineration and the use of sludge as an effective replacement for chemical fertilisers, especially phosphorus. Areas where the Directive may not fully match current needs were identified and included the limited scope of the Directive (which addresses only the agricultural use of sludge) and the lack of provisions on quality assurance and adequate monitoring. The results of this evaluation will inform the Commission’s decision on the need to progress with an impact assessment for a proposal to revise the Directive, as outlined in the New Circular Economy Action Plan, adopted on 11 March 2020 (EC, 2020c).

## 2.3.5 Switzerland

### 2.3.5.1 Background

According to the Federal Office for the Environment (FOEN) the state of the water protection in Switzerland with respect to nutrients and micropollutants (trace compounds that enter water bodies through wastewater treatment plants and through diffuse inputs from sources such as agriculture) is described as follows (FOEN, 2018):

- With regard to nutrient pollution, the water quality of surface water bodies has improved significantly since the 1960s. However, despite substantial progress, the state of many surface waters is still inadequate. Small water bodies are heavily polluted by nutrients and plant protection products from agricultural use, while medium-sized and large water bodies contain micropollutants from households and industry as well.

- The problem of inputs of micropollutants into water bodies has been acknowledged. The implementation of micropollutant elimination measures began in 2016. According to the criteria established in the Waters Protection Ordinance, the cantons determine which wastewater treatment plants (WWTPs) are to be expanded and then carry out the measures. If an additional treatment phase is added to around 100 specially selected WWTPs in future, micropollutants can be removed from almost two thirds of all wastewater. The necessary investments are financed by a Switzerland-wide wastewater charge.

- The state of groundwater in Switzerland is still good enough to be able to obtain sufficient quantities of clean drinking water from groundwater sources. However, pollutants have been recorded in the groundwater at numerous monitoring stations of the National Groundwater Quality Monitoring Network (NAQUA), especially in intensively farmed regions. Groundwater is most severely affected by nitrate. Furthermore, residues of artificial, sometimes persistent, substances such as substances from the degradation of plant protection products have been detected in the groundwater at more than half the NAQUA monitoring stations. Even though these substances are largely within the limits of the Waters Protection Ordinance (WPO), they are considered generally undesirable in groundwater.

### 2.3.5.2 Waters Protection Act

The purpose of the Federal Act on the Protection of Waters (WPA) (FASC (Federal Assembly of the Swiss Confederation), 2020) is to protect waters against harmful effects. In particular it aims:

a. to preserve the health of people, animals and plants;
b. to guarantee the supply and economic use of drinking water and water required for other purposes;
c. to preserve the natural habitats of indigenous fauna and flora;
d. to preserve waters suitable as a habitat for fish;
e. to preserve waters as an element of the landscape;

f. to ensure the irrigation of agricultural land;
g. to permit the use of waters for leisure purposes;
h. to ensure the natural functioning of the hydrological cycle.

The WPA applies to all surface and underground waters.

According to Article 6 of the WPA (Maintaining the quality of waters) it is prohibited to introduce into a body of water, either directly or indirectly any substances which may pollute it; the infiltration of such substances is also prohibited. It is also prohibited to store or spread such substances outside a body of water if there is a genuine risk of water pollution.

According to Article 9 of the WPA (Federal Council regulations on the discharge and infiltration of substances) the Federal Council shall specify the water quality requirements for surface and underground waters. It shall enact regulations on:

a. the discharge of waste water into bodies of water;
b. the infiltration of waste water;
c. substances which may according to the method of their use enter into water and which, by reason of their properties or the quantities used, risk polluting waters or impairing the operation of wastewater treatment plants.

According to Article 27 of the WPA (Soil use) soils shall be used according to the state of the art, in such a way that waters are not adversely affected in any way, in particular avoiding both washing away and leaching of fertilisers and plant protection products.

#### 2.3.5.3 Waters Protection Ordinance

The Waters Protection Ordinance (WPO) (SFC (Swiss Federal Council), 2018) shall facilitate the protection of surface and underground waters from harmful effects and enable their sustainable use. For this purpose, all measures taken under this Ordinance must take into account the ecological goals for waters as formulated in Annex 1 of the WPO. For underground waters, the following ecological goals apply:

1. The biotic community of underground waters shall:
    a. be close to nature and appropriate to the location;
    b. be specific to unpolluted or only slightly polluted waters.
2. The aquifer (flow section, permeability), the upper and lower confining beds and the hydro-dynamism of the groundwater (groundwater levels, flow regime) should correspond to near natural conditions. In particular, the self-cleaning processes and the interactions between water and its surroundings should be guaranteed unreservedly.
3. The groundwater quality shall be such that:

a. the temperature conditions are near natural;
b. the water contains no persistent synthetic substances;
c. other potential water pollutants which could enter the water as a result of human activities:
    - do not accumulate in the biotic community or in the inert matter of the aquifer,
    - occur in concentrations that are within the range of natural concentrations where these are already present in natural state groundwater,
    - do not occur in groundwater where they are not present naturally
    - have no harmful effects on the use of the groundwater.

The requirements for groundwater which is used for drinking water or is intended as such are specified in Annex 2 of the WPO:

1. The water quality must be such that after the use of basic water conditioning, it complies with the requirements of the foodstuffs legislation.
2. The following numerical requirements apply (Table 2.1), subject to the particular natural circumstances. For substances originating from polluted sites, these requirements do not apply in the downstream area where the greater part of these substances is degraded or retained.

***Table 2.1: Numerical requirements for groundwater which is used for drinking water or is intended as such (Swiss Waters Protection Ordinance (WPO) (SFC, 2018))***

| No. | Parameter | Requirement |
|---|---|---|
| 1 | Dissolved organic carbon (DOC) | 2 mg/L C |
| 2 | Ammonium (sum of $NH_4^+$-N and $NH_3$-N) | In oxic conditions: 0.08 mg/L N<br>(corresponds to 0.1 mg/L ammonium)<br>In anoxic conditions: 0.4 mg/L N<br>(corresponds to 0.5 mg/L ammonium) |
| 3 | Nitrate ($NO_3^-$-N) | 5.6 mg/L N (corresponds to 25 mg/L nitrate) |
| 4 | Sulphate ($SO_4^{2-}$) | 40 mg/L |
| 5 | Chloride ($Cl^-$) | 40 mg/L |
| 6 | Aliphatic hydrocarbons | 0.001 mg/L per single substance |
| 7 | Monocyclic aromatic hydrocarbons | 0.001 mg/L per single substance |
| 8 | Polycyclic aromatic hydrocarbons (PAH) | 0.1 µg/L per single substance |
| 9 | Volatile organic halogens (VOX) | 0.001 mg/L per single substance |
| 10 | Adsorbable organic halogens (AOX) | 0.01 mg/L X |
| 11 | Organic pesticides (biocidal products and plant protection products) | 0.1 µg/L per single substance |

### 2.3.6 WHO Guidelines for drinking water quality (GDWQ)

Very few water standards have any legal basis or are subject to enforcement. Two exceptions are the European Drinking Water Directive and the Safe Drinking Water Act in the United States, which require legal compliance with specific standards. For countries without a legislative or administrative framework for such standards, the World Health Organization (WHO) publishes guidelines on the standards that should be achieved (WHO, 2017). According to the guidelines, the great majority of evident water-related health problems are the result of microbial (bacterial, viral, protozoan or other biological) contamination. The health concerns associated with chemical constituents of drinking water differ in that they arise primarily from the ability of chemical constituents to cause adverse health effects after prolonged periods of exposure. There are few chemical constituents of water that can lead to health problems resulting from a single exposure, except through massive accidental contamination of a drinking water supply. Moreover, experience shows that in many, but not all, such incidents, the water becomes undrinkable owing to unacceptable taste, odour and appearance.

The WHO uses an approach based on a risk assessment concept to develop guideline values for water quality. A guideline value (GV) normally represents the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption. A number of provisional guideline values have been established based on the practical level of treatment performance or analytical achievability. For many chemicals, no formal guideline value is proposed on the grounds that occurrence is only at concentrations well below those that would be of concern for health.

In order for a particular chemical constituent to be evaluated to determine whether a guideline value or health-based value should be derived, one of the following criteria must be satisfied:

- There is credible evidence of occurrence of the chemical in drinking water, combined with evidence of actual or potential toxicity
- The chemical is of significant international concern
- The chemical is being considered for inclusion or is included in the WHO Pesticide Evaluation Scheme (WHOPES), which coordinates the testing and evaluation of pesticides for public health, including those applied directly to drinking water for control of insect vectors of disease

Two approaches to the derivation of guideline values are used, one for ‘threshold chemicals’ and the other for ‘non-threshold chemicals’ (mostly genotoxic carcinogens). For ‘threshold chemicals’ there is a dose below which no adverse effect will occur. For such chemicals a tolerable daily intake (TDI) is derived using the most sensitive end-point in the most relevant study and applying an uncertainty factor / chemical-specific adjustment factor. As TDIs are regarded as representing a tolerable intake for a lifetime, they are not so precise that they cannot be exceeded for short periods of time. Short-term exposure to levels exceeding the TDI is not a cause for concern, provided the individual’s intake averaged over longer periods of time does not appreciably exceed the level set. The large uncertainty factors generally involved in establishing a TDI serve to provide assurance that exposure exceeding the TDI for short periods is unlikely to have any deleterious effects upon health. The guideline value (GV) is then derived from the TDI (see Section 4.3 for calculation).

In the case of compounds considered to be genotoxic carcinogens (i.e., non-threshold chemicals), guideline values are normally determined using a mathematical model. Guideline values are conservatively presented as the concentrations in drinking water associated with an estimated upper-bound excess lifetime cancer risk of $10^{-5}$ (or one additional case of cancer per 100 000 of the population ingesting drinking water containing the substance at the guideline value for 70 years). This value does not equate to the number of cases of cancer that will be caused by exposure to the substance at this level. It is the maximum potential risk, taking into account large uncertainties. It is highly probable that the actual level of risk is less than this.

The scientific basis for each guideline value is summarised in Chapter 12 of the guidelines (WHO, 2017). This information is important in helping to adapt guideline values to suit national requirements or for assessing the health significance of a contaminant that is of a higher concentration than the guideline value. Detailed chemical reviews are available at https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/en/.

The WHO Guidelines for Drinking water quality (GDWQ) are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking water are subject to periodic review, and documentation related to aspects of protection and control of public drinking water quality is accordingly prepared or updated.

### 2.3.7 United States Safe Drinking Water Act

The Safe Drinking Water Act (SDWA) was established in 1974 to protect the quality of drinking water in the United States. This law focuses on all waters actually or potentially intended for drinking use, whether from above ground or underground sources. The 1996 amendments to SDWA require that the US Environmental

Protection Agency (US EPA) consider a detailed risk and cost assessment, and best available peer-reviewed science, when developing these standards. Currently, the EPA has set legal limits on over 90 contaminants in drinking water. The legal limit, referred to as the maximum contaminant level (MCL), reflects the level that protects human health and that water systems can achieve using best available technology. The MCL weighs the technical and financial barriers with public health protection. EPA sets MCLs as close as possible to the health goal, which is known as the Maximum Contaminant Level Goal (MCLG). The MCLG is the maximum level of a contaminant in drinking water at which no known or anticipated adverse effect on the health of persons would occur over a lifetime and which allows for an adequate safety of margin. For known cancer-causing contaminants the MCLG is set at zero. This is because any chemical exposure could present a cancer risk. MCLGs are not enforceable.

EPA works with states, tribes, and many other partners to implement these SDWA provisions. The SDWA gives individual states the opportunity to set and enforce their own drinking water standards if they are at least as stringent as EPA's national standards. A detailed review of the SDWA has not been carried out here as the focus of this report is the protection of water resources in the EU. However, it was considered appropriate to include a reference to this regulation given that the US and EU are the only two regions worldwide that have imposed legal requirements related to drinking water standards. Further details including regulated contaminants, candidate lists and the process for developing and reviewing standards are available at https://www.epa.gov/dwstandardsregulations.

## 2.4 Chemical regulations

### 2.4.1 Plant protection products

In the European Union, placing a plant protection product on the market is regulated by Regulation (EC) No. 1107/2009 (EC, 2009) and its associated implementing Regulations ((EU) No. 546/2011 on uniform principles (EC, 2011), plus (EU) No. 283/2013 (EC, 2013b) and (EU) No. 284/2013 (EC, 2013c) on data requirements). Regulation 1107/2009 includes a specific protection goal for groundwater resources. Specifically, an active substance will only be approved where it has been established that the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater is not expected to exceed the lower of (i) the maximum permissible concentration laid down by the Drinking Water Directive (DWD) 98/83/EC; or (ii) the maximum concentration laid down when approving the active substance in accordance with Regulation (EC) No 1107/2009. This is based on the appropriate data, in particular toxicological data, or, where that concentration has not been laid down, the concentration corresponding to one tenth of the acceptable daily intake (ADI) laid down when the active substance was approved in accordance with Regulation (EC) No 1107/2009. The maximum parametric values set for ‘pesticides’ and ‘total pesticides’ in Annex 1, Part B of Directive 98/83/EC (the DWD; EC, 1998) are identical to the ‘groundwater quality standards’ values set in the Groundwater Directive 2006/118/EC (EC, 2006), i.e. 0.1 µg/L. Gimsing *et al.* (2019) note that in the vast majority of the cases, the maximum permissible concentration (or groundwater quality standard or parametric value) of 0.1 µg/L (0.5 µg/L for the sum of active substances) applies. However, if a substance is expected (via modelling) to exceed this limit it may still be authorised if it can be scientifically demonstrated that under relevant field conditions the concentration is not exceeded.

Regulation (EU) No. 283/2013 (EC, 2013b) describes the data requirements for active substances. The fate and behaviour in the environment requirements mandate a tiered testing strategy of laboratory and field studies to describe routes of degradation and partitioning to different environmental compartments. Relevant metabolites are generally identified when they account for more than 10% of the active substance applied (weight by weight; w/w) in the study, or >5% at two sequential measurements or if formation is increasing (maximum not reached at the end of the study) but accounts for at least 5% at the final measurement. Subsequently the substance properties and kinetics derived from laboratory and field studies are used to parametrise groundwater models to predict whether or not the predicted environmental concentration in groundwater ($PEC_{GW;}$ annual average concentration) exceeds the quality standard for active substances and metabolites. This is achieved by the use of scenarios in the model simulations that are considered representative of EU soils and climate. If risk assessment failures for representative uses are anticipated at this lowest tier (tier 1), higher tier refinements to the assessment may be performed. At tier 2, the input parameters for the groundwater modelling (namely Disappearance time 50 ($DT_{50}$) and formation fraction) may be derived from terrestrial field degradation studies, deemed to be more environmentally relevant than studies performed under laboratory conditions. At tier 3, leaching studies may be performed to refine the understanding of the mobility and leaching potential of metabolites in soil. Experimental outdoor lysimeter studies can also be employed as a higher tier to assess mobility and leaching potential to groundwater. At the highest tiers of refinement, customised field leaching studies designed to represent realistic worst-case conditions (tier 3) or data from extensive groundwater monitoring programs (tier 4) run for a number of years and underpinned by in-depth geological characterisation of the monitoring wells, may be utilised.

In the USA, the SDWA of 1974 was originally designed to ensure the safety of drinking water supplies. It gave authority to the US EPA to develop standards for different contaminants. In 1996, an additional program was added to cover protection of surface water that is used for drinking water (the Source Water Protection Program). For pesticides the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) authorises US EPA to control the availability of pesticides that have the ability to leach into groundwater. The procedures employed are similar to those in the EU. The only major difference being that there is not a property-based cut-off (i.e., a 0.1 µg/L groundwater threshold). In the case of groundwater and surface water, risk assessment is applied to determine if any unreasonable risk to man or the environment is likely.

EPA's Office of Pesticide Programs (OPP) employs a tiered approach utilising laboratory and field studies (US EPA, 2020) with mathematical models to calculate estimated environmental concentrations. Monitoring data may also be used. At tier 1 conservative exposure estimates (sites that are highly vulnerable to runoff or leaching) are compared to (eco)toxicological information. Substances that pass this tier are considered unlikely to cause harm to human health or the environment. At the next tier more refined exposure models are employed.

It is beyond the scope of this chapter to describe the groundwater models employed. However, the models are further discussed in Chapter 4 (Section 4.5).

## 2.4.2 Biocides

In the European Union, placing a Biocidal Product on the market is regulated by The Biocidal Products Regulation (EU) 528/2012 (BPR; EC, 2012). The BPR implies that for biocides the cut-off value for pesticides in groundwater is applied (see Section 2.4.1 above). The concentration in groundwater should therefore be <0.1 µg/L for active substance, relevant metabolites or breakdown/reaction products and substances of concern. The total concentration should be <0.5 µg/L. However, similar to REACH (see below), concentrations are calculated only for indirect exposure of humans through drinking water. As an indication for potential groundwater levels, the concentration in porewater of agricultural soil is taken as a conservative estimate. A 10-year period for accumulation is assumed which can be refined if degradation data are available. If the assessment for the groundwater compartment indicates an unacceptable risk further refinement can be investigated using models developed for the assessment of pesticide mobility, reflecting, more realistic groundwater conditions, or by using measured data (lysimeter studies or monitoring data).

## 2.4.3 Pharmaceuticals

### 2.4.3.1 Medicinal products for human use

Pharmaceutical regulatory systems in EU comprise a decentralised body, the European Medicines Agency (EMA), Heads of Medicines Agencies (HMA), National Competent Authorities (NCAs) and the European Directorate for the Quality of Medicines (EDQM). The requirements and procedures are laid down in Directive 2001/83/EC (EC, 2001) on the Community code relating to medicinal products for human use and in Regulation (EC) No 726/2004 (EC, 2004) on the authorisation and supervision of medicinal products for human and veterinary use. These legal acts are supported by numerous guidelines. These guidelines are prepared by the Committee for Medicinal Products for Human Use (CHMP) in consultation with the competent authorities of the EU Member States. They provide applicants with necessary information to prepare marketing-authorisation applications for medicinal products for human use. These consider the potential environmental risk to groundwater. However, there is no explicit consideration of drinking water resources or risk evaluation for human health via drinking water.

The environmental assessment is described in the current guideline on the environmental risk assessment of medicinal products for human use – First version (EMA, 2006). Consultation has recently closed on a revised draft version (EMA, 2018). However, it is not yet defined how and when the new guideline will be published. The assessment is a step-wise, phased procedure, consisting of two phases. The first phase (Phase I) estimates the exposure of the environment to the drug substance. Based on an action limit the assessment may be terminated. In the second phase (Phase II), information about the fate and effects in the environment is obtained and assessed. However, certain substance properties (e.g., high lipophilicity and potential endocrine disruption) may need to be addressed irrespective to exposure considerations.

At phase I, screening for persistence, bioaccumulation and toxicity in line with the REACH guidance is performed. This is followed by calculation of the predicted environmental concentration (PEC) for surface water ($PEC_{SW}$). The calculations are based on a default market penetration factor ($F_{PEN}$) of 0.01 (1% of the population is treated with the respective medicine) and the maximum daily dose. $F_{PEN}$ can be refined based on prevalence data or also a specific treatment regime can be taken into account. If the $PEC_{SW}$ value is equal to or above 0.01 µg/L, then a Phase II environmental fate and effect analysis is performed. In addition, lipophilic drugs with *n*-octanol-water partition coefficient (log $K_{ow}$) >4.5 are directly moved to Phase II, Tier B, because of their bioaccumulative potential. Phase II explicitly considers an exposure assessment for groundwater.

The main exposure route to groundwater is considered via bank filtration, which is the transfer from surface water into groundwater used as drinking water resources. Contamination is considered unlikely for substances with an average $K_{oc}$ >10000 L/kg or for substances that are readily biodegradable or for substances that have a $DT_{90}$ of <3 days (EMA, 2006). It is assumed that the exposure of groundwater via sewage sludge incorporated into soil can be disregarded in view of the high sorption affinity of these active substances with $K_{oc}$ > 10000 L/kg to the soil. Where relevant, a simplistic scaling factor of surface water to groundwater (25%) is used to estimate the groundwater PEC ($PEC_{GW}$). The $PNEC_{GW}$ is based on the NOEC from a chronic toxicity test with aquatic invertebrates (typically *Daphnia magna)* (EMA, 2006). Where the ratio $PEC_{GW}$:$PNEC_{GW}$ (the Risk Characterisation Ratio) is above 1, further evaluation of the fate of the substance and relevant metabolites (≥10% of amount excreted) in the aquatic environment is required.

At the highest tier of groundwater evaluation, refinement of the risk assessment, using data on transformation of the substance within the environment (i.e., the water/sediment systems), can be used. Specifics are not described, but the proposed revised guideline (EMA, 2018) suggests specific groundwater modelling for a realistic worst case scenario using SiMBaFi, a bank filtration simulation model (Zippel *et al.*, 2010).

When the possibility of environmental risks cannot be excluded, precautionary and safety measures are taken into account. These include labelling that aims to minimise the quantity discharged into the environment by appropriate mitigation measures. Authorisation of a human medicinal product cannot be withheld on the basis of environmental issues as environmental risk is not currently considered in the risk-benefit analysis of human safety, efficacy and quality (Küster and Adler, 2014).

The environmental risk assessment (ERA) for human pharmaceuticals is only conducted in the EU, USA and Canada. A comparison of these regulatory frameworks has recently been published (Lee & Choi, 2019). The major difference between the current ERA procedures is that the EU and the USA assess products, while Canada assesses the substance. As mentioned above, in the EU the results of the ERA do not constitute a criterion for the refusal of marketing authorisation. However, failure to submit an adequate environmental assessment may constitute a reason to refuse to file or approve the application in the USA. The EU and USA evaluation systems primarily address protection of aquatic and terrestrial ecosystems and, for lipophilic drugs, consider accumulation in biota or biomagnification in the food web in the higher tier assessment. In Canada, for the evaluation of the potential for exposure to humans and the components of the environment, it is recognised that consideration should be given not only to physico-chemical properties, such as the mobility and fluidity of the substance, but also to the amount, frequency of application and condition of chemicals released to the environment. All three regions do not carry out an ERA if it is clear that the product or substance does not have any impacts on the environment. However, the criteria for conducting an ERA are different by country. For example, an ERA is not warranted when surface water PEC <0.01 µg/L in the EU, environmental introduction concentration (EIC) <1 µg/L in the USA, and surface water PEC <0.1 µg/L in Canada. Finally, a major limitation of all these regulatory frameworks is that they only address new products or substances (i.e., existing drugs are currently excluded).

### 2.4.3.2 Veterinary medicinal products

The requirement for assessment of environmental safety for veterinary medicinal products (VMPs) was introduced into the EU legislation by Directive 92/18/EC (EC, 1992) on the approximation of the laws of Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products. Since that time, data on ecotoxicity have been required as part of the safety submission for a Marketing Authorisation. The Directive stated that the environmental assessment should be carried out in two phases. In the first phase the extent of environmental exposure should be estimated while in the second phase the fate and effects of the active residue should be assessed. The basic framework provided by the Directive was elaborated by guidelines published by the Committee for Medicinal Products for Veterinary Use (CVMP) in 1997, providing guidance to both applicants and to the regulators on how the assessment of environmental safety should be carried out. The CVMP guidelines have in the meantime been replaced with VICH (Veterinary International Conference on Harmonization) guidelines: Guideline on Environmental Impact Assessment (EIA) for Veterinary Medicinal Products – Phase I, published in 2000 (EMA, 2000); and Guideline on Environmental Impact Assessment for Veterinary Medicinal Products – Phase II, published in 2004.

The guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38 (EMA/CVMP/ERA/418282/2005-Rev.1- Corr.) of 24 June 2016 addresses the leaching of VMPs into groundwater. A $PEC_{GW}$ is calculated according to REACH guidelines. However, in this model, the partitioning only depends on equilibrium sorption to solids. The $PEC_{GW}$ should be compared with the value of 0.1 µg/L and if the $PEC_{GW}$ is greater than this value then the predicted environmental concentration in soil ($PEC_{soil}$) could be refined based on metabolism data. After this, more sophisticated models for estimating the $PEC_{GW}$ should be used.

A more specific assessment of the environmental and human health risks of VMPs is provided in document EMA/CVMP/ERA/103555/2015 of 30 April 2018 (Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater). The risk to humans of VMPs in groundwater is associated with the use of groundwater as a source of drinking water. The risk assessment in this guideline is therefore based on scenarios following human consumption of drinking water derived from groundwater. In order to assess the human health risk of groundwater contamination by VMPs, it should be assumed that groundwater may be used as drinking water without further purification. Thus, a maximum tolerable concentration in drinking water ($MTC_{dw}$) (µg/L) needs to be calculated following the methodology used by the World Health Organization (WHO, 2017).

If a risk for human health is identified (groundwater risk quotient $RQ_{groundwater}$ is equal to or exceeds 1.0), risk mitigation measures have to be applied or the risk should be considered as part of the benefit/risk assessment.

## 2.4.4 REACH

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) is a European Union Regulation dating from December 2006 ((EC) No. 1907/2006) (EC, 2006b). REACH addresses the production and use of industrial chemical substances and their potential impacts on both human health and the environment. REACH requires, according to Article 14(4), exposure assessment and subsequent risk characterisation to be carried out for substances subject to registration which are manufactured or imported in quantities equal to or greater than 10 tonnes/year and where the substance meets any of the criteria to be classified as hazardous according to CLP (Classification, Labelling and Packaging) Regulation ((EC) No. 1272/2008; EC, 2008c). Substances may chemically transform during use or in the environment, e.g., by hydrolysis, biodegradation or other chemical reaction. When such transformation products (or 'degradation products' or 'metabolites') are stable and/or toxic they should be taken into account in the environmental risk assessment. Detailed explanations of environmental exposure assessment are available in the ECHA guidance on Information Requirements and Chemical Safety Assessment Chapter R16: Environmental Exposure Assessment (ECHA, 2016a).

The exposure assessment must cover any exposure that may relate to hazards identified in the hazard assessment. The environmental protection targets to be taken into account are water and sediment organisms (freshwater and marine), predators in the aquatic food chain, sewage treatment plant microorganisms, soil organisms, predators in the terrestrial food chain and air. In addition, humans exposed via the environment also need to be protected. According to ECHA guidance R.16.1.3, an assessment of indirect exposure of humans via the environment is generally only conducted if the tonnage is > 1000 t/y, or if the tonnage is > 100 t/y and the substance is classified as STOT RE 1 (specific target organ toxicity - repeat exposure), or as a carcinogen or mutagen (any category), or as toxic to reproduction (categories 1A or 1B).

Indirect exposure of humans via the environment may occur through air inhalation, food consumption (e.g., fish, leaf crops, root crops, meat and dairy products) and drinking water. Exposure via the oral route can be estimated based on the concentration of the substance in food products and drinking water, and the amount of each food consumed, and water drunk. In EUSES (European Union System for the Evaluation of Substances), a generic and very conservative 'food basket' is defined that describes the quantities and types of different food types that are consumed and their consumption rates. The EUSES 'food basket' consumption rates for individual food types are derived from the highest country-average consumption rate observed across Member States. This leads to a worst-case 'food basket'. The concentration of a substance in food is related to its concentration in water, soil and air and to its potential for bioaccumulation or transfer between compartments. Drinking water can be obtained from surface water or from groundwater sources. For the calculation of groundwater levels, several numerical models are available (mainly for pesticides). These models, however, require a characterisation of the soil on a high level of detail. This makes these models less appropriate for the initial standard assessment. Therefore, as an indication for potential groundwater levels, the concentration in porewater of agricultural soil is used. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers. Details on the calculation method are provided in Appendix A.16-3.3.7 of ECHA Chapter 16 (ECHA, 2016a).

The REACH assessment approach is further discussed in Section 4.6.

## 2.5 Conclusion

The existing legislation related to the protection of water sources has been reviewed in this chapter. The legislation can be divided into two groups; i) water directives aimed specifically at water protection and ii) chemical regulations that aim for the safe use of chemicals.

EU legislation focused on water protection include the Drinking Water Directive (DWD), the Water Framework Directive (WFD) and the Ground Water Directive (GWD). Together they cover surface, ground, bathing and drinking water and aim to protect aquatic ecology, habitats and drinking water resources as well as improve the quality of drinking water. While the DWD has been relatively well implemented, its approach to monitoring water quality at the point of consumption uses parameters determined over 20 years ago. Therefore, the European Commission has recently proposed to revise the directive in order to upgrade drinking water standards in line with the latest WHO recommendations and improve access to water for all. The coherence of the DWD with the WFD is especially important as the protection of drinking water resources is an indispensable part of the plans and measures under the WFD. An important missing link between the DWD and the WFD has been identified in that the former does not refer to the protection of water resources to be used for the abstraction of drinking water. Furthermore, Article 7 of the WFD states that drinking water should be able to be produced with a reduced level of purification treatment required.

However, drinking water concerns are inadequately reflected by current prioritisation of chemicals within the WFD. The DWD defines chemical parameters for some compounds, such as pesticides and their transformation products (0.1 µg/L), which are not included among the WFD priority substances (Brack *et al.*, 2017). The WFD is a living directive – the surface water watch list being updated in principle every two years and the list of substances designated as priority substances reviewed every six years.

The Urban Waste Water Treatment Directive (UWWTD) is a pollution focused directive that concerns the collection, treatment and discharge of urban waste water, and treatment and discharge of waste water from certain industrial sectors. The Sewage Sludge Directive (SSD) regulates the use of sewage sludge from waste water treatment plants as a fertiliser to prevent the quality of the soil and of the surface and ground water being impaired. Both directives are subject to potential revision to take into account new technical advances on treatment techniques for waste and emerging pollutants but also to exploit the potential the waste water treatment sector can contribute to the circular economy agenda (EC, 2020c).

The Swiss federal act on the Protection of Waters (WPA) applies to all surface and underground waters. The requirements for groundwater which is used for drinking water, or is intended as such, are specified in Annex 2 of the Waters Protection Ordinance (WPO).

The EU chemicals regulations reviewed include plant protection products, biocides, medicinal products (human and veterinary) and REACH (industrial chemicals). The registration of plant protection products requires the assessment and risk characterisation of the groundwater compartment. Specifically, an active substance will only be approved where it has been established that the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with a quality standard of 0.1 µg/L or the concentration corresponding to one tenth of the acceptable daily intake (ADI) based on toxicological information. The environmental impact assessment for veterinary medicinal products addresses the leaching of VMPs into groundwater and the risk to humans associated with the use of groundwater as a source of drinking water. A maximum tolerable concentration in drinking water is calculated following the methodology used by the World Health Organization. In contrast, although potential environmental risk to groundwater is considered for human pharmaceuticals there is no risk evaluation for human health via drinking water. Within the Biocide and REACH frameworks, groundwater concentrations are calculated. The assessment of man via the environment is generally only conducted under REACH if the tonnage is >1000 t/y or if the tonnage is >100 t/y and the substance is classified as STOT RE 1, or as a carcinogen or mutagen (any category), or as toxic to reproduction (categories 1A or 1B) (ECHA, 2016a).

In summary, existing EU frameworks provide reactive and prospective measures to protect water resources. The EU WFD would offer a holistic approach with an integrated framework for the management of surface water, groundwater and drinking water at a European level if the priority substances would cover all chemical types (e.g., plant protection products, biocides, veterinary and human medicines and industrial chemicals). Chemical regulations provide prospective measures covering groundwater and/or risks to humans via consumption of drinking water as part of the required risk assessment. Such a risk based approach would be in keeping with the frameworks for setting drinking water standards. The WHO guideline values represent the concentration of a chemical that does not result in any significant risk to human health over the lifetime of consumption while the legal limits for contaminants set by the US EPA in the SDWA reflect a level that protects human health and that water suppliers can achieve using best available technology.

# 3. MOBILITY AND PERSISTENCE: DETERMINANTS OF CHEMICAL LEACHING TO WATER SOURCES

## 3.1 Summary

In the UBA proposal on PMT (Neumann and Schliebner, 2019), persistence (P and vP) is assessed following the P criteria as defined in Annex XIII of the REACH Regulation (‘Criteria for identification of PBT/vPvB substances’; ECHA, 2017a). Mobility (M and vM) endpoints to identify substances likely to contaminate water sources are based on the organic carbon (OC) normalised adsorption coefficient $K_{oc}$ (L/kg). The UBA proposal on toxicity (T) has described additional criteria, beyond those already established by the PBT/vPvB assessment under the REACH Regulation ((EC) No 1907/2006; EC, 2006b). These additional toxicity proposals are discussed in Chapter 7 of this report.

M/vM and P/vP are assessed separately. Those chemicals which fulfil the UBA definition of both P/vP and M/vM are taken into consideration for PMT/vPvM categorisation. This approach may produce false positives due to the unrefined proposed triggers. Substances may also be classified as false negatives and be excluded from further assessments although they may pose a risk of reaching groundwater. There is, therefore, a need for a combined consideration of the environmental fate characteristics of the substance and interactions within the environment, including soil degradation and sorption processes and geospatial soil characteristic differences. The proposed cut-offs are considered apt for a preliminary level of screening, rather than any definitive regulatory classification. The main limitations on use of $K_{oc}$ alone to describe mobility are:

- The $K_{oc}$ concept used for the M/vM classification is not valid for soils with low organic carbon content or for ionisable substances where alternate sorption mechanisms may predominate.
- Non-linear sorption is not considered. Concentration dependent sorption is often observed for chemicals, resulting in non-linear (mostly Freundlich type) isotherms showing stronger relative sorption with decreasing concentrations.
- Slow kinetic sorption also called ‘aged sorption’ is not considered. This process, causing hysteretic sorption (a difference between adsorption and desorption isotherms), causes a considerable increase in chemical sorption with time and should not be ignored.
- Formation of non-extractable residues (NER) which are, by definition and in practice, highly resistant to desorption, thus preventing passage through the soil profile.
- Competitive sorption which is not considered in the $K_{oc}$ concept can lead to exchange of a sorbed species by another.

The mobility of substances has been discussed by the Task Force and suitable metrics incorporated into tiered approaches that aim to identify the leaching risk:

- Leaching indices and modelling combining the main chemical characteristics such as degradation and sorption.
- Ranking approach as used by the CIS Working Group to set up the Groundwater Watch List.

- Risk assessment approach based on exposure modelling, taking into account the leaching potential using models that consider the essential processes and take into account relevant climatic scenarios.

## 3.2 Introduction

The combination of persistence and mobility criteria as an approach to characterising a chemical's potential to contaminate water sources, as proposed by UBA (Neumann & Schliebner, 2019), is discussed in the following text.

The proposed screening and definitive criteria for persistence (P and vP) are the same as those defined in Annex XIII of REACH (ECHA, 2017a) and assessment should be carried out in acordance with Chapter R.7 (Endpoint specific guidance) and Chapter R.11 (PBT assessment) of the REACH guidance.

Mobile and very mobile (M and vM) endpoints have been proposed to identify persistent substances likely to contaminate water sources through movement between environmental compartments. Definitive criteria proposed for M and vM are based on the organic carbon (OC) normalised adsorption coefficient $K_{oc}$ (L/kg). Substances would be categorised as mobile (M) if the log $K_{oc}$ is < 4.0 (pH range 4–9) and very mobile (vM) if the log $K_{oc}$ is < 3.0 (pH range 4–9). In the absence of $K_{oc}$ data, a n-octanol-water partition coefficient (log $K_{ow}$) (for neutral compounds) or n-octanol/water distribution coefficient (log $D_{ow}$) (for ionisable compounds) are recommended by UBA as an indication for mobility if the log $K_{ow}$/log $D_{ow}$ is below 4.5 (Neumann & Schliebner, 2019).

Toxicity criteria are unrelated to the potential for leaching to water sources and are discussed in Chapter 7.

The objectives of this chapter are:

- To assess the UBA property-based approach, with particular emphasis on the proposed use of $K_{oc}$ and $D_{ow}$ as metrics for mobility, in combination with persistence criteria.
- To discuss alternative approaches involving 'indices', based on combinations of substance properties, which have previously been proposed for assessing potential for leaching of chemicals from soil to water sources.
- To assess if a modelling approach is appropriate and recommend which sorption parameters should be adopted, depending on the extent of the data already available or whose determination can be envisaged within the scope of an assessment.

## 3.3 Assessment of the approach proposed by UBA

The following sections review the evaluation scheme proposed by UBA and provide scientific justification as to their application and also discuss their advantages as well as their limitations when applied to a real-world situation within a complex natural environment.

Section 3.4 discusses alternative published approaches to the UBA proposal to screen and evaluate leaching potential for substances in groundwater.

### 3.3.1 Sequential assessment of P/vP and M/vM

Under the UBA proposed PMT/vPvM concept (Neumann & Schliebner, 2019), P/vP and M/vM properties of a substance are assessed sequentially. The potential for a substance to contaminate water compartments results from a competition between the rates of transformation and transport within and between environmental compartments (for further discussion see (Crookes & Fisk, 2018)). Consequently, it is possible that a highly mobile substance can break through to a water compartment even if it does not meet the persistence criteria, simply on account of migration being faster than degradation. Furthermore, substances that are classified as persistent and mobile will not necessarily leach to groundwater if transformation in soil is fast enough to sufficiently degrade a substance during transport processes.

These considerations demonstrate that it is essential to consider persistence and mobility in parallel, whilst understanding the environmental compartment to which a substance is initially introduced or predicted to reside.

### 3.3.2 Critical review of P/vP metrics

Fulfilment of M/vM and P/vP criteria is proposed by UBA to be based on comparison of ‘worst-case’ mobility and persistence data to the assigned threshold values (Neumann & Schliebner, 2019). For persistence the longest reported degradation half-lives in various environmental media are to be used.

From a precautionary principle standpoint, this may appear justifiable. However, in the case of persistence, the half-life data refer not only to soil, sediment and freshwater but also to media in which degradation may be less relevant to drinking water, such as estuarine or marine water. This needs to be carefully considered when looking at the route of entry of a substance to the environment and subsequent movement between compartments.

It should also be noted that the data requirement of definitive simulation degradation studies for substances under REACH is driven by the annual tonnage of the chemical produced or imported into the EU or the outcome of an exposure assessment. Many Registrants use screening level studies and/or modelling (e.g., quantitative structure-activity relationship (QSAR)) for fulfilling their persistence data requirements and therefore, measured half-life or transformation data ($DT_{50}$) for concluding P/vP is not available.

It finally needs to be considered that the cut-off values for the persistence criteria in the different compartments were taken from the PBT approach which has a completely different purpose, i.e., to identify substances that have potential to accumulate in biota in the environment, then potentially having unpredictable effects in the long term and cessation of emission will not necessarily result in a reduction in substance concentration. The suitability of these cut-off values for the processes at hand is yet to be established. To that end, the chemical transport processes through the unsaturated or saturated phase of the soil or sediment should be taken into account.

## 3.3.3 Critical review of M/vM metrics

The $K_{oc}$, $K_{ow}$ and $D_{ow}$ metrics proposed by UBA for assessing mobility are surrogates for expressing sorption of a substance to a given solid and its migration relative to the flow of sub-surface water, with retardation being inversely related to mobility. It is recognised that the proposed metrics may be adequate for preliminary screening of a large dataset of chemicals, but they present scientific shortcomings that preclude them from being used for definitive regulatory classification, as is discussed below.

### 3.3.3.1 Sorption metrics ($K_d$, $K_{oc}$)

The most relevant parameter for expressing the binding strength of a chemical to soil is the water-to-soil distribution coefficient at a given temperature ($K_d$; L/kg). Two different formulations of this parameter are in common use; the linear sorption isotherm and the non-linear, concentration dependent, Freundlich isotherm where the $K_d$ value becomes a Freundlich factor ($K_f$) value and the Freundlich exponent (1/n) describes the degree of non-linearity (for experimental determination, derivation of calculations and discussion please refer to other texts, e.g.: Office of Prevention, Pesticides and Toxic Substances (OPPTS) guidance; OECD Test Guidelines 106 and 121 (OECD 2000; OECD 2001); EC, 2014b; Green & Karickhoff, 1990; Doucette, 2000; Beltman *et al.*, 2008).

$K_d$ is both soil-specific and substance-specific, i.e., dependent on both the sorbent and the sorbate (test substance) and can therefore be used to compare the relative mobility of different substances in similar soils that have been thoroughly characterised. In order to achieve a 'comparative' value across different soil types, $K_d$ is 'normalised' by division of the fraction of organic carbon present in the solid phase ($f_{oc}$, kg/kg). This gives a new partition coefficient, the organic carbon normalised adsorption coefficient $K_{oc}$ (L/kg) = $K_d/f_{oc}$, which is considered to be an intrinsic property of non-polar organic chemicals being sorbed and hence independent of soil type (Karickhoff *et al.*, 1979; Green & Karickhoff, 1990; von Oepen *et al.*, 1991; Wauchope *et al.*, 2002; Jarvis, 2016).

The OECD 106 Test Guideline (OECD, 2000) aims to estimate the adsorption/desorption behaviour of a chemical for different soil types. The goal is to obtain a sorption value which can be used to predict partitioning under a variety of environmental conditions; to this end, equilibrium adsorption coefficients for a chemical on various soils are determined as a function of soil characteristics (organic carbon, clay content, soil texture, and pH).

The guideline states that soil parameters that are believed most important for adsorption are:

- organic carbon content;
- clay content and soil texture;
- pH (for ionisable compounds);
- the effective cation exchange capacity (CEC);
- the content of amorphous iron and aluminium oxides (particularly for volcanic and tropical soils);

- the specific surface area.

However, regulatory and modelling demands for an OC normalised value ($K_{oc}$) means that only this normalisation method is usually reported.

For REACH registered chemicals, only approximately 10% of the registered 23118 unique substances (https://echa.europa.eu/information-on-chemicals/registered-substances, accessed 18 December 2020) have an experimental $K_{oc}$ value[5]. Where a measured $K_{oc}$ is not available, surrogate methods (read-across, $K_{ow}$ or QSAR) are often used to predict the $K_{oc}$.

In the OECD 106 adsorption/desorption test, the test substance is ideally dissolved in a 0.01M solution of calcium chloride ($CaCl_2$) in distilled or deionised water. The 0.01 M $CaCl_2$ solution is used as the aqueous solvent phase to improve centrifugation and minimise cation exchange. Therefore, for ionisable substances, 0.01 M $CaCl_2$ will block any cation exchange and other ionic partitioning and may suggest (erroneously) that organic carbon partitioning is the principal partitioning mechanism. These $K_{oc}$ determinations will therefore be inaccurate. When considering the prominence of $K_{oc}$ in mobility screening schemes and in exposure modelling, this constraint of the methodology must be considered, particularly for ionisable substances. The limitation of the use of $K_{oc}$ has been recognised in several research papers (see below).

The use of the $K_{oc}$ model for assessing soil sorption is broadly accepted for non-polar substances and it can be considered substance-specific but soil-independent. However, this is a simplified model and despite its convenience should still be treated with caution and only used as an approximation. A review by Wauchope *et al.* (2002) notes that '*The temptation to regard $K_{oc}$ as a universal constant has been strong in spite of much accumulated evidence that it is not*'. Other authors have voiced similar criticisms (e.g. von Oepen *et al.*, 1991; Jarvis, 2016). The UBA report (Neumann & Schliebner, 2019) notes that the deviation of sorption metrics from simple behaviour are difficult to generalise, for example to account for clay and mineral sorption. However, soils are all complex and the issue of mobility is complex. This should be recognised and reflected in any hazard criteria that could be used to justify risk management measures of chemicals. Deviations from simple behaviour are discussed in the following Section (Section 3.3.3.2).

#### 3.3.3.2 Deviations of sorption metrics from simple behaviour

The $K_{oc}$ model is most appropriate for describing sorption of neutral apolar substances to surface soil layers with relatively high organic carbon contents, but the approach breaks down when interactions of substances with the mineral components of soils occur. These interactions become increasingly significant as the organic carbon content of a soil decreases (Koskinen & Harper, 1990; Delle Site, 2001; Li *et al.*, 2018). Due to degradation and dispersion/diffusion, environmentally relevant concentrations in sub-soils and aquifers are mostly below the concentrations used in adsorption studies (Schulze-Makuch, 2011; Myleyaganam and Ray,

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[5] 2277 substances extracted from the eChemPortal ECHA REACH property search (https://www.echemportal.org/echemportal/property-search), with reliability 1 and 2. Then duplicate CAS No. (Chemical Abstracts Service number) or name removed using MS Excel.

2016). As a consequence, the environmentally relevant sorption is often underestimated by these indices. For polar and ionisable substances, the $K_{oc}$ model is even more unreliable, particularly (but not exclusively) for soils with low OC contents. The coefficient of variation of $K_{oc}$ for any given compound has been stated to be typically in the range of 40-60%, and the difference between reported minimum and maximum values may be as great as an order of magnitude (Wauchope *et al.*, 2002; Jarvis, 2016). Ionic or ionisable substances make up a significant proportion of registered substances in the EU. A statistical evaluation from 2010 showed that approximately half of the substances registered under the REACH regulation are ionisable compounds (Franco *et al.*, 2010). Similar findings have been published for pharmaceuticals, where 64% of a contemporary set of drugs contained an ionisable group (Manallack, 2009).

### *Consideration of Mineral Components*

The clay component of all soils includes minerals containing alumina and silica, which have a net negative surface charge because $Si^{4+}$ can be partially replaced by $Al^{3+}$. However, the soil as a whole is electrically neutral, since this negative charge is balanced by the positive charge of various cations present in the soil, namely $Ca^{2+}$, $Mg^{2+}$, $K^+$, $Na^+$, $H^+$, etc. The negative charge of anions of organic humic and fulvic acids present in the soil is also neutralised by such cations, in this case with a dependency on the degree of dissociation of the various acid functions, i.e., increasing with pH. The capacity of the soil to bind cations is known as its cation exchange capacity (CEC), often expressed in milliequivalents per 100 grams (mEq/100 g) of soil, with typical values varying from <3 for sandy soils with low OC contents to >20 for clayey, high-OC soils. Strong sorption may be observed for cationic substances to negatively charged clay minerals (Jarvis, 2016).

Green and Karickhoff (Green & Karickhoff, 1990) suggested that the $K_{oc}$ approach may no longer be appropriate when the ratio of clay to OC content exceeds 40%. In a study by von Oepen *et al.* (1991), in which the minimum OC content investigated was as high as 1.58%, it was concluded that '*For more polar substances, e.g. acids (pH-dependent sorption) or amines, where sorption to clay minerals becomes important, it is impossible to obtain a soil-independent sorption coefficient, $K_{oc}$*'. In addition to the involvement of the mineral components of the soil, this variation may be due partly to the fact that soil organic matter does not have a single composition or structure and may be considered '*a mixture of solid and semi-solid, bulk and thin film materials with a range of properties depending on the history and age of the sample*' (Wauchope *et al.*, 2002).

### *Low Organic Carbon Content*

Aquifer soils are prominent examples of low OC content media. Typical OC values of <0.1% are observed (Piwoni & Banerjee, 1989; Hartog *et al*., 2004; Lee & Park, 2013; Fox *et al*., 2017). This is much lower than that of typical European top soils, which average between ~1.3 and ~4.5% OC in the upper 30 cm layer (Panagos *et al.*, 2013). Jobbágy & Jackson (2000), and references therein, note that the OC content of a soil falls off sharply with increasing depth and that typical global OC values between 2- and 3-meters depth are in the order of 0.05% to 0.4%, depending on the nature of surface biome. The authors of 'Remediation Hydraulics' note that '*we have observed the use of default assumptions for organic carbon fraction that exceed the values that we typically encounter by 10-fold, or more. This aquifer parameter is too critical to presume without sample collections, and the default assumption for aerobic aquifers should be very low i.e. 0.05%, or lower to be conservative*' (Payne *et al.*, 2008). Typical default values such as those used in the US EPA's Soil Screening User's Guide use a value of 0.2% when estimating migration of chemicals to groundwater (US EPA, 1996), and

Brussels Region's Environmental Agency environmental risk assessment guidance (Bruxelles Environnement, 2019) specifies a default subsurface OC value of 0.1% for estimating the rate of lateral transport of groundwater pollutants within aquifers.

### *Non-linear isotherms*

Apart from non-compliance with the popular and convenient $K_{oc}$ model, the sorption of organic chemicals to soils exhibits numerous deviations from the simple behaviour embodied in the linear isotherm corresponding to the $K_d$ metric. These complexities have been discussed in some detail by Wauchope *et al.* (2002) and others (Doucette, 2000; Delle Site, 2001) and are reviewed briefly here. They are included in the present chapter only for the purpose of emphasising the fact that no simple metric ($K_{oc}$, $K_d$, Freundlich parameters) can fully capture the sorption behaviour of a broad range of substances exposed to a variety of soils. If a chemical follows Freundlich behaviour, then its mobility at higher concentrations will be under-predicted by $K_d$ or $K_{oc}$ measurements made at lower concentrations and *vice versa*. Since environmentally relevant concentrations in sub-soils and aquifers due to degradation and dispersion/diffusion are mostly below the concentrations used in adsorption studies, the environmentally relevant sorption is often underestimated by these indices.

### *Slow kinetics and irreversible sorption*

Sorption and desorption of substances do not reach equilibrium instantaneously but occur over several time scales that reflect the kinetics of the complex series of steps involved (Pignatello and Xing, 1996; Beulke *et al*., 2004). Depending on the degree of mixing, rapid reversible diffusion of the sorbate and attachment to relatively accessible sites of the surface of soil constituents may occur in a matter of minutes. A slower, but fully reversible, second sorption phase requires between a few hours and 1–2 days. This has been attributed to slow diffusion within the pores and channels of the solid or limited molecular diffusion in the macromolecular organic matter. Depending upon the environmental matrix of contact, the formation of irreversibly bound residues may occur almost instantaneously. A classic example is the herbicide Paraquat, which undergoes strong adsorption to soils, particularly clay containing soils very rapidly (Constenla *et al*., 1990; Amondham *et al*., 2006). Lastly, a very slow but reversible process, often referred to as 'aged sorption' occurs over a period of weeks to years, removing the chemical from solution with the possibility to free the sorbate from the soil by relatively harsh extraction procedures. Since aged sorption is known to be a relevant and important process restricting the leaching of pesticides through soils, a guidance on how aged sorption studies should be conducted, evaluated and used in the regulatory leaching assessment was developed (EC, 2021).

Apart from increased reversible sorption (aged sorption) also the formation of non-extractable residues (NER) within solid matrices reduces the chemical transport in soil and sediment. As soils and sediments age, organic substances become increasingly recycled through metabolic pathways into recalcitrant non-characterisable fractions of organic matter (Kögel-Knabner, 2017). Incorporation via biogeochemical transformation on time scales exceeding a few days, results in a substance becoming the carbon source for resulting fractions such as humin, humic substances, humous, humic and fulvic acids. Extreme changes in environmental conditions would be required to remobilise even the smallest quantities of residual substance associated with an aged soil (Mordaunt *et al.*, 2005; Horwath, 2007).

***Hysteresis***

Values of apparent $K_d$ are often lower when measured in sorption equilibration experiments than in ensuing desorption runs in which the supernatant aqueous phase is replaced by fresh aqueous phase. Consequently, the values of $K_d$ lag behind the changes in the effect that is causing it e.g., slow diffusion or macromolecular interaction (Wauchope *et al.*, 2002).

***pH dependence***

Changes in pH generally have little impact on the sorption of neutral, non-polar substances. However, many chemicals in commerce have acid or basic functions that are partially or totally ionised at environmentally relevant pH values (Manallack, 2009; Franco *et al.*, 2010). For these ionisable substances, changes in pH affect not only the speciation of the substance, but also the nature of the soil or sediment sorption sites. Depending on the values of the acid dissociation constants (expressed as $pK_a$) relative to the ambient soil and water pH, the apparent $K_d$ (or $K_{oc}$) may be quite sensitive to variations in pH.

***Competitive sorption***

Numerous cases of competition for sorption sites have been reported. A few examples are the displacement of the following sorbed species:

- The organic cations of xenobiotic species, by the inorganic cations of salts present in pore water (Hamaker and Thompson, 1972, as cited in Doucette, 2000)
- Glyphosate herbicide, by phosphate used as a fertiliser (Munira *et al.*, 2018)
- The short-chain perfluoroalkyl carboxylic acid anion $C_3F_7COO$-, by longer-chain (more hydrophobic) perfluoroalkyl carboxylates and sulfonates (Gellrich *et al.*, 2012).

***Conclusion***

The use of the $K_{oc}$ model for assessing soil sorption is broadly accepted for non-polar substances, however this simplified model should be treated with caution and only used as an approximation. This section has indicated some of the complexities involved in understanding the mobility of substances in soils. Similar complexities arise in sediments too, but have generally not been studied so extensively.

#### 3.3.3.3 Limitations of the $D_{ow}$ metric

The *n*-octanol/water distribution coefficient $D_{ow}$ (L/L) is proposed by UBA as the main screening criterion for mobility (Neumann & Schliebner, 2019). $D_{ow}$ is equal to $C_o/C_w$, where $C_o$ (mg/L) is the concentration of the chemical in *n*-octanol and $C_w$ (mg/L) the corresponding concentration in water (summing both ionised and non-ionised forms, if applicable), when the two phases are in equilibrium.

$D_{ow}$ values are only roughly comparable with $K_{oc}$ values for ionisable substances, meaning that the use of $D_{ow}$ values interchangeably with $K_{oc}$ values in the proposed mobility criteria are not appropriate even at a screening level. In addition, *n*-octanol has generally been used as a surrogate for lipids when screening for potential bioaccumulation of chemicals into biota, but it should not be used as a surrogate for organic matter since *n*-octanol does not account for the potentially important properties of soil or sediment described above.

The empirically derived formula by Briggs (Briggs, 1981) has been used to estimate the soil adsorption coefficient ($K_d$) for plant protection products from the log $K_{ow}$:

$$K_d = 4.5\left(\frac{100\sqrt{K_{ow}}}{\%\text{Soil organic matter}}\right)$$

$K_{oc}$ is calculated from the $K_d$:

$$K_{oc} = 100\left(\frac{1.724\ K_d}{\%\text{Soil organic matter}}\right)$$

REACH registrants are encouraged to provide log $K_{ow}$ values for both the neutral and dissociated forms of their substance. However, the majority of dossiers contain QSAR derived log $K_{ow}$ values. $D_{ow}$ values can be predicted but models often require $pK_a$ and $K_{ow}$ values. If both these values are predicted, the uncertainty in both values will be magnified for $D_{ow}$ values. The training set for the model KOCWIN included within US EPA’s Estimation Programs Interface (EPI) Suite, contains a data set of substances with their experimentally determined log $K_{ow}$ and log $K_{oc}$ values (US EPA, 2012). It will be important to establish the impact of using log $K_{ow}$ or $D_{ow}$ values in place of a $K_{oc}$ value (or other more appropriate mobility descriptor) on the outcome of a mobility assessment before it is widely adopted.

## 3.4 Alternative approaches

### 3.4.1 The CIS Working Group Groundwater Watch List approach

As already mentioned in Section 2.3.2. of this report, the European Commission’s Common Implementation Strategy Working Group Groundwater (CIS WG GW) has developed methodology for a prioritised Watch List of substances to be monitored voluntarily in groundwater by Member States (CIS WG GW, 2018, Lapworth *et al.*, 2019). The Groundwater Watch List (GWWL) will gather occurrence data on substances posing a potential risk to groundwater and hence to be considered for possible regulation under the EU Groundwater Directive.

The proposed GWWL ranking and selection process involves the following steps:

1. Substances are initially identified based on either exposure likelihood resulting from their theoretical leaching potential, mobility, persistence and usage or existing monitoring data (their proven presence in groundwater)

2. Substances are then given a ‘groundwater leaching score,’ and identified as either a toxicological or ecotoxicological hazard

3. If sufficient monitoring data are available, the substances are deselected and added to a list with which to inform other relevant Ground Water Directive (GWD) annexes

4. If sufficient monitoring data are not available, the substances are added to the GWWL

5. Substances on the GWWL are then prioritised based on their identified toxicity risk. Those posing the highest risk are monitored until data are sufficient for them to be removed from the GWWL

The GWWL methodology is being refined as knowledge of groundwater and the behaviour of chemicals within this environment improves. The ranking and selection process goes further than assessment of leaching potential and persistence since it also takes into account usage data, monitoring data and the (eco)toxicological hazards of the candidate substances. It is based on a system in which scores for various input parameters are assigned, so as to create four ranked lists. The GWWL approach is simplistic in terms of leaching indices as it is based on the $K_{oc}$ or $K_{ow}$, despite mentioning that substances may be adsorbed to clay minerals or oxides (which may be important for ionisable compounds). This will not be discussed further in this section but a modified approach using more appropriate metrics, particularly for ionisable substances, may be helpful in the initial identification of potential candidates for further tiers of investigation (see Section 4.8). Despite some shortcomings, it is recognised that the GWWL approach is likely to play an important role in future EU regulation of groundwater contaminants.

### 3.4.2 Leaching indices and modelling approaches

Section 3.3.1 discussed the need for a simultaneous or joint assessment of P and M to consider the competition between migration and degradation during transport through the soil profile. This was recognised, if only in a rather simplistic fashion, in an approach originally proposed for pesticides by Gustafson (Gustafson, 1989). This approach enables leachability (a property combining both M and P) to be ranked in terms of the ‘GUS Index’, or ‘groundwater ubiquity score index’:

$$GUS = \log(t_{½,soil}) * (4 - \log K_{oc})$$

where $t_{½,soil}$ is the degradation half-life of the substance in soil, expressed in days.

This approach, or some variant of it (e.g., with a more suitable M metric than $K_{oc}$), is conceptually sounder than the use of separate criteria for P and M. The author of this index considered that ‘potential leachers’ are those for which GUS >2.8, while ‘non-leachers’ would have GUS <1.8, leaving a transition zone of moderate leachability between these two cut-off values (Gustafson, 1989).

While the GUS Index has been the one most commonly used index in assessing pesticide leachability, many others have been proposed. A total of 15 such indices for assessing pesticide leaching potentials have been reviewed by Akay Demir *et al.* (2019). Most of these indices are based on equations including sorption strength (generally expressed by $K_{oc}$) and half-life in soil, and neglect aquatic degradation. A few indices include additional parameters such as *n*-octanol-water partition coefficient, water solubility, vapour pressure, or

Henry's Law constant and a few use weighted linear combinations of other parameters, derived using Principal Component Analysis. An example of such a composite index is YASGEP-P, proposed by Akay Demir *et al.* (Akay Demir *et al.*, 2019) for ranking the leachability of 157 pesticides.

The equations used in defining all these alternative indices can be found in the review by Akay Demir *et al.* (2019), together with a description of their main features. They will not be further discussed here. Where there is sufficient data, the present report advocates a more detailed modelling approach for defining the relative and absolute leachability of chemicals. However, many substances lack sufficient data and therefore leachability indices may be useful for preliminary screening purposes. One limitation of this approach is the lack of an exposure assessment. This has also been recognised by the Groundwater Watch List (GWWL) approach described in Section 3.4.1.

### 3.4.3 Modelling approach

Significant work has been performed by the FOCUS (FOrum for Co-ordination of pesticide fate models and their USe) model initiative for plant protection products. Four FOCUS models (PELMO (PEsticide Leaching Model), PRZM (Pesticide Root Zone Model), PEARL (Pesticide Emission Assessment at Regional and Local scales) and MACRO (MACROpore flow model)) are used in Europe for the first-tier assessment of the leaching potential of pesticides to groundwater. The modelling endpoint is the average annual leachate concentration at a depth of 1 m representing a conservative approach for shallow groundwater close to the soil surface. The scenarios are generic and do not mimic specific fields but are designed to represent realistic worst-case scenarios that describe an overall vulnerability approximating the 90th percentile of possible situations that would enable leaching of a substance from different soil types, i.e., high rainfall and low organic carbon soils. Openly acknowledged limitations of these groundwater models recognise that the scenarios are based on Europe as it existed between 1997 and 2000 when they were developed and that the European Union has since grown and changed. However, the existing scenarios were checked for their relevance to the extended EU and it was found that they are still fit for purpose and provide regulators with a conservative estimate for the leaching potential of pesticides to groundwater for the whole EU (EC, 2014c).

The FOCUS strategy is to simulate all scenarios relevant to pesticide use. All scenarios would be relevant to the PMT proposal as this is also a European initiative. Identification of the pathways that lead to application or emission of REACH chemicals to soils could be identified, but is currently not available. For example, exposure through sludge application to land, or irrigation of land using surface water can be envisaged. Higher tier assessments for groundwater as shown in Figure 3.1 (below) can then be performed if sufficient data are available. Basic refinement at Tier 2 could include restricting the application of sludge to land at identified less vulnerable times (no application in Autumn/Winter) and decreasing the number or rate of applications. Further refinement could use additional $K_{oc}$ (or more appropriate metrics, e.g., dependency of sorption from soil properties other than OC) and $DT_{50}$ measurements, data on behaviour at different soil depths, plant uptake and aged sorption. For REACH chemicals these data are normally not available, so would either require default values (e.g., as used in FOCUS for subsoil degradation), estimates via QSAR tools or additional experimental resources before these refinements can be considered.

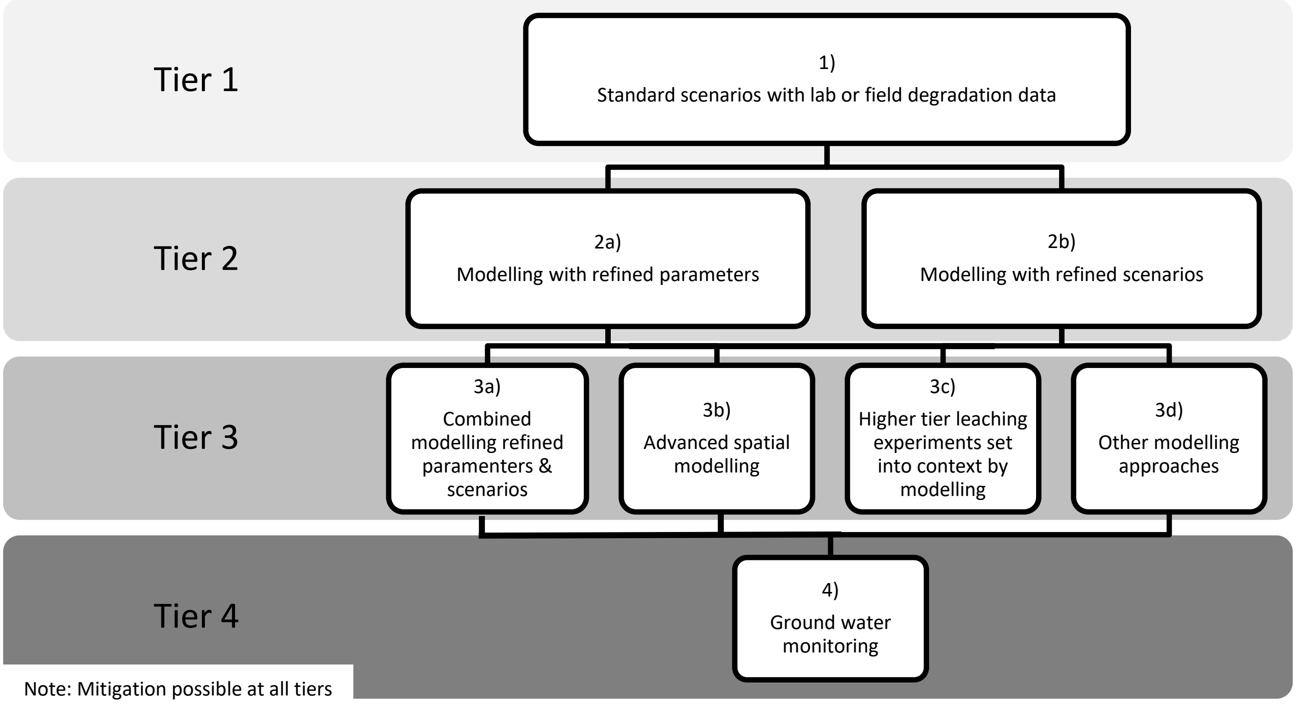

***Figure 3.1: Generic tiered assessment scheme for groundwater [Source: Adapted from Figure 1 in EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013]***

Overall, the benefits of the FOCUS approach are:

- Standard scenarios and models
- Guidance available on parameterisation (geomean $DT_{50}$, geomean $K_{oc}$ and maximal pesticide application rates)
- Easy to use
- Version control
- Standardised output and evaluation of results
- Multi-year experience in the regulatory context of PPP registration

These benefits lead to a common basis on which to discuss leaching issues, greater confidence of applicants that assessments will be acceptable to the relevant authorities, and debate which can focus on substance specific issues, rather than details of weather or soil parameterisation. Incorporating this type of tiered approach to REACH substances would be very challenging but for some substances where screening and initial assessments suggest a potential issue, this may be helpful and improve confidence in the hazard and exposure assessment data that registrants are able to provide.

The shortcomings discussed above (Section 3.3) of a trigger-based approach utilising $K_{oc}$ and P thresholds, as proposed by UBA (Neumann & Schliebner, 2019), has led to the authors of this report favouring a risk assessment methodology where there is sufficient data. Ideally, this would be based on sub-surface soil modelling, as discussed in Chapter 4 of this report. In principle this would have the advantage of allowing:

- The integration of realistic transformation by biotic or abiotic pathways simultaneously with transport processes. Hence considering the competing processes that would lead to improved groundwater and drinking water contamination assessments;
- The use of improved (i.e., non-$K_{oc}$ based) sorption functions, if available. These process descriptors may vary along the migration path of the contaminant's passage through the sub-surface soil as their properties change in successive layers or zones;
- Comparison of different hydrogeological scenarios ('typical' sub-surface compositions and structures, e.g., for a range of EU locations).

A tiered approach is proposed for selecting the most appropriate modelling parameter(s) for describing sorption, as a function of data that is available or that can be generated experimentally within the scope of a leachability assessment, in terms of both the budget and time that may be allotted.

The sorption parameters currently used in modelling exercises are predominantly based on $K_{oc}$, which can be estimated by a number of approaches, listed below by order of decreasing data availability and increasing relevance:

- $K_{oc}$ estimated from the molecular connectivity index, from $K_{ow}$, or using other correlations, as outlined in Section 3.4.3.1. This is appropriate, for example, if only the molecular structure of the substance to be assessed is known and no experimental sorption data are available;
- $K_{oc}$ estimated experimentally (only suitable for hydrophobic/non-ionisable substances) using the high performance liquid chromatography (HPLC) technique where suitable reference substances with reliable experimental $K_{oc}$ values are available as described in the OECD 121 test guideline (OECD, 2001);
- $K_d$ determined experimentally, e.g., according to the OECD 106 test guideline (OECD, 2000), for the specific soil composition(s) selected for the modelling exercise;
- $K_d$ / $K_{oc}$ determined experimentally, e.g., according to the OECD 106 test guideline (using a wide range of soil types);
- The Freundlich parameters $K_f$ and 1/n, determined experimentally, e.g., according to the OECD 106 test guideline over a relevant range of solute concentration.

It is clear from the parameters recommended above ($K_d$, $K_{oc}$ or Freundlich parameters) that, with the exception of the FOCUS models, many of the complexities and uncertainties in describing sorption, discussed in Section 3.3.3, cannot be adequately taken into account in the current state of scientific development of leaching models.

The lower tiers, involving $K_{oc}$, are recommended solely for screening purposes, rather than for definitive regulation. Indeed, it would be scientifically inappropriate to base any new legislation on $K_{oc}$ merely for the convenience of being able to exploit available estimated or experimental data, since these metrics often only poorly describe soil binding of ionisable substances at any level of organic carbon content and of most substances in low-carbon soils.

In a very limited number of cases (mostly pesticides) further $K_{oc}$ values may be available derived from higher-tier studies where the test chemical and environmental matrices represent more realistic environmental processes, e.g., ageing residues prior to performing OECD 106 tests, utilising representative sub-surface soils and associated groundwater, lysimeter studies or field dissipation studies.

New developments are ongoing, and this continually evolving strategy could be open to amendment for REACH substances. This is not a static approach.

### 3.4.3.1 Estimation of $K_{oc}$

There are many prediction methods available to estimate $K_{oc}$ values. Many models are based on a linear relationship between $K_{oc}$ and $K_{ow}$. Some developed models using this method are applicable to a wide variety of chemicals (for examples see (Baker *et al.*, 1997)), while others are only appropriate for a specific class of chemicals (for examples see (Sablić *et al.*, 1995)). The accuracies of the $K_{oc}$ predictions are dependent on the accuracy and reliability of the data used to build the model. These models should only be used when the substance of interest is within the scope (applicability domain) of the model. This can be defined in terms of chemical structure and a property range. Another common group of models available are based on the linear relationship between the log $K_{oc}$ value of a substance and the logarithm of its water solubility (for examples see Gerstl, 1990).

If no physicochemical data are available for a chemical, there are methods available to estimate a $K_{oc}$ value that only require knowledge of the molecular structure. These models describe the structure using molecular connectivity indices (MCI). MCIs are methods of describing the structure of a molecule in mathematical terms and can include information on molecular size and shape, including molecular volume, branching, unsaturation and atomic make-up. As with the models predicting $K_{oc}$ using physicochemical properties, some models are applicable to all chemicals and some are class specific.

There are also examples of other prediction models based on linear solvation energy relationships (LSER) (Baker *et al.*, 1997), characteristic root index (CRI) (Sacan & Balcioglu, 1996) and group contribution methods (Karickhoff, 1983).

*In silico* determination must be used with caution. Numerous software tools are now available to generate a $K_{oc}$ estimate. These include EPISuite™ (US EPA, 2012), OECD QSAR Toolbox[6], OPERA[7], ACD/Labs[8]. Values generated using software should always be treated cautiously especially in terms of suitability, e.g., ionisable substances. If possible, details of the substances that comprise the training sets (internal and external) should

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[6] https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm

[7] OPEn structure–activity/property Relationship App (Mansouri, 2017; Williams, 2017)

[8] https://www.acdlabs.com/

be available so that the applicability domain of the substance of interest can be assessed. If predicted values match experimental values for similar chemicals in the training set then there is greater confidence in the predicted value.

Regulatory tools for $K_{oc}$ estimation include the OECD TG 121 (OECD, 2001), which is an indirect experimental method using HPLC for the estimation of the adsorption coefficient $K_{oc}$ designed for soils and sewage sludge. It is based on the corrected retention time of the substance on a specific HPLC column (for examples see (Hong *et al.*, 1996)). Test substances are injected onto an HPLC column with a cyanopropyl stationary phase (cyanopropyl contains both lipophilic and polar functional groups). The measured retention time is then compared to the retention times of substances with known $K_{oc}$ values using the same HPLC conditions which is used to predict the $K_{oc}$ values of the substance of interest. The method is most reliable when used with substances for which chemically similar reference substances are used for calibration or validation of the test system. The method has been validated with non-polar reference substances, with log $K_{oc}$ values ranging from 1.5 to 5.0.

The method is not applicable for substances which react either with the eluent or the stationary phase. It is also not applicable for substances that interact in a specific way with inorganic components (e.g., formation of cluster complexes with clay minerals). The method may not work for surface-active substances, inorganic compounds and moderate or strong organic acids and bases. For ionisable substances, two tests should be performed with both ionised and non-ionised forms in appropriate buffer solutions but only in cases where at least 10% of the test compound will be dissociated within pH 5.5 to 7.5. Also, care has to be taken to avoid precipitation of buffer components or test substance.

### 3.4.3.2 Definitive and refinement tools for $K_d$ and $K_{oc}$ determination

Definitive measurement of adsorption/desorption ($K_d$, $K_{oc}$ or Freundlich parameters) can be performed following the methods presented in the OECD TG 106 (OECD, 2000). However, as described in Section 3.3.3.1, the method can be prone to inaccurate determination of the partitioning properties of a substance by not fully considering the chemical's structure.

Aged sorption studies can be performed using a range of approaches, including modified OECD TG 307 (soil metabolism; OECD, 2002b) and leaching in soil columns OECD TG 312 (OECD, 2004a). These have been described in 'Guidance on how aged sorption studies for pesticides should be conducted, analysed and used in regulatory assessments', October 2019 (Chemicals Regulation Division of the UK Health & Safety Executive (CRD), 2019). This text, and references therein, includes guidance on the incorporation of laboratory and field data into models such as PEARLNEQ, ModelMaker™ and MatLab that can be used in conjunction with the FOCUS guidance text (EC, 2014c and FOCUS, 2014; EFSA, 2015) to inform the risk assessment for plant protection products in groundwater. Data from the modified OECD TG 307 and the OECD TG 312 (OECD, 2004a) should yield more environmentally relevant data that reflect the long-term slow increase in sorption that affects the behaviour over increased time scales of weeks to months.

Aged sorption studies of this nature are relevant for chemical entities entering the terrestrial environment via sewage sludge applications to agricultural soils (e.g., chemicals in down-the-drain consumer goods). The high

OC content of sewage sludges (35% in primary sludge, 25% in digested sludge (Berthod *et al.* (2016)) can have a further significant influence on the adsorption /desorption characteristics within amended soils.

It should be emphasised that this level of data availability is normally only available for plant protection products and some veterinary products and not for other sectors including REACH chemicals.

## 3.5 Conclusion

A joint consideration of degradation rates and ability to cross natural barriers (sediment, soil) is necessary to make a scientifically sound prediction of whether a chemical can reach drinking water sources or not. The simple criterion of a threshold $K_{oc}$ value may be appropriate for an initial screening approach but is simplistic and does not consider the complex sorption behaviour chemicals can undergo in soils and sediments or the loading or application rate of the chemicals. Alternative approaches to the simplistic mobility criterion of $K_{oc}$, such as leaching indices, screening models and more sophisticated process-oriented leaching or groundwater models with appropriate scenarios should be considered in a tiered assessment.

**Knowledge Gaps and Research Needs**:

- Effect of low OC sub-surface soil and sediment on measurement of $K_{oc}$, $D_{ow}$
- Ionisable substances – validation of appropriate techniques for measurement of adsorption characteristics and differentiate between the effects of soil OC and mineral content
- Improved modelling techniques to determine adsorption characteristics of ionisable substances
- Aged sorption studies and realistic application scenarios for substances entering soils via indirect application.

# 4. Property-based vs risk-based approach to protecting water sources

## 4.1 Summary

This chapter reviews the various assessment approaches to predict chemical concentrations in drinking water. Tools developed for industrial chemicals (i.e., those registered under the REACH Regulation), biocides and plant protection products are compared, followed by different hazard threshold and risk assessment schemes. All modelling approaches integrate information on the use pattern and estimated release of a substance. These integrated metrics support the characterisation of fate and partitioning in the different environmental matrices. Using standardised cases, the models demonstrate that a simple mobility cut-off criterion does not sufficiently take into account the routes of exposures resulting from the diversity of use patterns between substances (e.g. industrial, PPP), the application or release rate, the partitioning between environmental compartments, and the interaction of degradation in soil or sediment. This indicates a need for more appropriate mobility data and more realistic modelling approaches that give a greater level of certainty when applied to a wide range of chemicals. However as discussed in Chapter 3, key metrics informing the exposure assessment are not suitable for a large proportion of chemicals. For certain industrial chemicals and plant protection products adequate modelling tools are available to partially assess their potential migration into drinking water resources. However, some uncertainties, such as bank filtration, remain as they are not appropriately covered by the existing models used in risk assessment, and thus are discussed as a research gap.

In order to rationalise the available tools and uncertainties a tiered approach is proposed in Section 4.8.

## 4.2 Introduction

In the case of the proposed PMT and vPvM screening criteria (Neumann and Schliebner, 2019), the soil adsorption coefficient normalised for organic matter content (log $K_{oc}$) of <4 is proposed as a trigger value for mobility (M). For vM a log $K_{oc}$ of <3 is proposed. Where a $K_{oc}$ is not available a n-octanol-water partition coefficient (log $K_{ow}$) (for neutral compounds) or n-octanol/water distribution coefficient (log $D_{ow}$) (for ionisable compounds) is proposed as an indication for mobility. The log $K_{oc}$ <3 trigger was selected as a harmonised value used in other European regulations and considered protective of compound movement to groundwater, although the accompanying reasoning does not consider the contribution of other sorption and degradation processes in soil. The higher threshold value of log $K_{oc}$ <4 was justified to screen compounds that might enter groundwater via bank filtration. For protection of groundwater from substances that are applied directly to the soil surface, it is questionable whether these log $K_{oc}$ thresholds are suitable values and this has been discussed further in Chapter 3.

The use of log $K_{oc}$ (or log $K_{ow}$, log $D_{ow}$) to identify a chemical's potential to move through soil is insufficient to characterise mobility in the environment, as fate and partitioning processes differ depending on the environmental compartment. Clearly, a substance with a short degradation half-life in soil is less likely to leach from soil to groundwater irrespective of its mobility, compared to one which has a slower degradation half-life in soil and of equal mobility (Kalberlah *et al.*, 2014). Parameters described in Chapter 3, only indicate a potential for mobility in soil. Other factors, such as degradation in soil and fate processes in river banks are equally important.

Chemicals can reach drinking water via a number of routes depending on their use and release patterns. Consideration of routes of exposure, persistence and mobility would be a more rational approach although it would necessarily be more complex to implement. Therefore, there is scope to consider the available tools and models to predict concentrations in drinking water and how they might be utilised in a tiered approach. In this chapter we discuss the relevant approaches under the framework of the World Health Organisation, the US EPA, the REACH regulation, the Plant Protection Products Regulation (PPPR) and the Biocidal Product Regulation (BPR)

The frameworks vary on the basis of the types of uses and the routes of exposure. Approaches for industrial chemicals evaluate exposure by taking into consideration substance use(s) and associated emissions to air, water and soil. Approaches developed in line with direct application to land (e.g., plant protection products) deal mainly with transport from surface (soil) application via leaching processes. Hydraulic transport from the soil surface to groundwater takes place over periods of weeks to years depending on the structure and properties of the topsoil, underlying substrates and climate or weather. The factors influencing leaching in the upper soil horizons are relatively well studied and understood. For biocide and plant protection substances several tools have been developed to model and predict the leaching of chemicals to groundwater for the purposes of risk assessment. Some of these are discussed below.

The differences between frameworks are illustrated with a hypothetical chemical for comparison purposes. These comparisons are then used to provide the basis for a proposal for a tiered assessment scheme that could deliver a more targeted approach to assess potential for drinking water sources contamination.

## 4.3 World Health Organisation (WHO) human health threshold approach

As already set out in Section 2.3.6, the World Health Organisation (WHO) uses an approach based on a risk assessment concept to develop guideline values for water quality (WHO, 2017).

The guideline value (GV), which considers chronic exposure, is derived as follows:

$$GV = (TDI \times bw \times P) / C$$

with: GV in [mg/L]

TDI = Tolerable daily intake [mg/kg_bw/d] (an estimate of the amount of a substance in food and drinking-water that can be ingested over a lifetime without appreciable health risk, and with a margin of safety)

bw = body weight [kg] (5 kg infants, 10 kg for a child, 60 kg for an adult)

P = fraction of the TDI allocated to drinking water = 0.2

(i.e., 20%; *note: this takes into consideration that exposure to, or intake of chemical contaminants from, drinking water is much lower than that from other sources such as food, air and consumer products*)
C = daily drinking water consumption [L] (0.75 L for an infant, 1 L for a child, 2L for an adult)

An acute health-based value can be derived for acute and short-term exposures for chemicals that are used in significant quantities and are involved in an emergency, such as a spill into surface water sources. The acute health-based value is derived as follows:

Acute health-based value = (ARfD x bw x P) / C

with: Acute health-based value in [mg/L]
ARfD = Acute Reference Dose [mg/kg_bw/d] (the amount of a chemical, normally expressed on a body weight basis, that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer)
P = fraction of the ARfD allocated to drinking water = 1 (100%)

The guideline value (GV) approach shown above could be incorporated into a risk assessment tool that requires input of basic toxicological end points (TDI) and would compare them with calculated exposure as described in the sections below.

## 4.4 US Environmental Protection Agency (EPA) approach

Regulation and approval of pesticides in the United States is administered by the EPA and governed by two main statues; Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA, 7 U.S.C. §136 et seq. 1996) and the Federal Food, Drug and Cosmetic Act (FFDCA, 21 U.S.C. §301 et seq. 2002) and amended by the Food Quality Protection Act (FQPA, Public Law 104-170 1996).

Under FIFRA, approved pesticides 'will not generally cause unreasonable adverse effects on the environment' defined as:

- any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or;
- a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under Section 408 of the Federal Food, Drug, and Cosmetic Act.

Section 408 of the FFDCA authorises EPA to set tolerances, or maximum residue limits, for pesticide residues on foods. In setting tolerances, EPA must make a finding that the tolerance is 'safe'. Safe being defined as a 'reasonable certainty that no harm will result from aggregate exposure to the pesticide residue'. The aggregate exposure to the pesticide is calculated from maximum residues in multiple sources (food, water, residential exposure and other non-occupational sources) and is commonly known as the 'Risk Cup Approach'.

Pesticide approvals in the US are based on risk assessment. Unlike the EU, there are no hazard cut-off values. Aggregate exposure (risk cup) is an important part of the EPA risk assessment, where the total exposure from all approved uses is considered. Residues in food, water etc. arising from any new proposed uses are added to the ‘risk cup’ to check for exceedance before approval. Substances with a common mode of toxicity can be added to the same ‘risk cup’.

In exposure evaluation of pesticides, the EPA uses a tiered procedure in order to focus on the most important issues. For drinking water, a variety of models have been used to assess concentrations in surface and groundwater. For groundwater a Tier 1 assessment, which is most appropriate in the context of this document, the SCI-GROW (Screening Concentration in Groundwater; Barrett, 1997; US EPA, 2003) model was widely used, however it has now been archived by the EPA and is no longer available for download. Pesticide concentrations estimated by SCI-GROW represent conservative or high-end exposure values because the model is based on groundwater monitoring studies which were conducted by applying pesticides at maximum allowed rates and frequency to vulnerable sites (i.e., shallow aquifers, sandy, permeable soils, and substantial rainfall and/or irrigation to maximise leaching).

The SCI-GROW estimate is based on simple environmental fate properties of the pesticide (aerobic soil degradation half-life and linear adsorption coefficient normalised for soil organic carbon content, $K_{oc}$) and the application rate. SCI-GROW provides conservative estimates of pesticides in groundwater, but it does not have the capability to consider variability in leaching potential of different soils, weather (including rainfall), cumulative yearly applications or depth to aquifer. The model is helpful as an early screening tool, particularly where limited data are available. Also, it should be noted that SCI-GROW has some limitations e.g., the model was only validated with $K_{oc}$ values in the range 32 to 180 L/kg and has an upper input limit of 9995 L/kg (log $K_{oc}$ = 4) (although higher values can be entered, results are not valid). SCI-GROW has not been implemented within the European plant protection products regulatory framework.

Although SCI-GROW provides conservative outputs, its simple range of inputs and lack of flexibility for the refinement of an assessment led to its replacement by PRZM-GW (Pesticide Root Zone Model; Carousel *et al.*, 2005; currently version 5 is approved for regulatory use).

PRZM-GW is a conceptual model based on a rural drinking water well beneath an agricultural field, which draws water from an unconfined, high water-table aquifer. The depth of the well and well-screen length are site-specific (i.e., scenario specific). Processes included in the conceptual model that influence pesticide transport through the soil profile include water flow, chemical specific dissipation and transportation parameters (i.e., degradation and sorption), and crop specific factors, including transpiration, pesticide interception and management practices. The customization of PRZM-GW for the US regulatory system makes it uncertain if it is relevant to uses in the EU. Additionally, its comprehensive chemical parameter requirements make it unsuitable as a screening assessment model for general chemicals. As a result, the SCI-GROW model in principle offers a more suitable, general and conservative Tier 1 tool for groundwater assessment.

It should be noted that for pesticide evaluation, drinking water from surface water is also considered by the EPA (as part of the ‘risk cup’). For human exposure, the EPA use the Pesticide in Water Calculator (v2.001 currently approved for regulatory use[9]). This model provides both groundwater and surface water concentrations using the models PRZM5 and VVWM (variable volume water model). The target water bodies

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[9] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

are a standardised pond and lake into which pesticides are transported via spray drift and aqueous and sediment run-off. It should be noted that bank filtration is not included in this model. However, as discussed above, the parametrisation is for specific scenarios in the US and is not considered suitable for direct use in the EU.

In addition, catchment scale models such as the Soil and Water Assessment Tool (SWAT), developed in the US, which are designed to predict the impact of management on water, sediment, and agricultural chemical yields in ungauged watersheds, are available. However, due to its complexity of operation it is not recommended as an initial screening tool.

## 4.5 European Plant Protection Products (and Biocidal Products) assessment approach

The FOCUS Groundwater approach (FOCUS GW; EC, 2020b) is the main model used in the European plant protection products framework. The approach is complex, designed around the groundwater models PEARL[10], PELMO[11], PRZM and MACRO[12] with nine specific climate/soil scenarios to represent European agriculture. The FOCUS models accommodate leaching over the long term, considering yearly applications for up to 26 years (the first 6 years' results are not used but provide a 'warm-up' period) which can be extended to 46 and 66 years if the substance application is limited to every second or third year. This could serve as a workaround for chemicals which are extremely persistent and for which a maximum plateau is not reached within the period of 26 years.

Although designed as a Tier 1 assessment tool, the FOCUS GW models are sophisticated process based numerical models which demand a significantly higher level of input (data) than SCI-GROW, e.g., additional chemical properties, use patterns, specific soil and climate data, and crop properties such as growth stages at application and during the vegetation period. However, it has wide regulatory acceptability for plant protection active substances and can also be used for metabolites. The output of the FOCUS GW model is pesticide and metabolite concentrations in the soil pore water at a 1 m depth. Clearly water at this depth would not be used directly for drinking water abstraction, however, the modelled concentrations are considered protective of groundwater. It should be noted that the model does not include the potential entry of chemicals to groundwater from surface water (for example via bank filtration).

The registration of biocidal active substances under the Biocidal Product Regulation (BPR) includes the protection of groundwater. The evaluation is based on a risk assessment approach, which evaluates exposure in a tiered approach. The potential for exposure to groundwater is evaluated in a first tier with the same

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[10] Pesticide Emission Assessment at Regional and Local scales

[11] Pesticide Leaching Model

[12] Macropore flow model

approach as REACH (EUSES model) and then FOCUS GW is implemented for higher tier assessments (where necessary).

There are currently no models approved in the EU registration process for the estimation of surface water concentrations at water abstraction points. For regulatory approval of PPP at the EU level, surface water is evaluated via the FOCUS Surface Water models (FOCUS SW[13]). Based on a tiered system, the lower Tiers 1 and 2 are easy to operate and require only simple inputs. The higher Tiers 3 and 4, are reliant on detailed crop use and chemical parameters and are far more complex to implement. The purpose of FOCUS SW is to provide edge of field concentrations for environmental risk assessment. Chemical inputs to water are principally via spray drift and run-off. For drinking water assessment, it is possible to use edge of field concentrations together with catchment dilution factors.

In contrast there are national approaches available in the Netherlands and Germany that consider drinking water concentrations for abstraction of drinking water from surface water or bank filtration. For example, the model DROPLET developed and used in the national registration of the Netherlands (van Leerdam et al., 2010) uses modified FOCUS SW Tier 3 outputs and specific catchment dilution factors to calculate water concentrations at nine abstraction locations. For screening purposes, a model based on FOCUS SW Tier 3 is unlikely to be practicable. However, work is initiated in the context of water treatment requirements to extend this approach to the whole EU.

For national PPP registration in Germany the simple surface water model EXPOSIT (BVL, 2017) is used that includes bank filtration factors to estimate the bank filtrate concentration at drinking water abstraction points. The bank filtration factors describe the reduction of the concentration of the surface water by the filtration process. These factors are dependent on the substance properties or are directly derived from experimental studies. However, the predicted concentration in the bank filtrate depends on several aspects: the emission rate of the substance; the calculated concentration in the surface water; and the reduction by the bank filtration. In general, an extension of this approach to other chemical classes would be possible but would require an exposure assessment of these substances in surface water and the information on the potential of bank filtration to reduce their concentration.

## 4.6 REACH assessment approach (and biocidal products)

The transport of a chemical to drinking water is an integral part of the exposure assessment framework used in European regulations for the registration and management of industrial chemicals. The quantitative approach supporting the safety assessment under the REACH and the Biocidal Product Regulations is outlined in the exposure assessment guidance (ECHA, 2016a; ECHA, 2017b) (Figure 4.1). This framework was already in use prior to the REACH regulation, in the context of the evaluation of new notified substances and existing substances (Technical Guidance Document (TGD) on Risk Assessment - Part II; EC, 2003a). The main environmental risk assessment tool is the EUSES (European Union System for the Evaluation of Substances)

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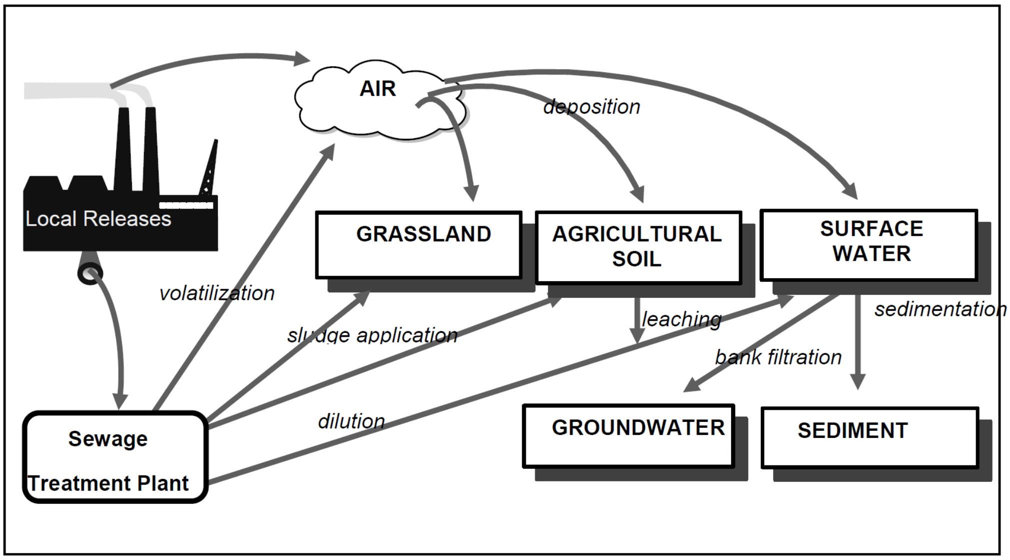
[13] https://esdac.jrc.ec.europa.eu/projects/surface-water

model, which was more recently coded into several newer applications in support of REACH registrations (e.g., ECHA CHEmical Safety Assessment and Reporting tool (CHESAR), ECETOC Targeted Risk Assessment (TRA) tool, Easy Targeted Risk Assessment (EASY TRA)).

The EUSES model addresses routes of exposure relevant to the screening level assessment of industrial chemicals to support environmental risk assessment, as well as indirect exposure of humans via the environment. As per ECHA guidance, an assessment of indirect exposure of humans via the environment is conducted if the tonnage is >1000 t/y or if the tonnage is >100 t/y and the substance is classified as: STOT RE[14] 1; as a carcinogen or mutagen (any category); or as toxic to reproduction (categories 1A or 1B). The route of exposure for humans includes consumption of food, drinking water and inhalation of air (Figure 4.2). Exposure resulting from oral intake by humans is compared to the human threshold for long-term systemic exposure via the oral route (referred to as PNEC oral long term systemic (ECHA, 2016a) or General Population derived no-effect level (DNEL) long-term oral (ECHA, 2016b)). The source of drinking water considered in the EUSES model is untreated groundwater or treated surface water (see EUSES 2.1 model calculations III, Section III.5.2.4 ‘Concentration in drinking water’; ECHA, 2020). The groundwater compartment parameterisation is not representative of a groundwater aquifer used as a source for drinking water preparation, since the EUSES model takes the chemical concentration in porewater from the 10 or 20 cm topsoil. Drinking water preparation from surface water is included in the model taking into account extensive treatment of surface water via storage in open reservoirs and via dune treatment, however Part I of the TGD outlines the low accuracy of the estimated removal efficiencies (EC, 2003b). This is associated with the challenge of defining efficiencies for treatment techniques used in treating surface water for use in drinking water (ECHA, 2016a). There is limited information on the relevance of the current approaches to river bank filtration used as natural attenuation. Consequently, groundwater or surface water predictions serve as worst case screening level assessments.



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[14] Specific target organ toxicity – repeated exposure

***Figure 4.1: Direct and indirect exposure to groundwater in REACH guidance R.16 (previous version) [Source: European Chemicals Agency, http://echa.europa.eu/ (ECHA, 2012)]***

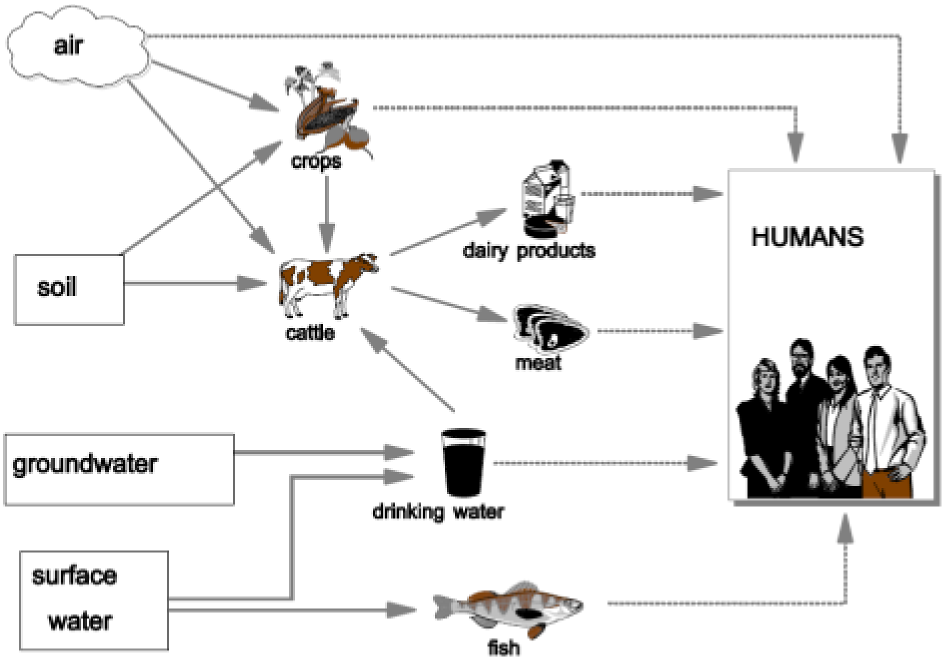

***Figure 4.2: Risk assessment of man via the environment in REACH guidance R.16 [Source: European Chemicals Agency, http://echa.europa.eu/ (ECHA, 2016a)]***

In EUSES, the PEC drinking water is derived from either the annual average PEC in surface water or the PEC groundwater, selecting the worst-case exposure (See EUSES 2.1 model calculations III; ECHA, 2020).

Exposure to soil (and eventually groundwater) is either from direct deposition from air and/or indirect exposure from the application of sludge to land. Sludge is a by-product of wastewater treatment used as fertiliser (Figure 4.1). Transport to soil by application of sludge and subsequent leaching from agricultural soil to groundwater may be the primary route of exposure to groundwater for non-volatile substances with potential adsorption to sewage sludge emitted to wastewater.

Sludge application to land is still practiced in a number of European countries, although some Member States report other management practices (EC, 2017b). Approaches for management of sewage sludge may evolve at the European level (see Section 2.3.4). In Switzerland, the use of effluent sludge as an agricultural fertiliser has been prohibited since 1 October 2006. Industrial chemicals may be indirectly applied to land when adsorbed to organic matter constituting the sewage sludge. Consequently, emissions to the wastewater treatment plant (WWTP) and fate and partitioning processes within the WWTP determine the potential exposure in soil and groundwater, as well as in surface water.

The predicted environmental concentration in groundwater ($PEC_{GW}$) is estimated, in a very conservative manner, as equivalent to the soil pore water concentration of the topsoil (ECHA, 2016a). Figure 4.3 illustrates differences in the route of exposure and the determination of the concentration in groundwater in the framework of REACH and in modelling approaches for plant protection products (PPP).

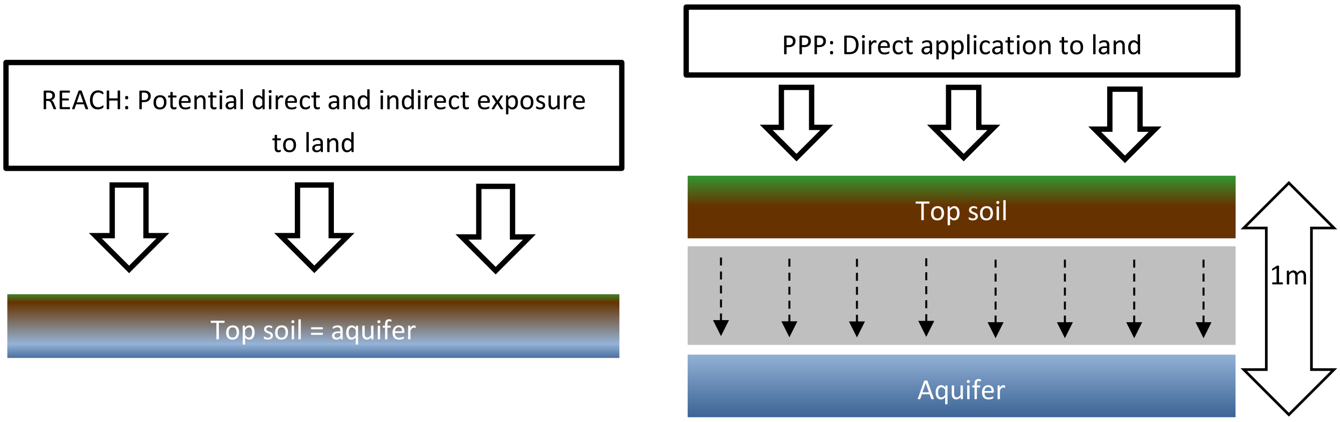

*Figure 4.3: Differences in route of exposure and determination of groundwater concentration in REACH and PPP frameworks*

However, following the principle of tiered approaches in risk assessment, the EUSES model output can be refined; including refined release characterisation, higher-tier fate and partitioning information, and/or parameterisation on the basis of measured data. Nevertheless, and as acknowledged in existing guidance, the model remains a conservative approach, since the pore water of a topsoil is not representative of the characteristics of a drinking water aquifer with regard to hydraulic transport, dilution or fate processes associated with transport to deeper soil layers, where anaerobic conditions may be predominant.

The exposure in surface water considers dilution of the WWTP effluent in surface water and partitioning to suspended solids. A purification factor is applied on the basis of the potential for partitioning, volatility and aerobic biodegradation rate. In line with the conservative approach, no biodegradation would be considered for substances with screening level information, since the half-life for biodegradation in bulk surface water ($DT_{50}bio_{water}$) at which a purification factor less than one could be considered is ≤10 days, whereas the default degradation half-life for substances meeting the criteria as 'readily biodegradable' is 15 days (EC, 2003b).

## 4.7 Case study

The focus of the case study it to illustrate the differences between the available tools and models supporting the prediction of concentrations in drinking water for the risk assessment frameworks previously described. The differences between frameworks are illustrated with a hypothetical chemical for comparison purposes.

Information needed to support an exposure assessment includes the substance properties, such as the physico-chemical, environmental fate properties, the characterisation of the environmental compartment(s) of release and the associated rates of emissions.

### 4.7.1 REACH approach (EUSES)

In the REACH case study, simulations of environmental transport from a wastewater treatment plant to surface water and to the groundwater compartment via sludge application have been performed using the EUSES model. This evaluates the influence of the local release rate to influent wastewater ($\mathrm{Elocal}_{\mathrm{WATER}}$), the conclusion from biodegradation screening assessment, which determines the half-life parameterisation in the different environmental compartments, as well as the partitioning to organic carbon ($K_{oc}$). Partitioning has been assumed to be adequately described by the $K_{ow}$ or $K_{oc}$. However, as described in Section 3.3.3, this is not appropriate for approximately half of REACH registered chemicals and an even higher proportion of pharmaceuticals. The first part of the case study focuses on transport to groundwater while the sourcing of surface water for use in drinking water preparation is discussed subsequently.

#### 4.7.1.1 Drinking water sourced from groundwater

Concentrations in groundwater were derived in accordance with the ECHA guidance R.16 as equal to the soil pore water concentration, after 10 consecutive yearly applications of sludge to land (ECHA, 2016a). The metric ‘fraction transport in groundwater at steady state’ is helpful in identifying model deviations from the assumption of steady state (fraction of steady-state). Such deviation may be expected for slowly degrading substances not degrading between sludge applications.

As indicated above, the exposure to groundwater may occur as a consequence of fate and partitioning in the WWTP and subsequently in soil. In order to assess similarities and differences between the EUSES model and models used for the evaluation of PPPs, the application rate to soil was aligned in magnitude for both approaches using an application rate for agrochemicals (see Appendix A).

As the purpose of the assessment was to explore the influence of fate and partitioning beyond the soil compartment, the release to WWTP $\mathrm{Elocal}_{\mathrm{WATER}}$ routinely used as key input to EUSES modelling was conservatively derived for a given release pathway and substance profile. The selected scenario assumes a single release pathway via WWTP of a water-soluble substance with a log $K_{ow}$ of 4. A fixed input value for $\mathrm{Elocal}_{\mathrm{WATER}}$ of 0.7 kg/d was subsequently used for all EUSES simulations.

The biodegradation characteristics and associated half-lives in WWTP and soil are aligned to default values outlined in the ECHA guidance (Chapter R.16; ECHA, 2016a). While the degradation rates in WWTP reflect the direct conclusion of the biodegradation testing, the half-lives in soil are extrapolated from standard biodegradation studies factoring in the influence of the soil-water partition coefficients (Table 4.1).

***Table 4.1: Biodegradation characteristics: Extrapolated rate constants or half-lives for biodegradation in different environmental compartments based on the conclusion of biodegradation screening studies (ECHA, 2016a)***

| **Conclusion from biodegradation screening assessment** | **Rate constant in WWTP (1/h)** | **Half-life in soil for substance with $Kp_{soil}$[a] <100 L/kg (days)** | **Half-life in soil for substance with $Kp_{soil}$ <1000 L/kg (days)** |
|---|---|---|---|
| Readily biodegradable | 1 | 30 | 300 |
| Readily biodegradable failing the 10-day window | 0.3 | 90 | 900 |
| Inherent biodegradable, fulfilling specific criteria | 0.1 | 300 | 3000 |
| Inherent biodegradable, not fulfilling criteria | 0 | 300 | 3000 |
| Not degradable $10^6$ day | 0 | 1000000 | 1000000 |

[a] Partition coefficient solid-water in soil

The groundwater PECs were determined in this case study with a defined release of 0.7 kg/d to WWTP (see Table 4.2), while evaluating the influence of the biodegradation characteristics and partitioning to organic carbon.

***Table 4.2: PEC groundwater in µg/L from an assumed release of 0.7 kg/d to WWTP [Fst - st = Fraction of steady state]***

| | **$K_{oc}$ (L/kg)** | | | | | |
|---|---|---|---|---|---|---|
| **Biodegradation characteristics** | **1** | **10** | **100** | **500** | **1000** | **10000** |
| Readily biodegradable | 0.11 | 0.69 | 1.39 | 1.48 | 1.41 | 4.21 |
| Readily biodegradable failing the 10-day window | 0.20 | 1.37 | 3.40 | 3.77 | 3.64 | 11.00 |
| Inherently biodegradable, fulfilling specific criteria | 0.27 | 2.07 | 7.10 | 9.30 | 9.26 | *Fst – st <1* |
| Inherently biodegradable, not fulfilling criteria | 0.31 | 2.34 | 8.01 | 10.50 | 10.40 | *Fst – st <1* |
| Not degradable (half-life $10^6$ days) | 0.34 | 2.80 | *Fst – st <1* | *Fst – st <1* | *Fst – st <1* | *Fst – st <1* |

The predicted concentrations in groundwater outlined in Table 4.2 vary over two orders of magnitude. A linear increase in PEC groundwater with $K_{oc}$ for a given biodegradation characteristic is not observed since the half-life in soil also depends on the solid/water partitioning coefficient (Table 4.1). Substances with $K_{oc}$ ≥100 and assumed half-lives in soil ≥3000 days (i.e., 'inherently biodegradable' or 'not degradable'; refer to Table 4.1) are associated with the highest exposure. Nevertheless, the parameter fraction of steady state 'Fst – st' <1 indicates deviations from the model assumption of steady-state, suggesting the need for alternative approaches to predict exposures resulting from sludge application over a 10-year period.

At the opposite end of the spectrum, substance properties reflecting a low potential for partitioning to organic matter or a rapid degradation in WWTP and soil are associated with the lowest exposure in groundwater. The simulation provides insights into the competing partitioning mechanisms driving exposure in soil. Exposure in soil from sludge application only becomes a relevant exposure pathway for substances emitted to wastewater treatment plants having the potential to adsorb to sludge and thus be transported to soil. In the current parameterisation, partitioning to organic carbon plays an important role to inform the partitioning coefficients between water and sludge or soil. As a result, substances with a low $K_{oc}$ result in a low potential for binding to organic matter present in the sludge resulting in low exposures to soil and groundwater.

### 4.7.1.2 Drinking water sourced from surface water

Low partitioning to sludge can alternatively result in substances partitioning into the water phase of the wastewater treatment and thus lead to emissions in the WWTP effluent and exposure in surface water. In the second part of this case study, concentrations in surface water were predicted and are outlined in Table 4.3 below. Once again, a fixed input value for $Elocal_{WATER}$ of 0.7 kg/d for a substance with high water solubility and low propensity to partition to air in WWTP (1000 mg/L and 1.3 Pa) was used for all simulations. The local surface water concentrations vary over approximately one order of magnitude. The predicted exposures in water are highest for the biodegradation characteristics where biodegradation in WWTP is not accounted for, namely 'inherently biodegradable, not fulfilling criteria' and 'not degradable'. Further, the predicted concentrations are higher for lower $K_{oc}$ values, i.e., less adsorbing substances. In the EUSES model, the $K_{oc}$ is used for the estimation of the solids-water partitioning coefficient in sewage sludge and on suspended matter, thus for higher $K_{oc}$ values removal by partitioning is considered in addition to degradation. As above, a linear increase in PEC groundwater with $K_{oc}$ for a given biodegradation characteristic is not observed since the half-life in soil also depends both on the biodegradation characteristics and the solid/water partitioning coefficient $K_p$ (Table 4.1).

***Table 4.3: Annual average local PEC in surface water in µg/L from an assumed release of 0.7 kg/d to WWTP***

| | $K_{oc}$ (L/kg) | | | | | |
|---|---|---|---|---|---|---|
| **Biodegradation characteristics** | **1** | **10** | **100** | **500** | **1000** | **10000** |
| Readily biodegradable | 3.86 | 3.85 | 3.82 | 3.71 | 3.57 | 2.54 |
| Readily biodegradable failing the 10-day window | 9.93 | 9.92 | 9.84 | 9.50 | 9.12 | 5.94 |
| Inherent biodegradable, fulfilling specific criteria | 18.10 | 18.00 | 17.90 | 17.20 | 16.40 | 9.72 |
| Inherent biodegradable, not fulfilling criteria | 30.30 | 30.20 | 29.90 | 28.50 | 26.90 | 14.10 |

| | $K_{oc}$ (L/kg) | | | | | |
|---|---|---|---|---|---|---|
| **Biodegradation characteristics** | **1** | **10** | **100** | **500** | **1000** | **10000** |
| Not degradable (half-life $10^6$ days) | 30.50 | 30.50 | 30.10 | 28.80 | 27.20 | 14.50 |

As noted above, the PEC drinking water is derived from either the annual average PEC in surface water or the PEC groundwater, selecting the worst-case exposure. This current case study can be used to illustrate the environmental route of exposure used in deriving the predicted drinking water concentration for the various scenarios (Table 4.4). The use of surface water for the model substance of high solubility and low propensity to partition to air in WWTP (1000 mg/L and 1.3 Pa) would be selected as the worst-case exposure in most cases (indicated via light blue highlighting). Considering that purification removal is only parametrised for log $K_{ow}$ >4, Henry's law constant >100 Pa $m^3$/mol and aerobic biodegradation half-life of ≤10 days (See EUSES 2.1 model calculations III, Section III.5.2.4 Concentration in drinking water; ECHA, 2020), this represents a worst-case situation for the surface water compartment. Scenarios indicated in light green in Table 4.4 are those where groundwater would be selected as the relevant route of exposure to humans. Scenarios indicated in dark green suggest groundwater as the route of exposure, however the groundwater model deviates from the assumption of steady-state (see Table 4.2). Similarly, the scenario indicated in dark blue indicates surface water as a worst case, bearing in mind the groundwater assessment is not at steady-state (Table 4.2). As discussed, several fate and partitioning properties inform the exposure assessment. This analysis is not applicable to substances with different solubility and volatility profiles, as these properties may influence the fate in WWTP and potentially during storage and treatment of surface water prior to use in drinking water.

***Table 4.4: Illustration of the route of exposure driving the EUSES drinking water assessment for a model substance of high solubility and low volatility and domain of model applicability [light green = groundwater selected as the relevant route of exposure; light blue = surface water selected as the relevant route of exposure; dark green = groundwater selected but groundwater model deviates from steady-state; dark blue = surface water selected and groundwater model deviates from steady-state]***

| | $K_{oc}$ (L/kg) | | | | | |
|---|---|---|---|---|---|---|
| **Biodegradation characteristics** | **1** | **10** | **100** | **500** | **1000** | **10000** |
| Readily biodegradable | 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | 🟩 |
| Readily biodegradable failing the 10-day window | 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | 🟩 |
| Inherent biodegradable, fulfilling specific criteria | 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | ▩ |
| Inherent biodegradable, not fulfilling criteria | 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | ▩ |
| Not degradable $10^6$ day | 🟦 | 🟦 | ▦ | ▩ | ▩ | ▩ |

It is worth noting that the drinking water concentration when derived from surface water has little or no consideration of water treatment technologies, beyond the considered extensive storage and treatment. Attenuation processes that may occur in bank filtration, such as fate during the residence time of sub-surface transport, are currently not characterised in the EUSES approach at least for substances with only screening level information on degradation characteristics. Unless higher tier fate data are available, screening assessment for substances with a log $K_{ow}$ ≤4 or Henry's law constant < 100 Pa $m^3$/mol would conservatively assume the consumption of untreated surface water. It is furthermore unclear whether the purification factors reflect current drinking water preparation practices.

The EUSES model includes a number of conservative assumptions in the estimation of drinking water concentrations. Namely, the prediction of the groundwater concentration assumes yearly application of sewage sludge to the same field over a 10-year period, does not include the potential for degradation in sludge, nor the aged adsorption processes, prior to application to land and assumes the top soil porewater concentration as a surrogate for groundwater. In the context of a tiered risk assessment framework, model prediction may be refined by integration of more specific release characterisation to the environment or by inclusion of information fate and partitioning data supporting an improved multimedia exposure prediction.

It is also of note that, in practice, drinking water suppliers follow groundwater protection schemes, of which the simplest form is the definition of protection zones around wellheads to mitigate influx from bacteria and contaminants (BLU, 2010, WHO, 2006). The intent of the protection zone is to reduce the transfer of bacteria, organic and inorganic contaminants to drinking water, therefore groundwater used for the supply of drinking water is sourced from areas where the application to land is strictly controlled in relation to the application of fertilisers whether the form is sludge, manure or synthetic fertilisers, and plant protection products.

The first part of the case study was developed for illustrative purposes by making a number of assumptions, namely by selecting a unique exposure scenario assuming complete release to a WWTP as the sole emission pathway. In addition, the hypothetical substance is of low volatility resulting in losses in WWTP to air <1%. Assessments under the REACH regulation account for all registered uses of substances having a variety of physical-chemical and fate characteristics. This chapter illustrates the importance of considering information with a holistic approach, by inclusion of substance and use information.

### 4.7.2 Plant protection products (and biocidal products) assessment approach

In the second part of this case study, simulations of environmental transport from the soil to the groundwater compartment have been performed using SCI-GROW and FOCUS-PELMO GW models as examples of simple and complex groundwater concentration estimations, respectively. The application rate to soil used in the model simulation are aligned in magnitude with the EUSES model (see Appendix A).

The predicted groundwater concentration, as a function of soil degradation half-life and soil adsorption coefficient normalised for organic carbon content ($K_{oc}$) for a chemical in both the SCI-GROW and FOCUS-PELMO GW models is shown in Table 4.5 below. The term half-life is used to describe the time taken for half the mass of a chemical to degrade using single first order degradation kinetics which are normally used in predictive models. The term $DT_{50}$ is used to describe the time taken for half the mass of a chemical to degrade regardless of the kinetic fit. A range of $K_{oc}$ and half-life in soil values were entered with a relatively high application rate for currently used pesticides of 1000 g/ha (hectare) per year as a single application (equivalent to 0.892 pounds/acre for SCI-GROW) for both models. Dosing was not selected to align with realistic application rate but to serve the purposes of comparing screening tools. Other parameters for FOCUS-PELMO GW using the conservative scenario 'Hamburg' (sandy soils with low organic matter, which also represents a larger surface area of the EU compared with some of the other FOCUS GW scenarios) are indicated in the table footnotes.

***Table 4.5: Drinking or groundwater concentrations [µg/L] for an example chemical at various degradation half-lives in soil and partitioning ($K_{oc}$) values for an application rate of 1000 g/ha (per year as a single application)***

| **Half-life in soil (days)** | **$K_{oc}$ (L/kg)[a]** | | | | | |
|---|---|---|---|---|---|---|
| | **50** | **100** | **500** | **1000** | **5000** | **10000** |
| | | | **SCI-GROW** | | | |
| **1** | 0.0008 | 0.0006 | 0.0003 | 0.0002 | 0.0001 | [b] |
| **10** | 0.0470 | 0.0357 | 0.0183 | 0.0136 | 0.0069 | [b] |
| **60** | 1.2812 | 0.6447 | 0.1220 | 0.0588 | 0.0107 | [b] |
| **120** | 3.5477 | 1.5732 | 0.2185 | 0.0920 | 0.0122 | [b] |
| **180** | 6.3251 | 2.6111 | 0.3045 | 0.1188 | 0.0132 | [b] |
| **500** | 26.5167 | 9.1633 | 0.6933 | 0.2238 | 0.0160 | [b] |
| **1000** | 69.3327 | 21.2864 | 1.2042 | 0.3422 | 0.0182 | [b] |
| | | | **FOCUS-PELMO GW** | | | |
| **1** | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| **10** | 0.134 | 0.008 | <0.001 | <0.001 | <0.001 | <0.001 |
| **60** | 55.900 | 20.600 | 0.104 | <0.001 | <0.001 | <0.001 |
| **120** | 151.000 | 77.800 | 2.360 | 0.098 | <0.001 | <0.001 |
| **180** | 217.000 | 130.000 | 8.970 | 0.643 | <0.001 | <0.001 |
| **500** | 353.000 | 278.000 | 72.400 | 13.200 | <0.001 | <0.001 |
| **1000** | 407.000 | 345.000 | 150.000 | 34.200 | <0.001 | <0.001 |

[a] For FOCUS-PELMO GW $K_{oc}$ entered with a 1/n =1 (see footnote on next page)

[b] Values of $K_{oc}$ greater than ~5000 L/kg give non-variable results so upper range not used; it should be noted that values in this category will result in significantly lower groundwater concentrations than those with a $K_{oc}$ of 5000 (L/kg)

FOCUS GW was run with the following additional parameters:

Crop: winter cereals, application 4 May, no interception

Chemical properties: solubility 1000 mg/L, volatility 0 Pa, Molecular weight 300, $Q_{10}$ 2.58, no plant uptake

Scenario: Hamburg

It is clear from the data in Table 4.5 that although the absolute concentrations vary considerably, the pattern of potential leaching (drinking water/groundwater concentrations) is effectively similar. The potential for chemicals to reach groundwater is influenced by half-life in soil and $K_{oc}$. Although, tempting, it is not possible to provide an absolute cut-off for where leaching is no longer possible. This is due to the fact that application rate controls the magnitude of the concentrations predicted with both models. The influence of application rate is presented in Table 4.6 with SCI-GROW data. Similar results are obtained with FOCUS GW (data not shown). Unless factors such as solubility are exceeded, modelled groundwater concentrations will be approximately linearly related to application rate[15].

***Table 4.6: Variation of drinking water concentrations with increasing application rate (SCI-GROW)***

| **Application rate (lb/ac)[a]** | **Drinking water concentration (µg/L)** | |
|---|---|---|
| | **$K_{oc}$ 5000 L/kg, half-life 1 d** | **$K_{oc}$ 500 L/kg, half-life 180 d** |
| 0.00892 | 0.0000009 | 0.00304 |
| 0.0892 | 0.000009 | 0.0304 |
| 0.892 | 0.00009 | 0.304 |
| 8.92 | 0.0009 | 3.04 |

[a] Note SCI-GROW only accepts pounds/acre (lb/ac) as input. 0.892 lb/ac ≈ 1 kg/ha (hectare)

### 4.7.3 Case study conclusion

The conclusion of this case study illustrating the REACH and PPP approach is that any attempt to provide a simple cut-off for drinking protection that ignores the interaction of routes of exposure, application or emission rates, degradation in soil and mobility is misleading and would fail to provide the required level of certainty when applied to a wide range of chemicals.

## 4.8 ECETOC Tiered approach

### 4.8.1 Summary

Considering the regulatory tools currently available under REACH, the BPR and PPPR that cover a range of potential refinements, a tiered approach to characterising potential human exposure from contaminants in drinking water has been developed by the Task Force. A tiered approach enables the results obtained from lower tiers to inform the required resources and methodologies for higher tiers (Embry *et al.*, 2014). The tiered

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[15] FOCUS GW uses data from the Freundlich adsorption isotherm ($K_{foc}$ and 1/n values) to correct the adsorption as concentration in soil changes.

approach includes key information discussed in previous chapters for their relevance in collectively informing the potential for exposure in drinking water, which are use patterns, compartments of environmental release, release rates, as well as fate and partitioning properties.

Screening level exposure assessment including tools such as the GUS index, SCI-GROW and GWWL need to be used and further developed to consider the interaction of degradation, mobility and partly also emission resulting either in an exposure index or an expected worst-case concentration if emission is considered. If necessary, modelling approaches such as the EUSES type model support the identification of those substances with insignificant concern for indirect exposure of humans via drinking water. Those substances requiring further iterations in the risk assessment procedure would be examined using higher tier assessments, e.g., refined emission rate predictions, increased environmental fate understanding or the use of higher tier models.

It is recognised that for many substances (e.g., ionisable substances) the use of $K_{oc}$ or $K_{ow}$ to describe mobility is not appropriate (see Section 3.3.3). Currently, appropriate tools are not available to address these shortcomings and this should be a priority for future research. For example, the partitioning of ionisable substances may be examined using soils with a range of cation exchange capacity (CEC), soil pH, clay content etc. (see Section 3.3.3) in order to develop an appropriate normalised metric.

Here a tiered approach for the exposure and risk assessment of drinking water is proposed (Figures 4.4 and 4.5). After the initial screening (Tier 0), those substances with significant potential to migrate to drinking water move to Tier 1 modelling which focuses on the routes of exposure for drinking water including from groundwater and surface water via bank filtration. The EUSES model may be used to identify the worst-case exposure via surface water or groundwater as the source of drinking water. This Tier 1 level risk assessment can be used for screening of substances with sufficient data. The Tier 1 assessment may also include iterations in the assessment procedure with the use of refined information on use patterns and associated emission pathways (emission rate predictions), as well as inclusion of additional information on relevant environmental fate and distribution processes of the chemical in the relevant exposure compartment. The Tier 1 assessment will also guide the relevant route of exposure to be considered at higher tiers.

A Tier 2 assessment aims to increase the realism in the exposure assessment. FOCUS GW is a higher tier approach that could be applied to estimate the transport from soil to groundwater where sufficient data exists. A higher tier exposure assessment method to characterise fate in bank filtration has not been validated to date, thus is identified as an area for research. The case study described in Section 4.7 suggests scenarios where surface water would be predicted by EUSES to represent a worst-case exposure concentration for soluble, low volatility substances. The German UBA have developed a simple estimator based on pre-defined ‘mobility classes’ implemented in a spreadsheet model EXPOSIT (BVL, 2017) which is only used for National registrations of PPPs. Specific approaches such as the SiMBaFi database model developed for the evaluation of pharmaceutical active substances (Zippel *et al.*, 2010) and the DROPLET model for the evaluation of PPP were not included in the review. However, these models should be considered for the appropriate exposure scenario development e.g., predicted exposure in drinking water from bank filtration.

Iterations in the exposure assessment in groundwater at Tier 3 may include use of refined information on the level of emissions onto soil, the fate and partitioning information from measured data and/or the characteristics of the soil compartment.

### 4.8.2 Tier 0 screening for the transport potential / mobility to drinking water sources

The first stage of the proposed tiered assessment (Figure 4.4), Tier 0, builds on the UBA proposal, but it first examines the suitability of the substance for consideration as a potential groundwater contaminant. Exposure to drinking water exceeding the level of concern may occur if significant releases to the environment occur. The potential for significant exposure might be excluded based on use information, e.g. intermediates, closed systems. However, screening assessment would benefit from a scoring system as proposed for evaluation in the Cefic LRI research project (ECO 54[16]). The second step is to identify the substance and examine its structure and existing measured physical-chemical data. If the substance cannot be characterised e.g., it is classified as a UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substance, then it cannot be assessed as a whole for potential to migrate to drinking water and will not be identified in any standard monitoring program. Therefore, the assessment needs to focus on constituents of concern. Whilst it is recognised that components could potentially reach drinking water it is not currently practical to consider this possibility. Should the UVCB substance contain a suitable representative component or surrogate then this can be considered in the scheme. The next step examines the substance to assess if $K_{oc}$ is likely to be suitable for predicting its mobility in soil/sediment/sewage sludge. If the substance has ionisable groups at environmental pH values (typically pH 5-8), then the $pK_a$ should be examined (which is especially relevant for weak acids that can be present in molecular form or as anions which hardly sorb in natural soils due to the negative charge of the soil matrix). Ideally this should be based on measured data. However, this is often not available and has to be estimated (see Section 3.3.3). Typically, pH values 2 log units either side of the $pK_a$ indicates the ionisable group will be almost completely ionised or non-ionised (depending upon the moiety of the molecule e.g., acid or base). However, pH values 1 log unit either side of the $pK_a$ indicate approximately 10% ionisation and is consistent with the UBA approach, so a $pK_a$ range of pH 4-9 is considered reasonable. If the substance is predicted to ionise at environmental pH values, then a single $K_{oc}$ is not considered adequate for predicting the mobility of the substance (see Section 3.3.3).

Mobility of ionisable substances is still an area of research. However, the partitioning of ionisable substances may be examined by testing the adsorption behaviour in soils which cover a broad range of properties that can influence the sorption behaviour such as cation exchange capacity (CEC), soil pH, clay content etc. (see Section 3.3.3). This can be used to develop an appropriate metric (e.g. $K_{clay}$, $K_{CEC}$, etc.) that is normalised to one or several factors that were identified to influence the sorption. Potential research may include the use of more realistic sub-surface soil/sediment with low organic matter/carbon, using realistic aqueous phase with appropriate pH and mineral content (see Section 3.3.3). Correlating the observed partitioning with properties other than organic carbon (e.g., clay content) may yield more helpful normalisation methods for such a substance. Other issues relevant for sub-surface soils include questions such as, can biotic and abiotic degradation rates be combined with partitioning at low substance concentrations, and what effects do

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[16] LRI ECO 54: DEVELOPING A TIERED MODELING FRAMEWORK IN SUPPORT OF RISK ASSESSMENT OF CHEMICAL SUBSTANCES ASSOCIATED WITH MOBILITY CONCERNS https://cefic-lri.org/projects/eco-54-developing-a-tiered-modeling-framework-in-support-of-risk-assessment-of-chemical-substances-associated-with-mobility-concerns/

temperature and environmental conditions relevant to groundwater have on the processes? Once more knowledge is gained, then it may be feasible to develop and validate new models based on a better mechanistic understanding.

In the meantime, it is not scientifically valid to assume these substances fit the $K_{oc}$ models sufficiently to be recommended, but where this is done it should be recognised that the uncertainty of the predictions will be very high.

For non-polar, hydrophobic, substances the use of $K_{oc}$ is considered generally suitable for predicting partitioning in surface soils, except for those with very low OC content. As discussed in Section 3.3.3, the use of high-quality measured data is preferred.  In the absence of measured values, then the use of predicted values may be used. The mobility metrics have been discussed in more detail in Section 3.3.3.

The mobility and soil degradation half-life are considered in combination in Tier 0. Ideally a suitable estimation of the exposure would be included to prioritise those substances most likely to migrate into groundwater. As discussed in Section 3.3 the use of $K_{oc}$ alone to predict mobility is not recommended due to the high uncertainty associated with this metric. Alternative approaches using indices are described in Section 3.4. The Task Force considers the use of suitable indices to be more appropriate for initial screening in Tier 0. Those substances with a low potential for reaching groundwater e.g., ‘non-leachers’ with GUS <1.8, are no longer considered a risk for groundwater. In the GWWL approach the available (eco)toxicity data are also considered and where a risk has not been identified the substance is given a low priority. If monitoring data suggests a potential exposure, then more detailed investigation would be warranted. Such substances would be included in the higher tiers described below.

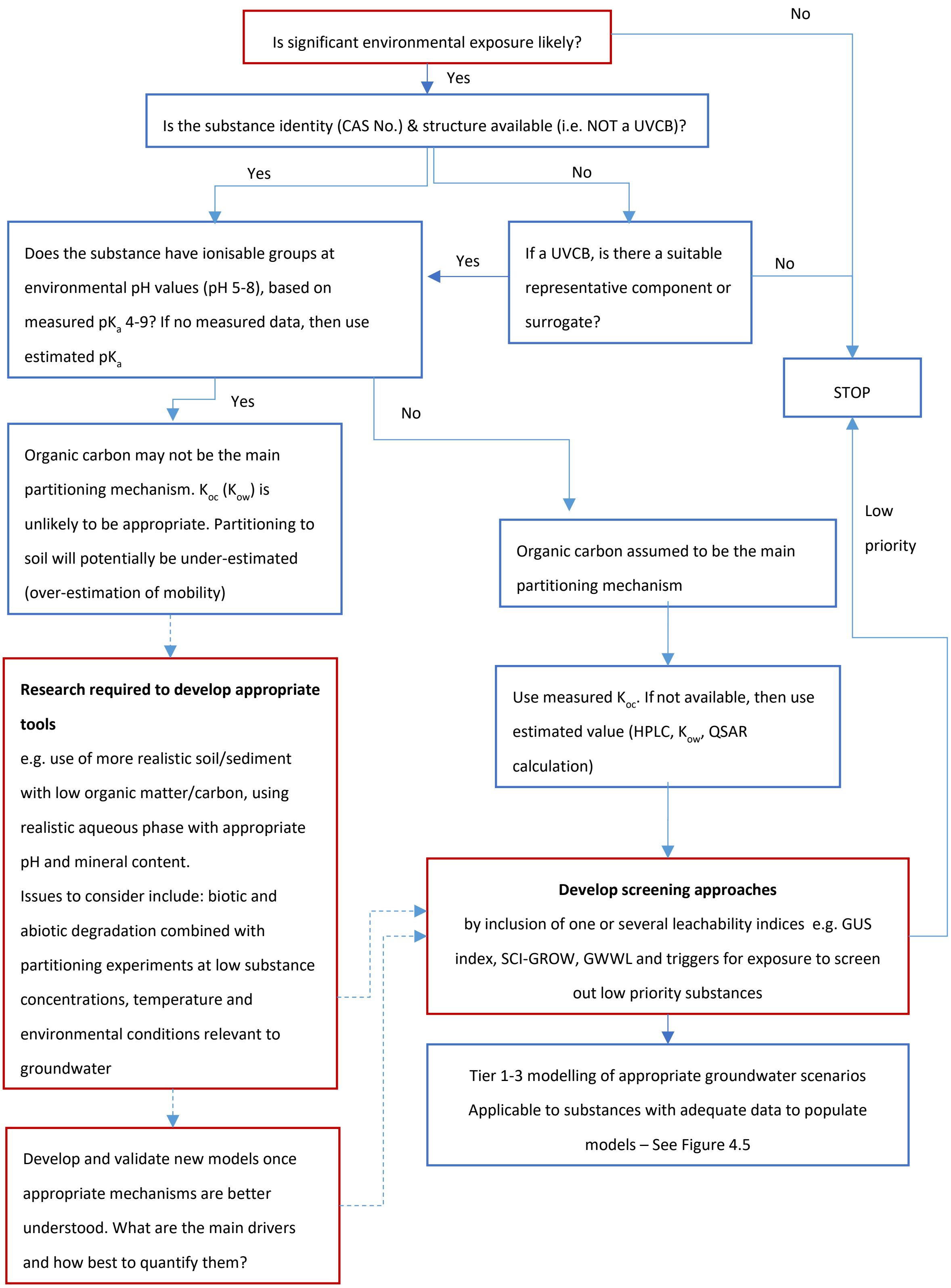

***Figure 4.4: ECETOC tiered approach for assessment of drinking water safety: Tier 0 screening for mobility in groundwater. Boxes in red point to science gaps, for which additional research is required***

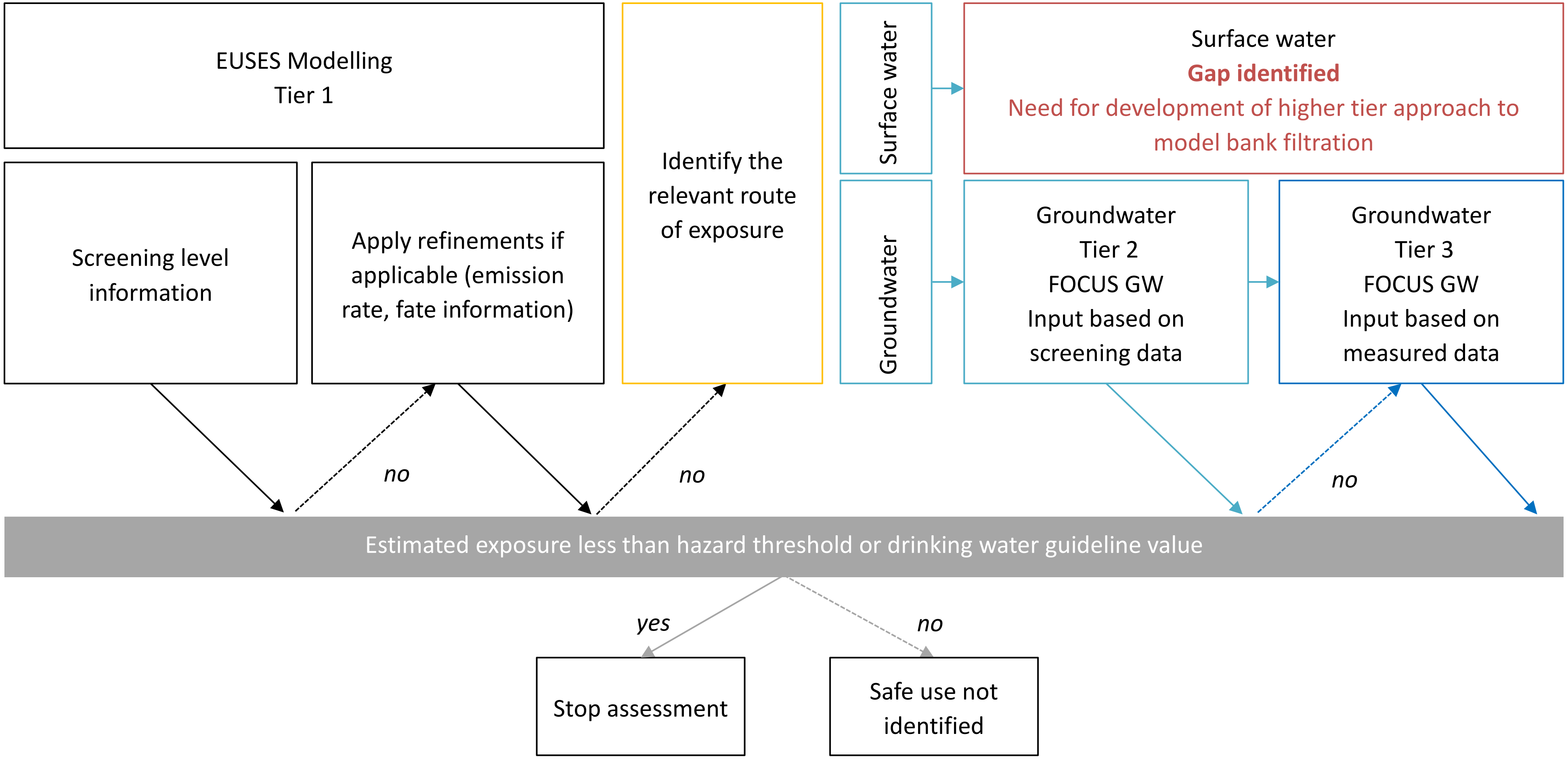

***Figure 4.5: ECETOC tiered approach for assessment of drinking water safety: Tier 1, 2 and 3 exposure modelling***

### 4.8.3 Exposure scenario for Tier 1 assessment of drinking water

The EUSES model addresses routes of exposure relevant to the Tier 1 level assessment of industrial chemicals and biocides to support environmental risk assessment, as well as indirect exposure of humans via the environment. The Tier 1 environmental exposure assessment can be refined by inclusion of additional or more specific information to characterise the release to the different environmental compartments and/or to inform fate and partitioning properties. The source of drinking water considered in the EUSES model is untreated groundwater or treated surface water, although purification of surface water for substances with a log $K_{ow}$ ≤4 or Henry's law constant >100 Pa $m^3$/mol would not be considered in the screening assessment. There is therefore limited information on the relevance of the current approaches to river bank filtration used as natural attenuation. Consequently, groundwater or surface water predictions serve as worst-case screening level assessments. This is discussed in detail in Section 4.6.

As acknowledged, the characterisation of exposure in drinking water sources from rivers via bank filtration is an identified area for improvement in the environmental exposure assessment. Discussion of the higher tiers here is focused on the groundwater exposure routes.

### 4.8.4 Exposure scenario for Tiers 2 and 3 assessment of groundwater exposure route

In the context of the prediction of groundwater concentration, a Tier 1 assessment via EUSES is based on worst-case assumptions as described in Section 4.6, while higher tier assessment according to FOCUS GW (see Section 3.4.3) will include information on pedo-climatic characteristics typical of a given European region. As discussed previously FOCUS GW requires a number of input parameters, and these may not be available for all chemicals requiring assessment. The parameters include agricultural use specific parameters such as the crop, application rate and timing, etc. For non-agrochemicals this application information is not relevant but temporal and spatial characteristics of the emission are required. It is therefore proposed that some FOCUS GW scenarios are identified or developed that provide an agreed level of protection. It also needs to be checked how a continuous emission of chemicals onto the soil surface or growing plants can be simulated (e.g., with daily input) or if the total annual emission could be simulated as a single input on a specific day during the leaching period which leads to a conservative estimate of the substance amount that is potentially transported to groundwater. As an example, in this section winter wheat with no interception and an application on the 4 May has been modelled using the Hamburg scenario. An example of an evaluation table is shown in Table 4.7. A soil half-life of 120 days (at 20 °C) and linear sorption was used.

*Table 4.7: Groundwater concentrations (µg/L) for an example chemical at various application rates and $K_{oc}$ values – FOCUS GW, half-life 120 days (at 20 °C) simulated with FOCUS-PELMO*

| **Application rate (g/ha)** | **$K_{oc}$ (L/kg)<br>FOCUS GW output (µg/L)** | | | | | |
|---|---|---|---|---|---|---|
| | **50** | **100** | **500** | **1000** | **5000** | **10000** |
| **100** | 15.1 | 7.78 | 0.236 | 0.010 | <0.001 | <0.001 |
| **500** | 75.5 | 38.9 | 1.18 | 0.049 | <0.001 | <0.001 |
| **1000** | 151 | 77.8 | 2.36 | 0.098 | <0.001 | <0.001 |
| **5000** | 755 | 389 | 11.8 | 0.491 | <0.001 | <0.001 |

It is acknowledged that parameter selection needs to be clearly defined and work will be required to identify a suitable scenario. However, it is envisaged that once these are agreed a series of tables could be produced covering the key $DT_{50}$ values in soil – a simple software tool could automate this. The resultant look-up tables would greatly simplify subsequent assessments. At Tier 3, FOCUS GW could support the exposure assessment in several soil types and dosing conditions.

## 4.8.5 Refinements at Tiers 1, 2 and 3

### 4.8.5.1 Release/application to the environment

The exposure assessment of industrial substances accounts for the uses from multiple applications. Estimates of exposure at the Tier 1 assessment are derived on the basis of generic exposure scenarios for all registered uses. Release pathways and worst-case conservative values of amounts of release are characterised for a wide variety of applications, as reported in SpERC scenarios (Cefic, 2012). Iterations of the exposure assessment at all tiers may include refined characterisation of releases to the environmental all compartments.

### 4.8.5.2 Partitioning in soil

Iteration of the exposure assessment at Tiers 1-3 may include refined partition coefficient input values reflective of the substance partitioning properties and the appropriate environment. In particular, the partitioning in surface soil of non-polar substances may initially be predicted on the basis of the octanol/water partitioning coefficient log $K_{ow}$ or other estimation techniques (see Section 3.4.3). The log $K_{ow}$ (or log $D_{ow}$ between pH 4–9) has been proposed by the UBA to screen for mobility.

As described in Section 3.3.3, for hydrophilic and ionisable chemicals the $K_{oc}$ model is unreliable, particularly (but not exclusively) for soils with low OC contents. As discussed in Section 4.8.2, research is needed to develop suitable descriptors which take into account interactions between these types of chemical and the soil/sediment matrix.

### 4.8.5.3 Degradation

Iteration of the exposure assessment at Tiers 1-3 may include refined degradation input values. Screening assessment typically includes fate information from screening degradation studies. Use of higher tier degradation information, if available, for the relevant exposure compartment should be included where possible. Currently, there are no QSAR models available to predict the rate of degradation of a chemical in soil with any certainty. Availability of data on a similar substance may be considered or additional testing information may be helpful.

It is noted that models discussed in the tiered approach conservatively characterise the transport to groundwater through a model aerobic soil environment restricted to 1 meter depth (with factors lowering the biodegradation rate below the first 30 cm of the topsoil) which may be representative for shallow aquifers, but not representative for many deeper aquifers. Site specific assessments, such as those performed in the context of remediation, consider additional fate processes associated with transport though greater soil depths at which anaerobic processes may become dominant depending on the redox potential (Eh).

## 4.9 Conclusions

Exposure via drinking water is included in risk assessment approaches from the WHO, US-EPA and European regulations. Approaches and the related quantitative models differ as they are aligned to the scope of the required assessments. Models for industrial chemicals take into account the life cycle of the substance by integration of information of use patterns and potential releases, while approaches for PPPs typically focus on the routes of exposures aligned to application to crops.

The potential for transport to groundwater is considered more appropriately evaluated on the basis of information on the compartment of release to the environment, the level of emissions, and the fate and partitioning characteristics of the substance under realistic environmental scenarios. For chemicals reaching groundwater from the application of sewage sludge to land, a prerequisite for potential exposure in groundwater is the adsorption of the substance to sewage sludge and the use of sludge as a fertiliser to land. In these cases, the subsequent desorption from the sludge and further sorption/desorption in the soil layers should be considered. For soil-applied chemicals a mobility cut-off criterion based on soil adsorption ($K_{oc}$) alone is not sufficient to describe the migration of a substance through sub-surface soil layers to groundwater.

Further, mobility in soil is a multifactor property where the potential for degradation in soil and partitioning should be considered together. The predicted concentration in groundwater is also dependent on the rate of application. Predictions of exposure may vary over several orders of magnitude depending on the use pattern and substance properties, so it is recommended to consider a health-based concentration in drinking water, to compare with the exposure concentration.

A tiered approach has been developed by the Task Force. An initial Tier 0 screening level risk assessment, using tools such as the GUS index, SCI-GROW and GWWL, develops the UBA proposal further to include combined degradation and mobility along with an exposure element. In higher tiers, where more refined data are required, a more sophisticated modelling approach is recommended.

Various models are available to provide conservative predictions of concentrations in groundwater. At Tier 1, the EUSES model can provide a conservative estimate of groundwater concentration (assumed as equal to the shallow porewater concentration). Higher tier models from the agrochemical arena are already established and have a proven record for identifying potentially mobile compounds transported from the top soil to groundwater aquifers. These models are considered as suitable higher tier refinement options for the assessment of biocides under the BPR. In a regulatory context, there is the conflict between the need for simplicity of approach for expedience versus complexity for environmental realism. In the tiered approach proposed in Section 4.8, this balance has been considered at each step.

For hydrophilic and ionisable chemicals, the $K_{oc}$ model is unreliable, particularly (but not exclusively) for soils with low OC contents. Research is needed to develop suitable descriptors which take into account interactions between these types of chemicals and the soil/sediment matrix.

The current proposed tiered approach has its limitations since the transport of contaminants via bank filtration systems is addressed in EUSES with a conservative approach and is not addressed in the higher tier models. The route of exposure of surface water to drinking water via bank filtration requires increased characterisation in validated models to support a tiered approach for regulatory decision making in Europe. The need to develop a model to predict the fate of surface water contaminants in river bank filtration has recently been identified as a Cefic LRI research project (ECO 54)[17].

The modelling approaches should also include best practice procedures used in drinking water protection schemes and the efficiencies of treatment methods routinely used for the preparation of drinking water.

**Knowledge Gaps and Research Needs:**

In addition to the needs indicated within Chapter 3,

- Improve comprehension of bank filtration processes with respect to transfer of contaminants to and from water bodies
- Integrate this knowledge of bank filtration into environmental distribution models, such as EUSES
- Review current practices in sludge management and refine default parameters supporting the exposure assessment of industrial chemicals finding their way into soils via sewage sludge application
- Establish set of assumptions and generic hazard and risk scenarios in “look-up” tables to permit higher-tier modelling to be performed on chemicals where higher-tier environmental fate studies are not available.

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[17] LRI ECO 54: DEVELOPING A TIERED MODELING FRAMEWORK IN SUPPORT OF RISK ASSESSMENT OF CHEMICAL SUBSTANCES ASSOCIATED WITH MOBILITY CONCERNS https://cefic-lri.org/projects/eco-54-developing-a-tiered-modeling-framework-in-support-of-risk-assessment-of-chemical-substances-associated-with-mobility-concerns/

- Advance screening test methods and approaches for the mobility assessment of ionisable substances by combining elements of fate and partitioning.

# 5. REVIEW OF MONITORING DATA AND EVALUATION OF PROPOSED P/vP AND M/vM CRITERIA

## 5.1 Summary

Analytical monitoring data in surface and groundwater were used partly as justification of the PMT concept proposed by UBA (Neumann and Schliebner, 2019). Therefore, this section uses many of the same monitoring data, and some recently available studies, to evaluate the relationship between P (persistent) and M (mobile) criteria and the observed exposure (e.g., measured concentrations in surface and groundwater). The available monitoring data were compared with the M criteria, organic carbon normalised adsorption coefficient ($K_{oc}$) or n-octanol/water distribution coefficient ($D_{ow}$ (pH 7)), and against P criteria as either measured biodegradability data (e.g., ready biodegradation test) or *in silico* predicted biodegradation status. The main result was that detection was not correlated with the P or M metrics. This highlights the potential importance of understanding local emission patterns, or heterogeneity in local fate processes. Properties that affect P and M are used in general risk assessments to predict typical exposures, based on typical use. Whilst the proposed P and M metrics may be adequate for preliminary screening of a large dataset of non-polar chemicals, the P and M criteria alone do not seem to be predictive of local concentrations and such screening criteria are expected to result in significant false positives and false negatives.

## 5.2 Introduction

The current PMT/vPvM concept is built on the assumption that substances fulfilling both P and M criteria have the potential to reach sources of drinking water. This chapter aims to test this assumption through the analysis of monitoring surveys of chemical contaminations in surface and groundwater with substances of different degradation rates and $K_{oc}$ / $D_{ow}$ values.

The results derived from well-designed monitoring programs, which are reflective of the real-world environment encompassing all processes and interactions that are encountered under natural conditions. As such, groundwater and surface water monitoring studies are considered to be the highest tier of testing possible. However, they still require careful examination since the local hydrogeology, and application rates, may affect the monitored substance concentrations. As a simple example, if the source (input) and point of abstraction are close together, then high levels of contaminant may well be detected, even for non-persistent chemicals, depending on its mobility over the short distance and time.

## 5.3 Comparison of REACH registered substances detected in UK groundwater with respect to PMT criteria

The concentrations of substances detected in UK groundwater by the Environment Agency (EA) have been published by the British Geological Survey (Lapworth, *et al.*, 2019). The 31 non-ionisable REACH registered substances detected in UK groundwater were assessed by the authors of this report against the UBA proposed PMT/vPvM criteria (Appendix B). These substances were selected as information relevant to the PMT assessment were likely to be available within their REACH registration dossiers. For the majority of the substances, there were no $K_{oc}$ data available so *n*-octanol-water partition coefficient (log $K_{ow}$) data were used. This was considered valid as the substances were non-ionisable substances. Of the 31 substances, 21 (68 %) did not meet the PMT/vPvM criteria. This suggests that these detected substances, that have the potential to become drinking water contaminants in the future, do not fulfil the proposed criteria (false negatives).

## 5.4 Evaluation of detected chemical concentrations in a Swiss riverbank filtration system with respect to P and M criteria

Riverbank filtration is used worldwide as a natural process to produce drinking water with relatively low environmental impact and at low capital costs (Maeng *et al.*, 2011). It has the potential to remove dissolved compounds mainly by sorption and biodegradation as surface water infiltrates through the riverbank (Figure 5.1). However, especially persistent and mobile substances are often not eliminated and end up in the abstracted raw drinking water. The residence time of the water in the bank and connected aquifer before abstraction can range from several hours (Hollender *et al.*, 2018) over days to years and decades (Albergamo *et al.*, 2019) depending on the bank sediment and aquifer characteristics as well as the distance to the well.

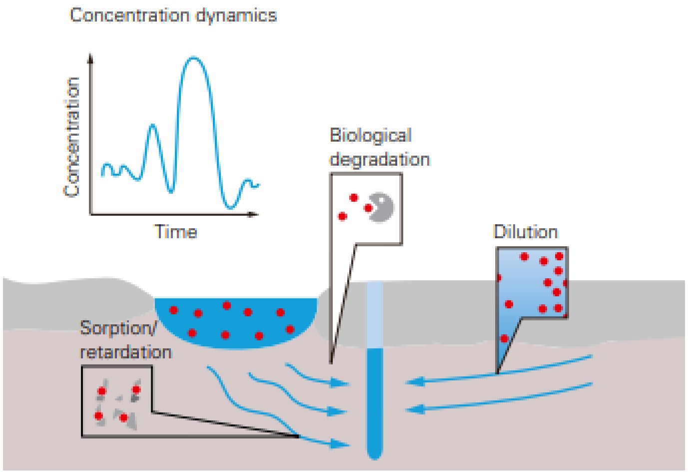

***Figure 5.1: Schematic representation of bank filtration from river to groundwater well, showing key processes that can lead to changes in pollutant concentrations [Source: Reproduced, with permission, from Hollender & Huntscha (2014)]***

Hollender *et al.* (2018) collected measurements in Swiss river water, and nearby groundwater, representing the drinking water abstraction scenario of concern. The target analytes span a range of ionisable organics including pharmaceutical, surfactant, and pesticide molecules. Using JChem[18], log $D_{ow}$ at pH 7.0 were determined based on log $K_{ow}$ and $pK_a$. The log $D_{ow}$ ranged from -5.2 to 6.8. The average concentration data were used to evaluate the relative change in concentrations from the river to the groundwater sampling site. The parameter, $D_{ow}$, is used as a proxy for $K_{oc}$, because it includes the impact of ionisation on the hydrophobic sorption properties, presumed to be the principal sorption mechanism of organic matter in soil. However, as discussed in Section 3.3.3, this presumption may not be valid and may underestimate the sorption in sub-surface soils.

Most quantifiable data are around a ratio of 1, meaning that river water concentrations were the same as those detected in nearby groundwater, with ratios that range from 3 to 0.3, which represent variability in the system. These data show no correlation in the relative fraction with log $D_{ow}$. There are several non-detects across the whole range of chemicals and across all the sites. Notably, all chemicals with log $D_{ow}$ >5 are below detection limits. Approximately 80% of the 543 analytes were not detected in the river or groundwater and are plotted in Figure 5.2 arbitrarily at Ratio $2x10^{-4}$. In some cases, there were measured concentrations in the river, but not the groundwater (Ratio = 0, plotted arbitrarily at 0.002). The frequency of non-detects is approximately the same across the log $D_{ow}$ scale and is considered a reflection of exposure and emissions and not partitioning behaviour. Based on this analysis there is no obvious log $D_{ow}$ cut-off as a proposed PMT criteria.

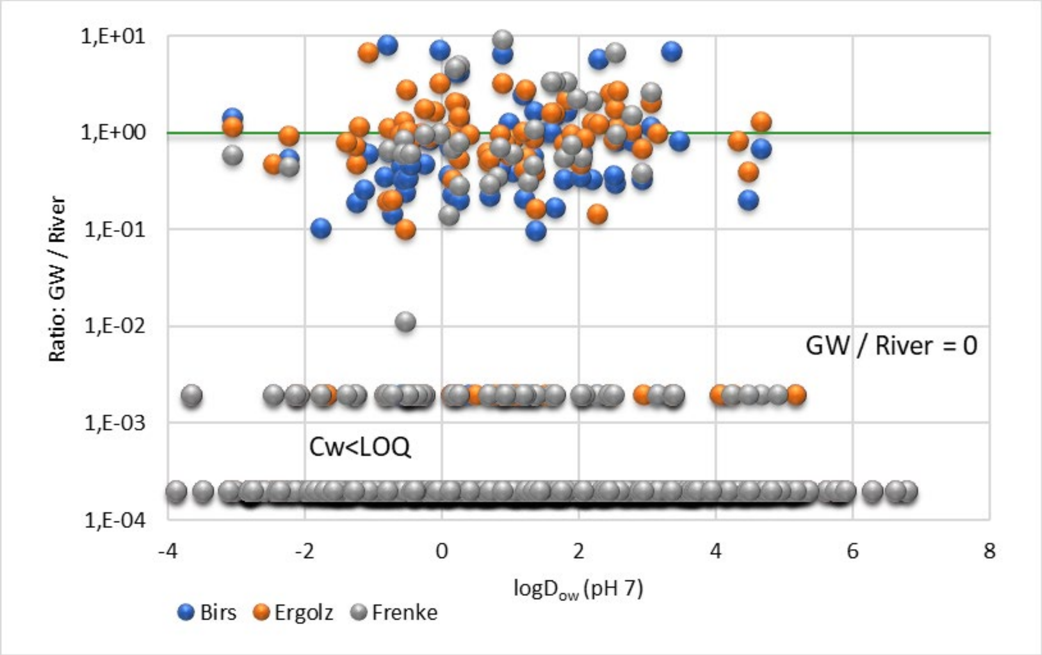

***Figure 5.2: Relative change in the concentration of selected chemicals between Swiss groundwater (GW) and surface water (River) against the log $D_{ow}$ of the molecules. To illustrate the scope of the database, chemicals with no***

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[18] https://chemaxon.com/products/jchem-for-office

***measurable concentrations are plotted at 2x10$^{-4}$, and chemicals with measurable concentrations in river but not groundwater (Ratio = 0) are plotted at 2x10$^{-3}$ [Data source: Hollender et al. (2018)]***

## 5.5 Evaluation of detected chemical concentrations in European groundwater and surface water with respect to P and M criteria

Available monitoring data were compiled from a number of sources and evaluated against common reporting limits for groundwater contaminants (0.1 µg/L) to characterise any trends with respect to log $D_{ow}$ and biodegradation. The monitoring dataset included the Hollender *et al.* (2018) study (Section 5.4), as well as several other studies that characterised concentrations in groundwater or surface waters, which are potential drinking water sources.

The other studies comprised the following:

Loos *et al.* (2009) evaluated concentrations of nearly 40 chemicals (surfactants, pesticides, pharmaceuticals) in 122 rivers across Europe. These constituents spanned log $D_{ow}$ from 0.5 to 5.3 and the average concentrations of these measurements were used in this analysis.

Huntscha *et al.* (2012) evaluated concentrations of 87 constituents in groundwater and surface water. This includes pharmaceuticals, pesticides, and other selected molecules that spanned log $D_{ow}$ from -4.2 to 4.2. The average concentrations of this dataset were used in this analysis.

The British Geological Survey (EA, 2019) collected concentrations in surface water and groundwater on pesticides, pharmaceuticals, and industrial chemicals such as plasticisers. The dataset includes concentration data on more than 50 chemicals from 2010–2019. Only data from 2015–2019 were used in this analysis to reflect recent emission profiles. Also, notably some high molecular weight (MW) plasticisers were detected in samples at or near their solubility limits, which is not reasonable and probably reflects contamination from sampling gear. Therefore, these data will not be used. The final database includes median concentration data for 48 chemicals with log $D_{ow}$ from 0 to 5.

Other studies reporting monitoring data that were used in the UBA reports (Arp & Hale, 2019; Neumann & Schliebner, 2019) were also included. Several of those studies only reported ranges, maximum or average values. Representativeness cannot be assessed with such metrics and they were not included. Moreover, several of those reports were not publicly available. The remaining studies used in the UBA report (Neumann & Schliebner, 2019; Table A1) provided monitoring data from Europe, North America, and other international locations (Kavcar *et al*., 2006; Benotti *et al.*, 2009; Gebbink *et al.*, 2017; Kaboré *et al.*, 2018; Tröger *et al.*, 2018).

Multiple entries of a given chemical for a given site were combined to calculate a median value. These median values were used to evaluate the trends discussed below. Median values were considered representative of typical exposures and were considered the most appropriate metric for evaluating regional characteristics and trends. Maximum measured values can be strongly influenced by local conditions (e.g., proximity to source), and the arithmetic averages of datasets are, likewise, biased by the highest values.

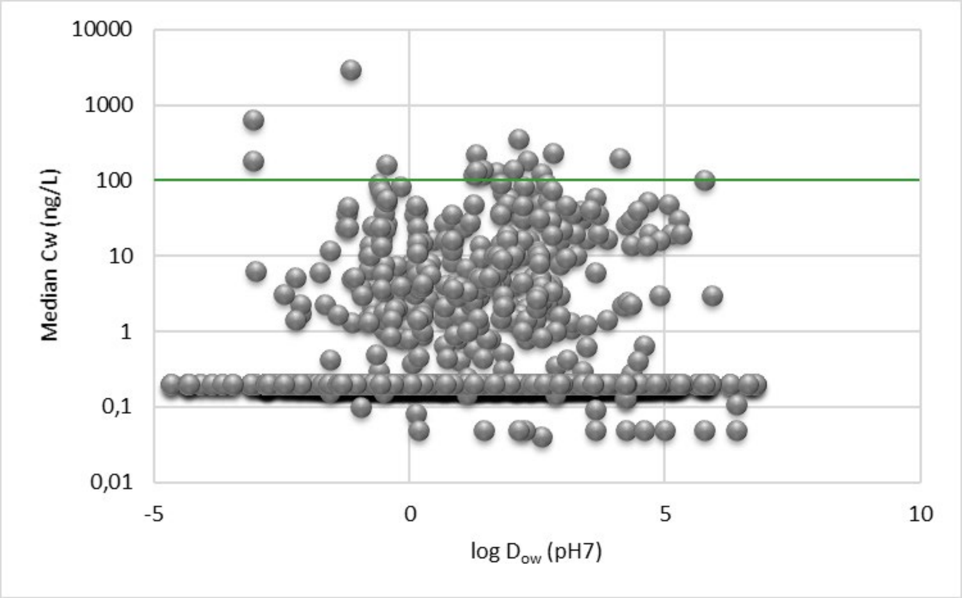

***Figure 5.3: Median concentrations of European groundwater and surface water analytes (Cw) relative a to common drinking water reporting limit of 0.1 µg/L, plotted against log $D_{ow}$. Non-detects are plotted at 0.2 ng/L for reference. [Data source: Monitoring data compiled from a number of sources]***

The compiled dataset of concentrations of chemicals in groundwater and surface waters in Europe were plotted against log $D_{ow}$ (Figure 5.3). The concentrations for these analytes are generally below the reporting threshold for groundwater contaminants of 0.1 µg/L. The concentrations range mostly from 0.001 to 0.1 µg/L with several non-detects (arbitrarily plotted at 0.2 ng/L). This is consistent across the different studies. There are some exceedances of the reporting threshold but there are no obvious trends with respect to log $D_{ow}$. It is notable that most of the median concentrations are lower than the threshold indicating a generally favourable drinking water quality condition in Europe.

These data were further analysed for the frequency of exceedance of the groundwater contaminant reporting threshold. The data (quantifiable and non-detects) were binned into log $D_{ow}$ intervals of 1 log units. The percentages of data that were above the threshold are reported in Figure 5.4. These data often represent an average of several data, which is an obvious source of uncertainty in the analysis. However, this feature is expected to affect the low concentration data as well as the higher concentration data, so it is considered acceptable. This threshold is not related to toxicity thresholds, so this assessment is considered very conservative.

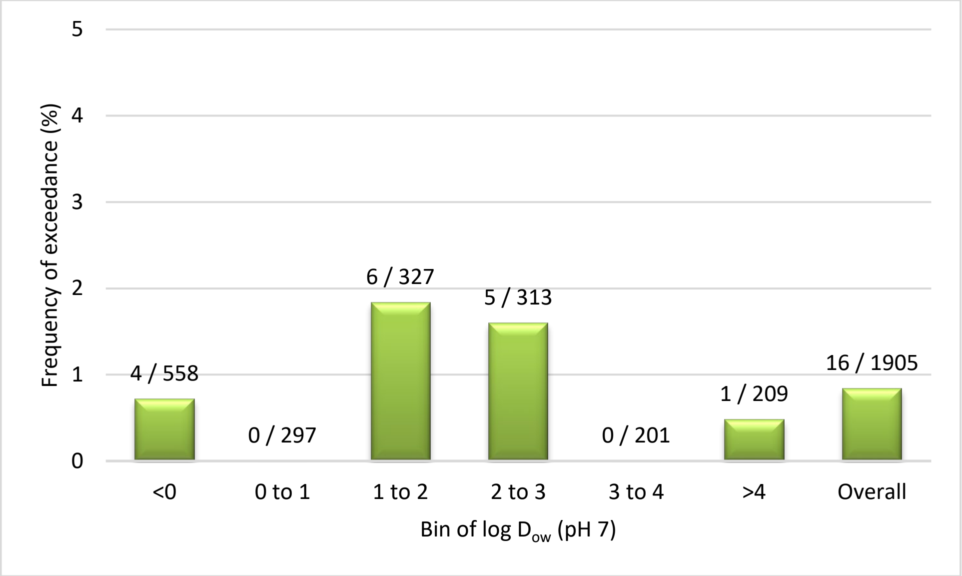

***Figure 5.4: Display of frequency of exceedance of median measured chemical concentrations in European surface water and groundwater (Figure 5.3) relative to the common groundwater contaminant reporting threshold (0.1 µg/L) in log $D_{ow}$ bins. Data labels show the actual counts of exceedances per number of observations in the bin range. [Data source: Monitoring data compiled from a number of sources]***

The frequency of exceedance for lowest log $D_{ow}$ interval (<0) was almost 0.7% of all data in that bin. The exceedance rate varied from 0 to 1.8% in the different log $D_{ow}$ bins. Chemicals with log $D_{ow}$ >4 were generally below the limits of detection. In the entire dataset, approximately 0.8% of all chemicals were detected above the groundwater contaminant reporting threshold of 0.1 µg/L. There is no apparent trend in the observed exceedances against log $D_{ow}$ suggesting that the log $D_{ow}$ as an M criterion is not predictive of typical exposures greater than common reporting thresholds.

This approach used many of the same datasets as the UBA approach but relies on median values as they are considered more typical of actual exposures. UBA used maximum values, which can be affected by local conditions, but simple detection is used as a *de facto* criterium for evaluation as PMT. The result is that 80% of the detected chemicals were suggested as potential PMT/vPvM constituents. The analysis in the present work relies on median concentrations relative to a common groundwater contaminant reporting threshold (0.1 µg/L) as an indication of concentrations that might prompt additional regulatory action (e.g., reporting, management). This reporting threshold was used for convenience and could be refined based on the context of an additional evaluation.

Analysis of this monitoring dataset was extended to include evaluation of the measured exposure as a function of the predicted ready biodegradation potential. The SMILES (simplified molecular-input line-entry system) and CAS numbers for the substances in the dataset were entered into the VEGA tool (Virtual models for property Evaluation of chemicals within a Global Architecture; Pizzo *et al.*, 2013) and resulted in predictions of ready biodegradation potential for about 75% of the database. Some SMILES were not available or were out of the tool's domain. The surface water and groundwater concentration data in Figure 5.3 were re-plotted against log $D_{ow}$ with the inclusion of indications of ready biodegradability (Figure 5.5). This analysis shows that there is no correlation between the ready biodegradability, log $D_{ow}$, and the measured concentrations. For example, all of the data overlap between the different categories. Also, it is notable that most of the data are non-detectable and are plotted arbitrarily at 0.2 ng/L, and the total number of analytes vary between categories. Therefore, in order to account for the number of entries in each category, the fraction of detectable values was calculated and reported in the legend of Figure 5.5. The percent of detectable chemicals varies from 15% to 18% between the different biodegradability categories. This is a very narrow range and the number of observable chemicals is not based on biodegradation potential but based on the sampling design. The VEGA model relies on data from a nearest neighbour to make a prediction. This analysis could be refined using measured ready biodegradation test results (see Section 5.6).

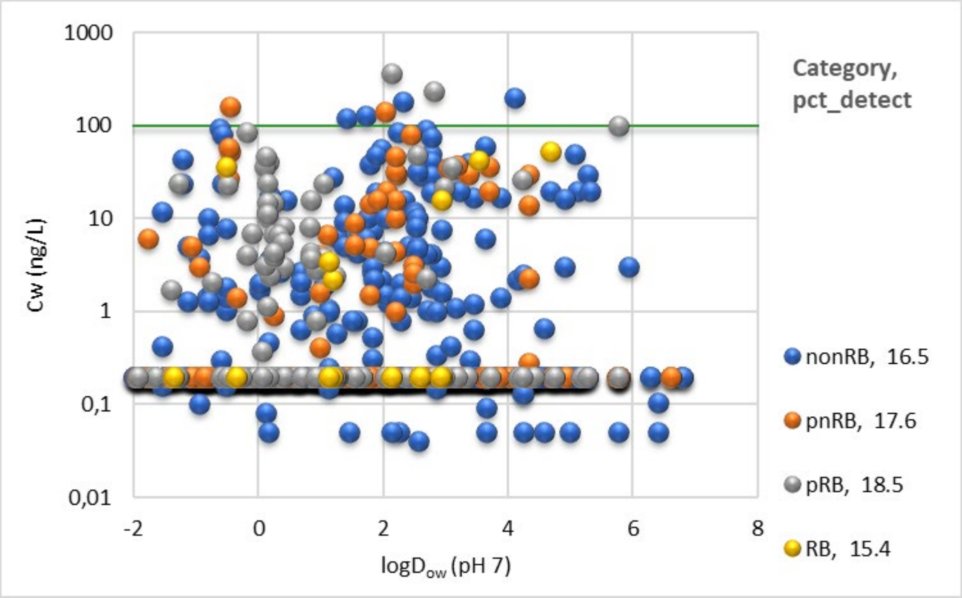

***Figure 5.5: Median measured chemical concentrations in surface water and groundwater (Cw) (Figure 5.3) plotted against log $D_{ow}$ and including indications of their predicted ready biodegradation test status. [nonRB = non readily biodegradable, pnRB = potentially non-readily biodegradable, pRB = potentially readily biodegradable, RB = readily biodegradable]. Most of the measurements show non-detects and to evaluate the impact of the size of each subset of data we report the percentage of chemicals in that category which had quantifiable measurements (pct_detect). [Data source: Monitoring data compiled from a number of sources]***

# 5.6 Evaluation of detected chemical concentrations in groundwater and surface water in England against P and M criteria

## 5.6.1 Data acquisition

### 5.6.1.1 Monitoring data

The Environment Agency (UK) conduct monitoring of surface water and groundwater and maintain a database of the concentrations of detected substances (EA, 2019). The full database was retrieved for this work. However, only data classified as 'Freshwater – Rivers', 'Groundwater – Pit', 'Groundwater – Borehole' and 'Groundwater – Spring' were considered for analysis. This was due to the large size of the data set making further analysis with all data extremely challenging. Any substances that had not been detected in both surface water and groundwater were removed from the dataset as both measurements were critical to this analysis. However, even once these criteria had been applied, the dataset was still considered too large for the purposes of this project. Therefore, data from one area of England was selected. The data from the whole of England was split into small geographic regions to try to maximise the likelihood that the surface water concentration could be related to the groundwater concentrations. The total number of surface water detections and the total number of groundwater detections for each chemical in each of these small geographical regions were compared. The three regions with the smallest difference between the number of groundwater data points and surface water data points were selected. Of these three regions, two regions contained many substances with very different numbers of surface water and groundwater data points, despite the total numbers of each being similar. Therefore, the remaining region was selected to be analysed further. The database includes 62 unique chemicals for which a total of 5600 analytical points (detects and non-detects) have been determined in both surface water and groundwater at various locations. The dataset is included in Appendix C.

### 5.6.1.2 Physicochemical and Environmental Fate data

Degradation and $K_{oc}$ data were retrieved for each of the 62 unique chemicals mentioned above.

It was not possible to find enough data for direct comparison with the P/vP criteria set in Annex XIII of REACH. However, most chemicals had at least one valid ready biodegradability test result according to OECD Test Guideline 301 (OECD, 1992a). The chemicals were thus binned into two categories: readily biodegradable chemicals and not readily biodegradable chemicals. Data on biodegradation were searched for in the following order of priority:

1. Ready biodegradability test result from ECHA disseminated dossier
2. Ready biodegradability test or simulation degradation result from PPP dossiers
3. Publicly available safety datasheet (Google search)

4. Biowin v4.0 (Epi Suite (Estimation Programs Interface Suite), US EPA, 2012) prediction when none of the above was available

Many REACH disseminated dossiers have used QSARs for $K_{oc}$, especially when these are low as this is a valid reason for REACH regulatory data waiving. PPP dossiers often use OECD TG 106, which often yields many different $K_{oc}$ values, among which it was too difficult to assess which one was the most relevant for the current work. For these reasons, $K_{oc}$ of the chemicals were determined by QSAR, using batch mode of the molecular connectivity index (MCI) of KOCWIN v2.0 (Epi Suite; US EPA, 2012). This approach is considered acceptable for this exercise as most screening investigations from UBA on chemical properties largely involved QSARs. However, as discussed in Section 3.3.3, this approach is not recommended. The $K_{oc}$ model is most appropriate for describing sorption of neutral hydrophobic substances to surface soil layers with relatively high organic carbon contents, but the approach breaks down when interactions of substances with the mineral components of soils occur. These interactions become increasingly significant as the organic carbon content of a soil decreases. For hydrophilic and ionisable substances, the $K_{oc}$ model is even more unreliable, particularly (but not exclusively) for soils with low OC contents.

The data on biodegradation and $K_{oc}$ retrieved for the dataset can be found in Appendix C. These data were used in the following Section to evaluate if detected chemical concentrations in groundwater and surface water were explained by the P and M criteria.

### 5.6.2 Concentration limit analysis

Regulation EC 1107/2009 (EC, 2009) sets the analytical reporting threshold of 0.1 µg/L for some pesticides and their metabolites in drinking water. This was therefore used as the concentration limit in this analysis. Exceedance Frequency (EF) is defined as the ratio between the number of detections for a chemical where its concentration exceeds 0.1 µg/L divided by the total number of concentration determinations for that chemical. Thus, each chemical has an EF between 0 and 1 in surface water (SW) and another EF (also between 0 and 1) in groundwater (GW). It was hypothesised that EF would correlate positively with mobility (i.e., EF is an indicator of mobility). For the present work, three EF ranges were arbitrarily considered (0; > 0.33; > 0.67). For instance, if chemical X has an EF above 0.33, this means that more than one third of the measured concentrations of chemical X are above 0.1 µg/L. On this basis, EFs were analysed against biodegradability of the substances and log $K_{oc}$, which is considered a surrogate for mobility. Chemical concentrations measured in surface water (SW) and groundwater (GW) were treated separately.

In order to investigate if there was a relationship between biodegradability, log $K_{oc}$ and EF, three potential log $K_{oc}$ cut-off values (2, 3 and 4) and three arbitrary chosen EF cut-off values (>0; >0.33; >0.67) were considered. Non-readily biodegradable (NRB) (47) and readily biodegradable (RB) (15) chemicals were treated separately. It should be noted that the number of RB chemicals is much lower than the NRB chemicals and may introduce a bias, but this was not investigated further. For each EF cut-off value, the proportion of chemicals that were both above this cut-off value and below each log $K_{oc}$ value was determined as well as the proportion of chemicals that were both above the EF cut-off value and above each log $K_{oc}$ value. If a log $K_{oc}$ cut-off value for mobility exists in this dataset, it should become apparent from (i) a substantial and sustained difference between the two calculated proportions of chemicals along log $K_{oc}$ and (ii) decreasing trends showing that these proportions substantially decrease after reaching this log $K_{oc}$ cut-off. The advantage of this approach is that the analysis is based on EF and $K_{oc}$ and degradation rate classes and not on absolute numerical concentration values where some very low or very high values could imbalance the analysis.

#### 5.6.2.1 Groundwater data

***Non-readily biodegradable (NRB) chemicals***

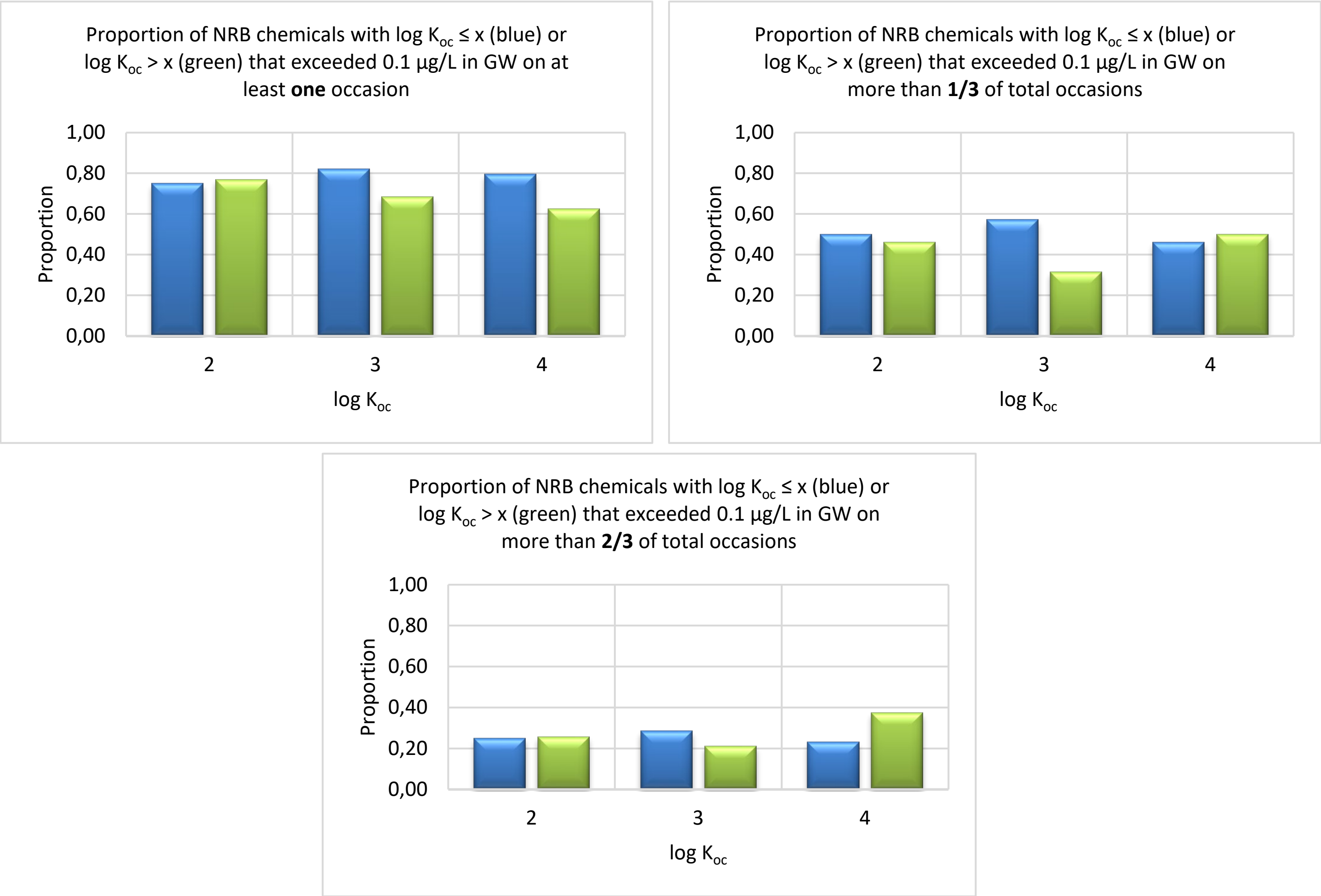

***Figure 5.6: Proportion of non-readily biodegradable chemicals with log $K_{oc}$ ≤ x (blue) or log $K_{oc}$ > x (green) that exceeded 0.1 µg/L in groundwater on at least one occasion (top left), more than 1/3 of total occasions (top right) or more than 2/3 of total occasions (bottom). [Data source: monitoring data compiled from a number of sources]***

Figure 5.6 presents the proportion of non-readily biodegradable chemicals that exceeded 0.1 µg/L in groundwater on at least one occasion, i.e., EF >0, more than 1/3 of total occasions, i.e., EF >0.33 or more than 2/3 occasions, i.e., EF >0.67, according to their log $K_{oc}$ value. On the top left figure, the blue bar at log $K_{oc}$ = 2 means 'Among all NRB chemicals that had log $K_{oc}$ ≤2, 75% had measured concentrations that exceeded 0.1 µg/L on at least one occasion'. The green bar at log $K_{oc}$ = 2 means 'Among all NRB chemicals that had log $K_{oc}$ >2, 77% had measured concentrations that exceeded 0.1 µg/L on at least one occasion'. First and foremost, concentrations above 0.1 µg/L were observed for 40–60% of NRB chemicals that had log $K_{oc}$ above 4. That shows that a substantial number of chemicals with low potential for mobility (high log $K_{oc}$) are detected in groundwater. For all EFs, the proportion of NRB chemicals with log $K_{oc}$ ≤3 that exceeded 0.1 µg/L in groundwater tended to be higher than the proportion of NRB chemicals with log $K_{oc}$ >3. This might suggest a role of $K_{oc}$ in the contamination of groundwater by NRB. However, this trend is not consistently observed for a log $K_{oc}$ cut-off of 2 or 4, showing that the trend observed at log $K_{oc}$ = 3 is an artefact. Log $K_{oc}$ of non-readily biodegradable substances does not appear to explain the groundwater contamination in the geographical area investigated.

***Readily biodegradable chemicals***

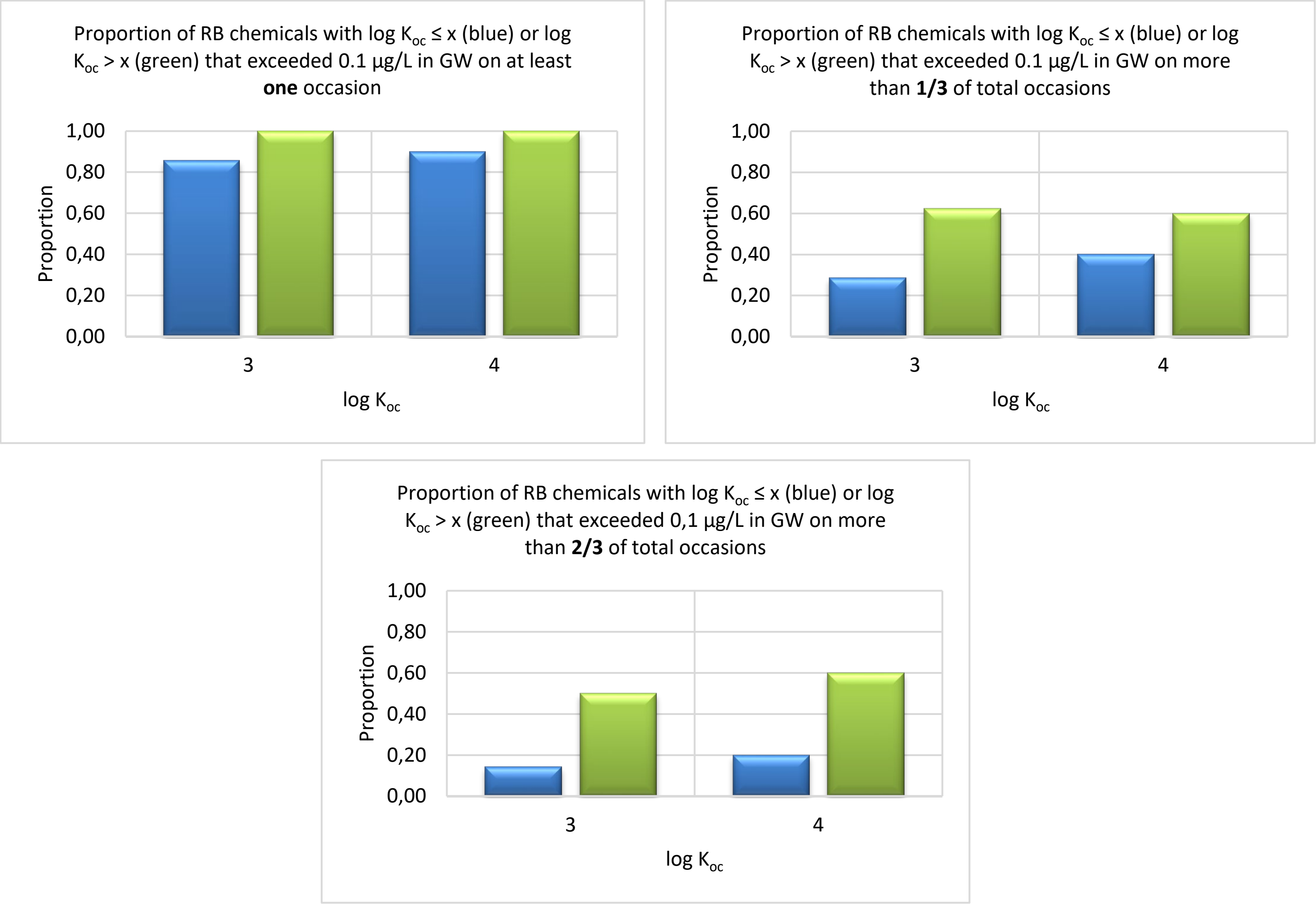

***Figure 5.7: Proportion of readily biodegradable chemicals with log $K_{oc}$ ≤ x (blue) or log $K_{oc}$ > x (green) that exceeded 0.1 µg/L in groundwater on at least one occasion (top left), more than 1/3 of total occasions (top right) or more than 2/3 of total occasions (bottom). [Data source: monitoring data compiled from a number of sources]***

Figure 5.7 presents the proportion of readily biodegradable chemicals that exceeded 0.1 µg/L in groundwater on at least one occasion, i.e., EF >0, more than 1/3 of total occasions, i.e., EF >0.33 or more than 2/3 occasions, i.e., EF >0.67, according to their log $K_{oc}$ value. It is striking that most of the readily biodegradable chemicals investigated exceeded 0.1 µg/L in groundwater on at least one occasion. This is notably more than for NRB chemicals. This was an unexpected result with regards to the ready biodegradability property of the chemicals.

In addition, readily biodegradable chemicals reached groundwater much more often above log $K_{oc}$ values of 3 or 4 than below these cut-off value. This analysis shows that biodegradability and $K_{oc}$ are not necessarily appropriate predictive criteria of groundwater contamination.

### 5.6.2.2 Surface water data

***Non-readily biodegradable chemicals***

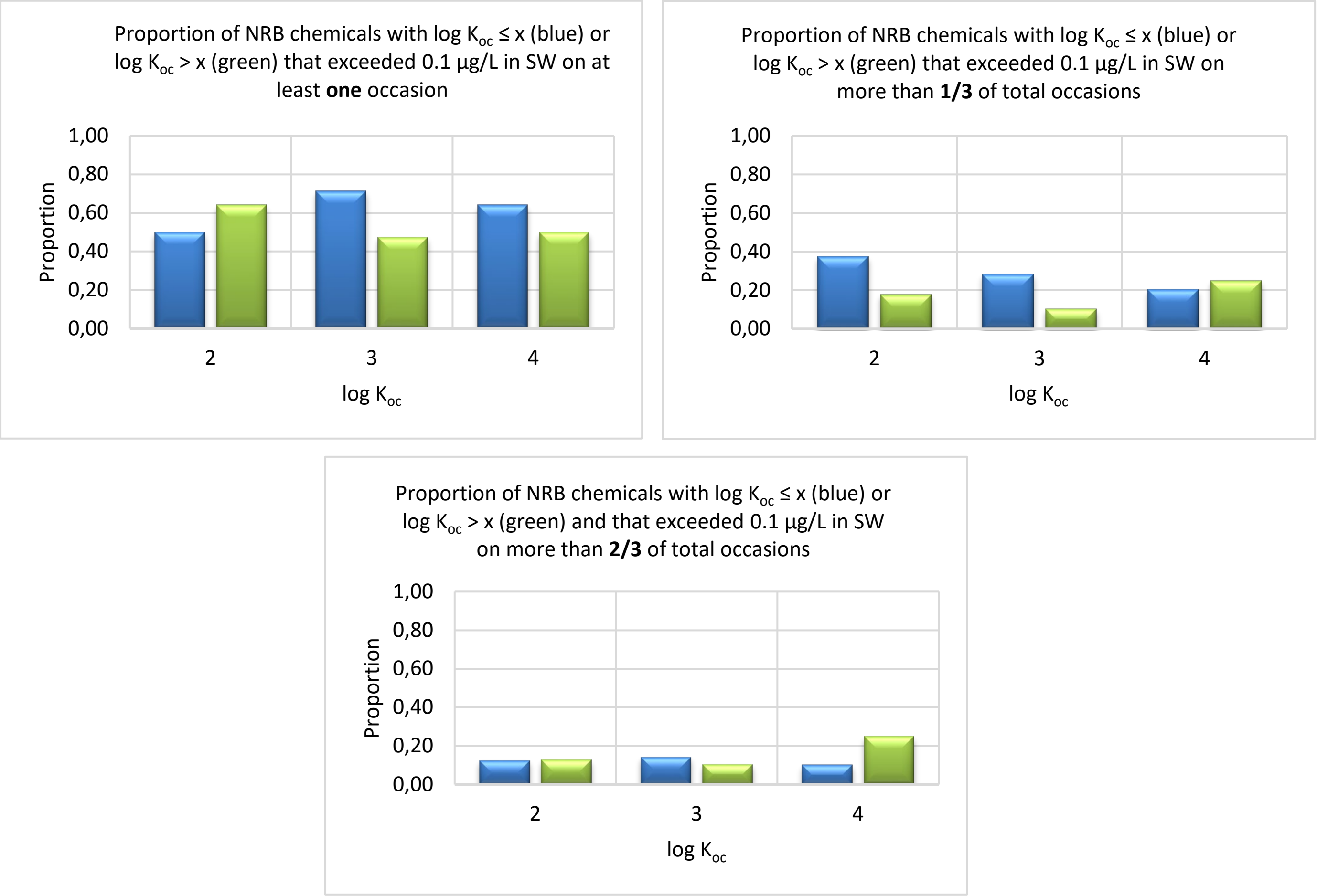

***Figure 5.8: Proportion of non-readily biodegradable chemicals with log $K_{oc}$ ≤ x (blue) or log $K_{oc}$ > x (green) that exceeded 0.1 µg/L in surface water on at least one occasion (top left), more than 1/3 of total occasions (top right) or more than 2/3 of total occasions (bottom) [Data source: monitoring data compiled from a number of sources]***

Figure 5.8 presents the proportion of non-readily biodegradable (NRB) chemicals that exceeded 0.1 µg/L in surface water on at least one occasion, i.e., EF >0, more than 1/3 of total occasions, i.e., EF >0.33 or more than 2/3 occasions, i.e., EF >0.67, according to their log $K_{oc}$ value. The proportions of NRB chemicals that exceeded 0.1 µg/L at various EF and were found in surface water was similar to the respective proportions found in groundwater. Concentrations above 0.1 µg/L were observed for 20–50% of NRB chemicals that had log $K_{oc}$ above 4. This shows that a substantial number of chemicals with low potential for mobility according to $K_{oc}$ are encountered in surface water. As for groundwater, the proportion of NRB chemicals with log $K_{oc}$ ≤3 that exceeded 0.1 µg/L in surface water tended to be higher than the proportion of NRB chemicals with log $K_{oc}$ >3. However, this trend was not observed systematically for a log $K_{oc}$ cut-off of 2 or 4, showing that the trend observed at log $K_{oc}$ = 3 is an artefact. Log $K_{oc}$ of NRB substances did not appear to explain the surface water contamination in the geographical area investigated. In conclusion, there is no indication that low log $K_{oc}$ is a major driver of surface water contamination for this set of NRB chemicals in the geographical area investigated.

***Readily biodegradable chemicals***

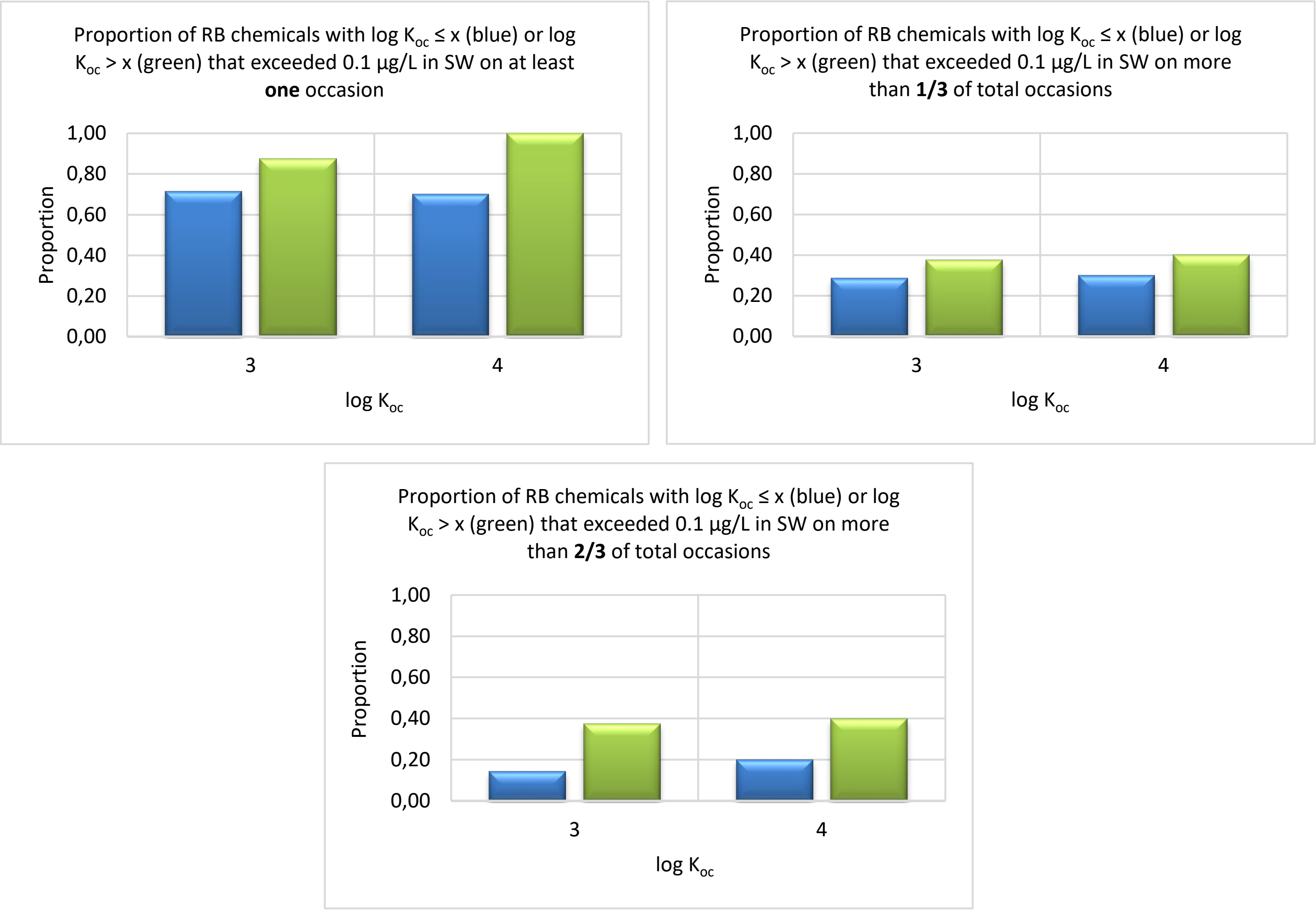

***Figure 5.9: Proportion of readily biodegradable chemicals with log $K_{oc}$ ≤ x (blue) or log $K_{oc}$ > x (green) that exceeded 0.1 µg/L in surface water on at least one occasion (top left), more than 1/3 of total occasions (top right) or more than 2/3 of total occasions (bottom) [Data source: monitoring data compiled from a number of sources]***

Figure 5.9 presents the proportion of readily biodegradable (RB) chemicals that exceeded 0.1 µg/L in surface water on at least one occasion, more than 1/3 of total occasions or more than 2/3 occasions according to their log $K_{oc}$ value. As for groundwater, most of the readily biodegradable chemicals investigated exceeded 0.1 µg/L in surface water on at least one occasion. RB chemicals reached surface water more often above log $K_{oc}$ values of 3 or 4 than below these cut-off value. This analysis shows that biodegradability and $K_{oc}$ are not necessarily appropriate predictive criteria of surface water contamination.

## 5.7 Conclusion

The analysis presented in this chapter utilised several available monitoring datasets to evaluate the scientific basis of the proposed P and M criteria (Neumann and Schliebner, 2019). The first analysis used multiple datasets to evaluate the role of log $D_{ow}$ at pH 7 (as a proxy for log $K_{oc}$) in the ratio of surface water to groundwater concentrations to evaluate potential for obvious cut-offs (e.g., potential increases in the ratios vs log $D_{ow}$). The general observation was that there was no correlation with log $D_{ow}$ below 5.0. A second analysis was performed to evaluate the frequency of exceedance in typical concentrations against common reporting limits (0.1 μg/L). This analysis also indicated no strong trend in exceedance frequencies with log $K_{oc}$ and that exceedance frequencies were generally low (<4%). A third analysis was performed to establish if properties such as biodegradability and $K_{oc}$ were key drivers of the presence of chemicals in surface water or groundwater.

According to the UBA mobility concept, log $K_{oc}$ is assumed to drive the extent of contamination by chemicals that fulfil the P criteria set under REACH. However, the analyses presented in this chapter did not show any indications that log $K_{oc}$ is a major factor of groundwater or surface water contamination by readily or non-readily biodegradable chemicals. In addition, it was observed that a high proportion of the readily biodegradable chemicals have been detected in both groundwater and surface water.

It is concluded that P and M criteria alone are not sufficient for predicting surface water or groundwater contamination. Tonnages, emissions, exposure pattern and routes of exposure may be major additional factors at play. The PMT/vPvM approach would fail to capture many contaminants (e.g., bisphenol A (BPA)) and would needlessly capture many others. The simple criterion of a threshold $K_{oc}$ value is too simplistic and does not consider the complex sorption behaviour chemicals can undergo in soils and sediments or the loading or application rate of the chemicals. Alternative approaches to the simplistic mobility criterion of $K_{oc}$, such as leaching indices, screening models and more sophisticated process-oriented leaching or groundwater models with appropriate scenarios should be considered in a tiered assessment. This conclusion has been developed further in Chapter 4.

**Knowledge Gaps and Research Needs:**

In addition to the needs indicated within Chapters 3 and 4,

- Additional in-depth analysis of robust groundwater monitoring data with the aim of identifying principle influencing factors leading to detects under natural, environmental realistic conditions.

# 6. CONSIDERATION OF METABOLITES IN THE CONTEXT OF THE PMT CONCEPT AND PROTECTION OF WATER SOURCES VIA RISK ASSESSMENT

## 6.1 Summary

The PMT/vPvM concept is proposed for application to REACH registered substances only, which typically represents the class of industrial chemicals excluding other chemicals such as pharmaceutical and agrochemicals active ingredients or food and feed additives. Within this concept, metabolites/transformation products are considered as relevant if a 0.1% threshold is reached or even passed (Neumann and Schliebner, 2019). Higher tier biodegradation tests, as described within the OECD 307 (OECD, 2002b), 308 (OECD, 2002a) and 309 (OECD, 2004b) Test Guidelines (TGs), are considered as relevant for the identification and quantification of metabolites of REACH-registered substances where both readily and inherent biodegradation tests (i.e., OECD TG 301 (OECD, 1992a) and 302 TG series (OECD, 1981a, b; OECD 1992b)) failed to demonstrate an adequate rate of biodegradation. However, the thresholds for a relevant metabolite as indicated in the TGs differ significantly from the threshold proposed in the PMT/vPvM concept. For industrial chemicals, the OECD TGs 307, 308 and 309 suggest that the expected environmental concentration of a substance should be tested. Taking this into account, the evaluation of a representative data set of REACH registered substances, revealed predicted environmental concentrations (PECs) typically in the range of 0.01 to 10 µg/L, which corresponds to a 0.1% (w/w) metabolite concentration of 0.01 to 10 ng/L.

Furthermore, adequate (measured) monitoring data of a large number of candidate substances under the EU Water Framework Directive revealed measured environmental concentrations ranged from 0.00001 to 2.7 µg/L, 0.0005 to 12.5 µg/L and 0.0005 to 20 µg/L for the median, 90th and 95th percentile, respectively (Carvalho *et al.*, 2016a). Taking again a 0.1% (w/w) metabolite threshold into account, this would result in typical metabolite concentrations in the range of 0.01 to 0.1 ng/L. For many water-soluble substances no adequate analytical method is available which allows for both sample concentration and analytical measurement of such low concentrations.

Both the EU and the US plant protection regulations consider 10% of the applied parent (or 5% if technically feasible) as a common limit for metabolite identification and risk assessment since identification and quantification at levels below this limit would be practically difficult. Also, the EMA guidance for environmental risk assessment of pharmaceuticals requires an evaluation of the risks of metabolites that are ≥10% of the applied parent (EMA, 2006).

The presence of naturally occurring metabolites may interfere with concentrations released from man-made productions and thus requires a more detailed analysis on a case-by-case basis.

Taking into account that mobile substances are likely to be hydrophilic and resulting metabolites are likely to be even more hydrophilic than the parent, the formation of NERs (Non-extractable residues) would be expected to be rather low. However, formation of NER very much depends on the functional groups present in the metabolite and the environmental matrix and may form more NER than expected. Nonetheless,

formation of NER is a significant process which limits translocation of chemical substances through soils and sediments. This would mean that concentrations of hydrophilic substances and their metabolites in drinking water may be significantly lower than the 0.1 µg/L threshold for drinking water.

## 6.2 Introduction

It has been proposed that the PMT/vPvM concept shall be applied to REACH registered substances (Neumann & Schliebner, 2019). Within this concept, a threshold for relevant metabolites/transformation products similar to the criteria under the ECHA PBT/vPvB concept of 0.1% (w/w) was proposed (Neumann & Schliebner, 2017). However, as analytical limits of quantification (LoQ) of substances are very much driven by the analytical methods used and the concentrations to be measured in standardised OECD simulation degradation tests, a fixed threshold 0.1% may not be appropriate in all cases. Therefore, the current chapter focused on the evaluation of how and when relevant metabolites should be considered within the PMT concept as well as in the context of protection of water sources via risk assessment. The evaluation of this approach is structured into the following sub-chapters:

- Which % concentration of metabolite is appropriate to consider
- Identify what is known from Plant Protection Products Regulation guidance regarding relevant metabolites
- Consider common/naturally occurring metabolites
- Consider increased mobility versus NER formation

Within the REACH guidance, biodegradation screening tests (i.e., OECD 301 TG and 302 TG series) are considered as suitable for PBT/vPvB screening. In cases where those tests fail to demonstrate an adequate biodegradation of the substance (i.e., at least readily biodegradable failing 10-day window or inherently biodegradable), a more detailed assessment of the degradation profile (i.e., determination of half-life for both parent and transformation/degradation products, quantification and identification of relevant metabolites) is required. For this purpose, three OECD TGs are recommended, covering three environmentally relevant compartments such as water (OECD TG 309), water-sediment (OECD TG 308) and soil (OECD TG 307). Besides some recommendations on the relevant metabolite concentrations, these test guidelines also provide useful recommendations on the typical/maximum test substance concentrations to be tested. Nevertheless, it should be mentioned that in some cases (i.e., some biocides), toxicity towards bacteria or other microorganisms may limit the maximum concentration of a substance to be tested in such a simulated biodegradation study. In other cases, higher substance concentrations may alter the kinetic degradation profile of the substance, influence adsorption characteristics or be above the water solubility limit.  In simulation studies, the applied dose should be conservative, yet realistic, and be in-line with the predicted environmental concentrations or the stipulated application rate in the case of directly applied substances (e.g., plant protection products).

## 6.3 Evaluation of relevant metabolite threshold concentrations

The OECD test guidelines No. 307, 308 and 309 were used to evaluate the suitable test concentration within simulated biodegradation studies, which could then be considered as a starting point for the evaluation of possible relevant metabolites taking into account the 0.1% threshold for relevance.

In addition, estimated environmental concentrations (PECs, i.e., in surface water) for various REACH registered industrial chemicals were evaluated and critically discussed with respect to its usefulness for the estimation of environmentally relevant metabolite concentrations.

Available monitoring data from the European Commission Joint Research Centre (JRC) monitoring based exercise of substances of concern within the European Water Framework Directive (WFD) were evaluated with respect to the measured environmental concentration range for the 90th, 95th percentile and mean values.

Based on the given measured concentration range for these WFD listed substances, estimated concentrations were calculated for the corresponding metabolites (0.1% level).

This section also collates and evaluates decisions by ECHA and its Board of Appeal (BoA) on Community Rolling Action Plan (CoRAP) substances under PBT/vPvB scrutiny with respect to the 0.1% threshold for relevant metabolites.

Based on the recommendations from the OECD test guidelines for simulated degradation tests, plant protection products should be tested at the maximum applied dose/application rate in both soil and water-sediment systems (OECD, 2002a,b; 2004b). For all other chemicals, the expected environmental concentrations in the relevant compartment should be used as maximum concentration (Table 6.1).

In some cases, the test guidelines allow also for higher concentrations (>100 µg/L) to be tested for the purpose of identification and quantification of major transformation products at a level of ≥10% (w/w of parent); however, given the fact that the pelagic test version of the OECD TG 309 contains an especially low bacterial density, the quantification of any transformation product may not reflect a more realistic degradation scenario at environmentally relevant concentrations due to the limitation of available bacteria in surface water.

***Table 6.1: Comparison of test set-ups of simulated degradation test guidelines according to OECD***

| OECD test guideline | 307 | 308 | 309 |
|---|---|---|---|
| Substrate | Soil | Water-sediment | Water |
| Max. duration (d) | 120 | 100 | 60–90 |
| $^{14}C$-requirement | Yes | Yes | (Yes) |
| Measurement of mineralisation as | $CO_2$ | $CO_2$ (aerobic)/$CH_4$ (anaerobic) | $CO_2$ |
| Bound residues considered | Yes | Yes | Not addressed within this TG |

| OECD test guideline | 307 | 308 | 309 |
|---|---|---|---|
| Test concentration | a) For crop protection products: max. application rate.<br>b) For general chemicals, the application rate should be estimated based on the most relevant route of entry.<br>For example, when the major route of entry is via sewage sludge, the sludge is dosed at a concentration that reflects the expected sludge concentration and the amount of sludge added to the soil should reflect normal sludge loading to agricultural soils.<br>If this concentration is not high enough to identify major transformation products, incubation of separate soil samples containing higher rates may be helpful. | a) For crop protection products: max application rate.<br>b) All other: expected concentration from environmental emissions; It may be necessary to apply higher doses (e.g., 10 times) in situations where test substance concentrations are close to LoD at the start of the study and/or where major transformation products could not readily be detected when present at 10% of the test substance application rate. | a) Concentrations should represent the expected range of environmental concentrations.<br>b) >100 µg/L for identification and quantification of metabolites.<br>c) less than 1–100 µg/L for biodegradation kinetics. |
| Test temperature | A temperature of 20 ± 2°C is recommended for all test substances which may reach the soil in temperate climates. For chemicals applied or released in colder climates (e.g., in northern countries, during autumn/winter periods), additional soil samples should be incubated but at a lower temperature (e.g.,10 ± 2°C).[a] | 10–30°C | Field temperature at collection or standard field temperature, or 20 – 25°C |
| Amount of soil/water | About 50 to 200 g of soil (dry weight basis) are placed into each incubation. | ≥50 g Sediment; water-sediment ratio 3.1 - 4:1. | Option 1: pelagic test (no sediment); Option 2: suspended sediment test: 0.01–1 g/L. |
| Relevant metabolites | ≥10% of applied dose at any time during the study. | ≥10%; or metabolites constantly increasing during | ≥10%; or metabolites constantly increasing during |

| OECD test guideline | 307 | 308 | 309 |
|---|---|---|---|
| | | the course of the study even if 10% is not reached. | the course of the study even if 10% is not reached. |
| Limit of detection (LoD) | At least 0.01 mg·kg$^{-1}$ soil (as test substance) or 1% of applied dose whichever is lower. | At least 0.01 mg·kg$^{-1}$ soil (as test substance) or 1% of applied dose whichever is lower. | At least 1 % of the initial amount applied. |
| Minimum purity of TS | at least 95% | at least 95% | at least 95% |
| Recoveries | Recoveries should range from 90% to 110% for labelled chemicals and from 70% to 110% for non-labelled chemicals. | Recoveries should range from 90% to 110% for labelled chemicals and from 70% to 110% for non-labelled chemicals. | Recoveries should range from 90% to 110% for labelled chemicals and from 70% to 110% for non-labelled chemicals. |
| Treatment of substrate | The soil should be processed as soon as possible after sampling. Vegetation, larger soil fauna and stones should be removed prior to passing the soil through a 2 mm sieve which removes small stones, fauna and plant debris. Extensive drying and crushing of the soil before sieving should be avoided. | Sediment samples and associated water should be collected from the same location. For the anaerobic study, sediment and associated water should be sampled and transported under exclusion of oxygen. The sediment is separated from the water and the sediment wet-sieved to 2 mm. Known amounts of sediments and water are mixed at the desired ratio in the incubation flasks. For the anaerobic study, all handling steps have to be done under exclusion of oxygen. | Start within1 day after sampling; natural water samples should be kept at 4 °C prior to use. |

[a] For active ingredients of plant protection products a temperature of 20°C (soil moisture pF 2) is used in the degradation studies and then the degradation rate is corrected on a daily basis in the models to simulate potential ground and surface water exposure; thus, there is no need for separate studies at lower temperatures (although this is described within the OECD TG 307).

To conclude, the expected environmental concentration of a chemical due to its intended use should be used to select the maximum applied test concentration in a simulation degradation test according to OECD TGs 307, 308 or 309. Adapting test temperatures to higher temperatures (i.e., from 12 to 20 or from 20 to 30°C) would most likely also impact the %-level of transformation products being formed during the course of a simulation degradation study and thus impact the relevance of such a given metabolite. Furthermore, this is likely to have a significant impact on the microbial distribution in the environmental matrix being tested.

For industrial chemicals, the expected environmental concentration is reflected within the substance specific REACH registration dossier as the predicted environmental concentration in the region[19] ($PEC_{regional}$). The $PEC_{regional,\ SW}$ values could be attributed to various types of applications (environmental release categories, ERCs) and were typically in the range of 0.01 to 10 µg/L (Table 6.2). In some cases, lower or slightly higher $PEC_{regional}$ values were predicted. However, these values do not necessarily represent a realistic environmental concentration of a substance for the following reasons:

- The PEC was calculated using a tonnage-based approach (% releases into the environment), rather than an application-based approach
- Similar PECs were derived from substances used in consumer products as well as for substances used in various types of applications (i.e., consumer products versus industrial uses)
- The primary aim of such a PEC derivation under REACH was to demonstrate a safe use of the chemical by its intended use, but not to derive an absolute PEC that is comparable to a measured environmental concentration (MEC).

***Table 6.2: Representative concentration range of calculated regional PEC surface water of > 1000 tonnes/annum substances, registered under REACH****

| Case No | $PEC_{regional,\ SW}$ range [µg/L] | ERC 1 | ERC 2 | ERC 3 | ERC 4 | ERC 5 | ERC 6 | ERC 7 | ERC 8 | ERC 9 | ERC 10 | ERC 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.00001 - 0.0001 | x | x | | | | | x | | | | |
| 2 | 0.001 - 0.01 | | x | | x | | | | x | x | | |
| 3 | 0.01 - 0.1 | x | x | | x | x | x | x | x | x | | |
| 4 | 0.01 - 0.1 | x | x | | | | x | | | | | |
| 5 | 0.01 - 0.1 | | x | | x | | | | x | | | |
| 6 | 0.01 - 0.1 | x | | | | | x | | | | | |
| 7 | 0.01 - 0.1 | x | x | | x | | x | x | x | x | | |
| 8 | 0.01 - 0.1 | x | x | | | x | x | | x | | | |
| 9 | 0.1 - 1.0 | x | x | | x | | x | | x | | | |
| 10 | 0.1 - 1.0 | x | x | | x | | x | | | | | |
| 11 | 0.1 - 1.0 | x | | | | | x | | | | | |
| 12 | 1.0 - 10 | x | x | | x | | x | | x | | | |
| 13 | 1.0 - 10 | x | x | x | | x | x | | x | | | |

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[19] Environmental exposure assessments under REACH are conducted at two spatial scales: local (in the vicinity of the source of release) and regional (a larger nominal area 10% size of EU, which includes releases from all sources in that area)

| **Case No** | **$PEC_{regional, SW}$ range [µg/L]** | **ERC 1** | **ERC 2** | **ERC 3** | **ERC 4** | **ERC 5** | **ERC 6** | **ERC 7** | **ERC 8** | **ERC 9** | **ERC 10** | **ERC 11** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 14 | 1.0 - 10 | x | x |  | x | x | x |  | x |  | x | x |
| 15 | 10 - 100 | x | x | x | x | x |  |  | x |  | x | x |

* Data were taken from confidential information of a subset of 15 REACH registered substances

The PECs calculated within the various REACH registration dossiers reflect a worst case, rather than a more realistic case, and require further refinement by the support of adequate monitoring data only if a risk is indicated. The PEC calculation exercise is limited to surface water and thus does not include $PEC_{soil}$ calculations, simply due to the fact that for $PEC_{soil}$ no adequate monitoring data was available or deemed suitable for the comparison of PEC versus MEC. MEC data for the soil compartment are typically available for active ingredients used in plant protection products, but not for industrial chemicals registered under REACH.

Taking the typical concentration range of the $PEC_{regional, SW}$ as the reference concentration for the test concentration in the OECD 308 and 309 simulation biodegradation tests into account, this would result in a metabolite concentration of 0.01 to 10 ng/L if the 0.1% threshold for relevance were applied. The corresponding limit of quantification (LoQ) required is then estimated to be in the range of 0.001 to 1 ng/L (Table 6.4).

Generally, MECs are not available on an EU-wide or even national level for the majority of industrial chemicals. However, substances which are considered as hazardous to human health and/or the aquatic environment were intensively discussed during the EU Water Framework Directive process (Carvalho *et al.*, 2016a). Substances for further prioritisation were evaluated according to their hazard profile and compared with adequate and reliable (measured) monitoring data. The results from this monitoring were compiled in the JRC draft report, entitled 'Monitoring-based Exercise: Second Review of the Priority Substances List under the Water Framework Directive' (Carvalho *et al.*, 2016a). Overall, this report contains monitoring data for 321 chemical substances such as plant protection products, industrial chemicals, biocides or pharmaceuticals. The monitoring data reflect validated measured concentrations from at least four European countries and thus provides an excellent database for typical environmentally measured substance concentrations within the EU in the aquatic environment. Using the 95th-percentile of the measured concentrations, as suggested within this JRC report, the substance concentrations ranged from 0.0005 to 20 µg/L, whereas the median concentration was even lower (i.e., 0.00001 to 2.7 µg/L; Table 6.3). Although the ECHA 'Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment' recommends the use of the 90th percentile, which is in the range of 0.0005 and 12.5 µg/L (ECHA, 2016a) it does not deviate significantly from the previously mentioned 95th percentile. For the further assessment of the relevant metabolite concentration, the 90th, the 95th percentile and the mean values of the measured substance concentrations were used.

***Table 6.3: Summary of 321 monitored substances within the Water Framework Directive (WFD) monitoring-based exercise report (summarised data from Carvalho et al., 2016a)***

|  | No. of countries | No of sites | No of samples | Median [µg/L] | 90th %ile [µg/L] | 95th %ile [µg/L] |
|---|---|---|---|---|---|---|
| Minimum | 4 | 48 | 51 | 0.00001 | 0.0005 | 0.0005 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Maximum | 23 | 7429 | 147284 | 2.7 | 12.5 | 20 |

Setting a threshold of 0.1% for relevant metabolites as suggested within the current PMT/vPvM concept, would result in a relevant metabolite concentration range of 0.0001 to <100 ng/L. Despite the larger metabolite concentration range, 2/3 of the so-called relevant metabolites would be in the range of 0.01 to 0.1 ng/L (Figures 6.1 – 6.2) and the corresponding LoQ is estimated to be even lower, in the range of 0.001 to 0.01 ng/L (Table 6.4). Furthermore, the data presented in Figure 6.1 and 6.2 shows that the majority of metabolites are expected to be well below current EU drinking water standards for groundwater (i.e., ≤0.1 µg/L) and therefore would imply that any focus on metabolites is misplaced and not necessary in the content of protection of drinking water resources.

***Table 6.4: Overview of typical predicted (PECs) and measured environmental concentrations (MECs) of various chemicals within the EU (summarised data from subset of REACH dossiers (Table 6.2) and WFD monitoring data (Table 6.3)) and calculated 0.1 % metabolite concentrations and optimal limits of quantification***

| Data source | Type of value | Parent concentration [µg/L] | Metabolite concentration (0.1% of parent) [ng/L] | Optimal limit of quantification [ng/L] |
|---|---|---|---|---|
| REACH | PEC | 0.01–10 | 0.01–10 | 0.001–1 |
| EU WFD | MEC | 0.01–0.1 | 0.01–0.1 | 0.001–0.01 |

PEC – predicted environmental concentration; MEC – measured environmental concentration; EU WFD – EU Water Framework Directive

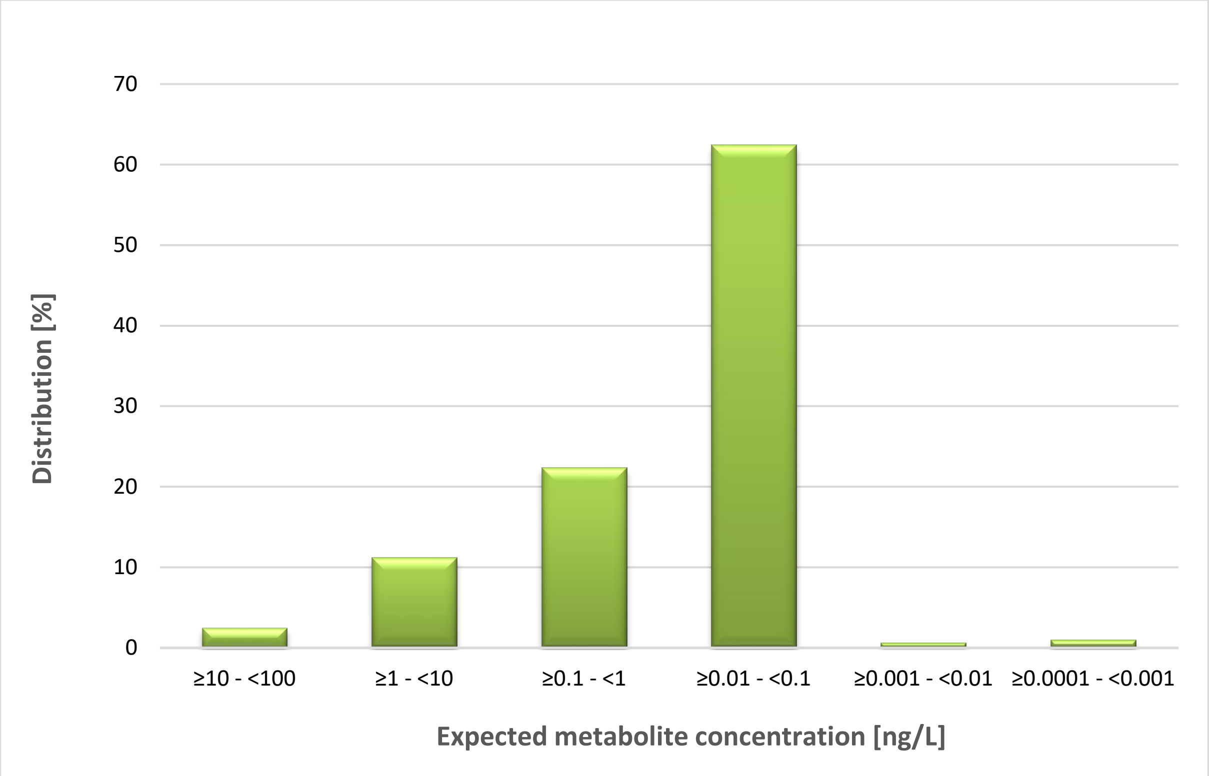

***Figure 6.1: Distribution of relevant metabolite concentrations [ng/L] based on the 95th percentile [Data source: Calculated from WFD monitoring data presented in Carvalho et al., 2016a]***

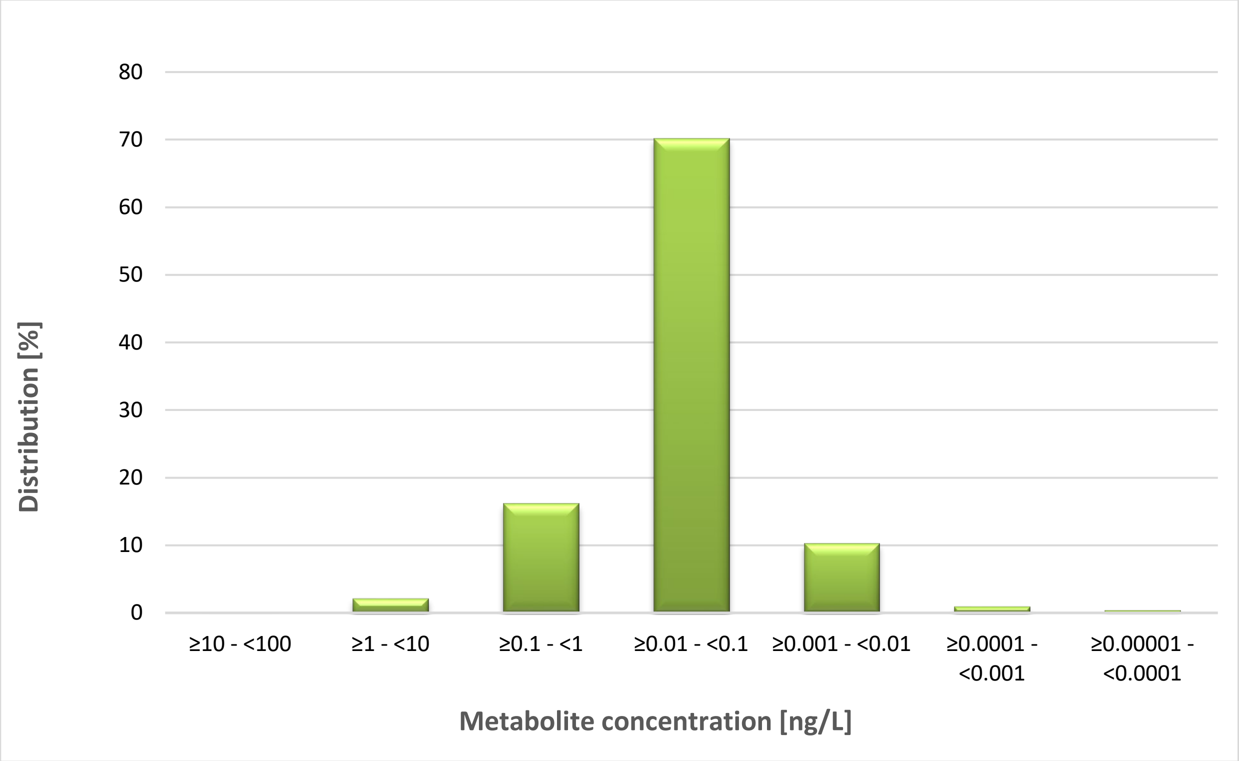

***Figure 6.2: Distribution of relevant metabolite concentrations [ng/L] based on mean values [Data source: Calculated from WFD monitoring data presented in Carvalho et al., 2016a]***

Several REACH registered substances have been included in the CoRAP for several reasons, including PBT and/or vPvB concerns (see also https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table). In several cases, additional data requirements regarding the environmental fate (i.e., simulation degradation tests) have been identified by the evaluating Member State and in agreement with the other Member States and ECHA. The conclusions from the substance evaluations are available via the ECHA homepage and summarised accordingly (Appendix D). In three out of 28 cases, decisions by ECHA were challenged by the applicant(s) and thus reviewed by the ECHA Board of Appeal (BoA) (Appendix D).

The request for additional higher tier degradation data for the various substances of concern includes all three types of simulation degradation tests (i.e., OECD TGs 307, 308 and 309). In the various decisions, the threshold for the identification of relevant metabolites is discussed to be highly variable. In many cases, it is stated that ‘metabolites should be identified at the 0.1% level, unless it can be demonstrated that this is technically not feasible’. However, in some cases, no additional reference (besides citing the OECD test guideline and indicating a test temperature of 12°C) to a relevant metabolite concentration was provided.

In one case, the BoA concluded that the substance properties do not allow for the identification of metabolites down to 0.1% and concluded that the quantification and identification of metabolites should be carried out on a case-by-case basis (BoA, 8 Sep. 2017, Appendix D).

In a recent decision by the BoA, it is stated that the agency (i.e., ECHA) agreed that the 10% threshold for the identification of relevant metabolites should be applied, as it is stated in paragraph 41 of the OECD TG 308 (BoA, 15 Jan. 2019, Appendix D). However, further final decisions have been issued by ECHA, which did not take this decision into account. Either they did not specify the level of relevance or indicated 0.1% as a threshold level for relevance. These discussions continue and it seems that consensus is still to be reached.

### 6.3.1 What is known from Plant Protection Products Regulation guidance regarding relevant metabolites

In the EU, metabolites of agrochemicals are routinely identified in a number of environmental studies including OECD TG 307, 308 and 309, discussed earlier. Identification of metabolites is an intrinsic part of understanding the route of degradation of chemicals in the environment. The threshold for identification is 10% of the applied parent substance (based on maximum annual use) or, if technically feasible, >5% on two consecutive sampling occasions or >5% on the final sampling occasion with an increasing trend of formation, Commission Regulation (EU) No 283/2013 (EC, 2013b) and Commission Regulation (EU) No 284/2013 (EC, 2013c).

All metabolites meeting the trigger levels must be evaluated for environmental safety which includes, for metabolites formed in soil, a prediction of potential groundwater concentrations. Only compounds with a predicted groundwater concentration of >0.1 µg/L (using FOCUS Groundwater models[20]) or that exceed an annual average of 0.1 µg/L in lysimeter studies are considered for relevance. In the EU a relevant metabolite is defined in Regulation (EC) No 1107/2009 (EC, 2009; Chapter 1, Article 3) as:

*'A metabolite is deemed relevant if there is a reason to assume that it has intrinsic properties comparable to the parent substance in terms of its biological target activity, or that it poses a higher or comparable risk to organisms than the parent substance or that it has certain toxicological properties that are considered unacceptable. Such a metabolite is relevant for the overall approval decision or for the definition of risk mitigation measures;'*

The detailed steps to identify relevant metabolites are laid out in Sanco/221/2000 – rev.10 (EC, 2003c). Briefly, compounds predicted to be >0.1 µg/L in groundwater are assessed for comparable biological activity to parent and relevant toxicology. Compounds with significantly less biological activity than parent and which do not reach the toxicological trigger values are deemed as 'non-relevant'. Non-relevant metabolites are permitted in groundwater at levels >0.1 µg/L, although an upper limit of 10 µg/L is suggested, but not implemented in all EU Member States. Metabolites which have significant biological activity and/or exceed the toxicological triggers are 'relevant' and limited to a maximum of 0.1 µg/L in groundwater.

Under this legislation the FOCUS Groundwater models and lysimeter studies are considered at Tier 1. Higher tier studies such as retrospective monitoring or field leaching studies can be used to refine the exposure risk (Commission Regulation (EU) No 283/2013 and Commission Regulation (EU) No 284/2013).

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[20] European Commission, Joint Research Centre, European Soil Data Centre: https://esdac.jrc.ec.europa.eu/projects/focus-dg-sante

In the US[21] minor degradates (those that form <10% of the applied compound) are typically excluded from the residues of concern, with the following possible exceptions:

- Minor degradates approaching 10% of the applied substance at the termination of an environmental fate laboratory study,
- Minor degradates with no observed degradation over an extended period in environmental fate studies, and
- Minor degradates of known or expected ecotoxicological concern:
  - When their toxicity is greater than that of the parent compound, or
  - When two or more degradates are formed, and their sum substantially changes exposure estimates modelled with the Total Residue (TR) method.

Additionally, degradates that are less toxic than the parent compound by an order of magnitude or greater (or the confidence intervals do not overlap or both) are typically excluded from the residues of concern unless they present a substantial exposure concern, such as being particularly persistent and/or demonstrating a potential to accumulate in the environment.

Therefore, for both regulatory regions, EU and USA, the common trigger for metabolite identification and risk assessment is 10% of applied parent or 5% if technically feasible. Furthermore, degradates exceeding 10% are not of concern if they lack relevant toxicity. Identification and quantification at levels significantly below 10% of applied parent would be practically difficult and inconsistent with existing regulations.

### 6.3.2 Consideration of common/naturally occurring metabolites

Cases where a parent or metabolite are the same as a naturally occurring compound make monitoring and evaluation of risk more difficult. Sources of naturally occurring compounds may be highly heterogeneous and environmental levels subsequently very variable. Establishment of baseline levels is therefore challenging. In plant protection a well-known example of this type of compound is 1,2,4-triazole which naturally occurs and has been observed widely in soils. It is also used in a variety of industrial processes as an intermediate. In agriculture the 1,2,4-triazole moiety is incorporated in a large number of active ingredients such as fungicides. A review of approximate production amounts from various sources in Germany is shown in Table 6.5. Based on the estimated yearly production/release volumes, it can be concluded that a significant amount of 1,2,4-triazole resulted from natural sources, which then contribute to any background concentration in a highly variable manner and thus may interfere with standard risk assessment approaches for these chemicals.

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[21] United States Environmental Protection Agency, Memorandum – Guidance for Residues of Concern in Ecological Risk Assessment, December 2012

*Table 6.5: Total annual production/release (tonnes, t) of free[22] 1,2,4-triazole or products containing the 1,2,4-triazole moiety in Germany (2010)*

| | |
|---|---|
| **Agricultural fungicides** | 357.2 t [1] |
| **Wood preservative** | 21.7 t [2] |
| **Antimycotics** | 0.87 t [3] |
| **Fertilisers** | >200 t [4] |
| **Industrial production** | 1000 t [5] |
| **Natural sources (forest)** | 408.4 t [6] |
| **TOTAL** | 1988 t |

[1] Worst-case: based on total of azole fungicides applied in Germany in 2010 (Kleffmann Group, personal communication) and assuming 100% release of 1,2,4-triazole moiety and free availability

[2] Worst-case: based on sales of tebuconazole only for wood preservation in Germany 2010 (Bayer CropScience, personal communication)

[3] Worst-case: based on assumption that all prescribed azole drugs were fluconazole (containing 2 x 1,2,4-triazole) and free availability (data collated by Bayer Pharmaceuticals and ECHA database for the EU)

[4] Based on estimated use of 1,2,4-triazole as a nitrification inhibitor additive for fertilisers (SKW Piesteritz, Germany, 2010)

[5] Detailed data not available but use of 1,2,4-triazole given in ECHA database for the EU is between 1000–10,000 t, 1000 t is assumed for Germany

[6] Worst-case: 1,2,4-triazole formed in natural forest soil measured at the equivalent of approximately 30 g/ha, total based on 11 million ha of forest in Germany (Heinemann, O. 2013. Background Abundance of 1H-1,2,4-Triazole in Selected German Forest Soils – Final, Bayer CropScience AG. Document No.: M-404570-01-1). Note: Other sources such as meadow and grassland not included.

As 1,2,4-triazole is toxic for reproduction, it is deemed a relevant metabolite for the purposes of regulation of agrochemicals containing the structure. Therefore, potential contamination of groundwater is limited to a maximum concentration of 0.1 µg/L. However, other sources are not subject to the same control and therefore could exceed the 0.1 µg/L limit without penalty. This situation is recognised by regulatory authorities but currently no harmonisation of regulations is being considered. However, in order to improve drinking water standards within the EU, it might be more effective to spend time harmonising different existing regulations rather than introducing new screening regulations on PMT/vPvM.

### 6.3.3 Consideration of NER formation and Reduced Mobility

Non-extractable residues (NER) of chemicals are formed through chemical and biological reactions in soil or sediment. They have been the subject of recent consideration in the regulatory context as a mechanism for supporting PBT evaluations (ECHA, 2018). They are of concern due to the hypothetical potential long-term exposure associated with the progressive release of entrapped residues that are unavailable to degraders. The NER fractions remain operationally defined due to the complex chemical nature of NER but are conceptually discussed as ‘entrapped’, ‘covalently bound’, and ‘biomass’. NER quantification requires the use of labelled (normally $^{14}C$) test substances and are normally only elucidated in high-tier environmental fate studies e.g., OECD TG 307, 308 and 309.

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[22] ‘Free’ indicates 1,2,4-triazole moiety cleaved from the parent molecule and existing on its own

‘Entrapment’ refers to low-energy binding mechanisms such as electrostatic interactions, or could refer to diffusion-limited releases such as chemicals trapped in pore spaces that could be released to bulk extraction with agitation. ‘Biomass’ is the result of metabolism that converts the chemicals into biomolecules. ‘Covalently bound’ is operationally defined. The energy in covalent bonds is approximately 10–1000 fold greater than van der Waal’s forces. Plus, true covalent bonds suggest the addition of new ligands, or branches onto the original molecule, which would result in a new molecule with new physicochemical properties.

NER have been studied since the 1960s yet there is still no scientific consensus on how to characterize or address NER (ECETOC, 2013a). All NER extraction methods result in operationally determined NER fractions. Instead of trying to evaluate NER, ECETOC has suggested the focus should be on characterising the bioavailability and risks associated with the residues (ECETOC, 2013a, b). This work also reports that documented scenarios of releases of NER rely on aggressive extraction methods or certain environmental scenarios (e.g., freeze-thaw, wetting-drying). Recent work has advocated a conceptual model and experimental extraction scheme to quantify and speciate various NER fractions (e.g., biomass vs bound vs sequestered) (Loeffler *et al.*, 2020). However, the extraction methods have limited validation in terms of limited number of research laboratories with this expertise and the relatively few chemical classes used in the experimental work. Performance of the method, also, can vary depending on properties of the substance investigated, which will invariably lead to increased uncertainty, inconsistency, and variability in the results. So NER remains operationally defined and given the unique nature of the testing could be costly and uncertain.

NER formation has mainly been studied for plant protection products. Numerous studies have observed that NER formation is much reduced in abiotic control soil samples compared with microbially viable samples which have received the same application rate. This observation points to biodegradation to primary metabolites as the major mechanism in the process of NER formation (Barriuso *et al.*, 2008).

In a purely scientific sense, NER, as the name implies, are defined as irreversibly adsorbed residues of a chemical entity which are not bioavailable in the dissolved phase on a timescale relevant for risk assessment and which cannot be extracted from an organic matrix (soil, sediment, sewage sludge, plant tissue) via the application of non-destructive, harsh extraction approaches (ECETOC, 2013a). NER is operationally often defined as material that is not extracted by different extraction methods.

The current literature has proposed a number of biotic and abiotic release mechanisms for operationally defined NER which may lead to the release and remobilisation of NER. These include microbial release mechanisms ( Khan & Ivarson, 1982; Dec & Bollag, 1988; Dec *et al.*, 1990; Eschenbach *et al.*, 1998), physical and meteorological events (e.g. wetting - drying and freeze - thaw cycles (Fierer & Schimel, 2002; Feng et al., 2007; Jablonowski *et al.*, 2012a; Jablonowski *et al.*, 2012b)) and presence of plant root systems (Fuhremann & Lichtenstein, 1978, Roberts & Standen, 1981, Yee *et al.*, 1985).

The breadth and detail of the available work in this domain remains limited and inter-research comparability is low, with studies having been performed at differing time periods, on different chemistries with varying goals and conclusions (ECETOC, 2013a). Nonetheless, the majority of these studies have suggested that the remobilisation of slowly desorbed or irreversibly bound residues is low and that the moiety released may be rapidly mineralised or degraded by microorganisms. This would indicate that the environmental fraction attributed to NER within a soil profile will not undergo leaching across different horizons. Also, chemical residues that are strongly sorbed to sediment or soil material are not considered relevant for drinking water scenarios.

The experimental and conceptual models are based on data and behaviour from a narrow class of compounds (pesticides), such that broad extrapolation of these ideas to other classes, and exposure scenarios, will result in confusion. Also, the connection between NER and PMT is unclear. Parent material associated with NER will reduce its availability and, therefore, contributes directly to the P assessment. With respect to M, however, NER may be considered immobile within soil and sediment profiles and will reduce its mobility. In this context, the concept of persistency leading to mobility are principles which are in contradiction with one another, and which lends itself to a double accounting effect. Under such an assumption, the NER fraction, which contributes to the overall soil persistence outcome, and, despite being irreversibly adsorbed, is also assumed to be readily available to leach within a soil profile. NER cannot be predicted with any certainty (ECETOC, 2013a) and is not correlated with $K_{oc}$. This suggests that other binding mechanisms are important in the formation of NER but this is not well understood (ECETOC 2013a).

Use of reporting levels (e.g., 0.1 µg/L) as a mechanism to identify potential concerns in drinking water would implicitly address the concern of NER. The measured dissolved concentrations are considered more relevant for risk assessment. Therefore, measured bioavailable concentrations would support drinking water protection more than hypothetical NER concerns.

## 6.4 Conclusion

The evaluation of derived PECs for REACH registered substances, followed by the measured concentrations of selected substances within the prioritisation process of the European Water Framework Directive, clearly indicates that the concentration of relevant metabolites would in many cases fall below any technically achievable analytical limit of quantification (LoQ) if a threshold for relevance of 0.1% of the parent were applied. Although ECHA states in its substance-specific CoRAP decisions for substances under PBT/vPvB-suspicion, that a 0.1% threshold should be attempted, the agency has acknowledged that this threshold might not be achievable due to technical/analytical limitations. In contrast to hydrophobic (lipophilic) substances, hydrophilic substances present a technical challenge since existing analytical methods are only to a limited extent amenable to these substances. Research will be required to develop tools to concentrate, separate and detect such low metabolite concentrations.

In its latest decision, both ECHA and ECHA's BoA (CASE A-004-2017) acknowledged that for the determination of relevant metabolites within an OECD 308 test, the 10% threshold as set within paragraph 41 of OECD TG 308 should be applied and the 0.1% threshold level is not appropriate.

Therefore, it can be concluded that the 0.1% threshold level for the identification of metabolites (so-called relevant metabolites) is not applicable. However, attempts should be made to meet the 10% threshold level criteria as set within the OECD 307, 308 and 309 test guidelines.

Both the EU and the US plant protection regulations consider 10% of the applied parent (or 5% if technically feasible) as a common limit for metabolite identification and risk assessment since identification and quantification at lower levels would be practically difficult. For active ingredients of plant protection products, it is very rare that a metabolite at 5 %AR (applied radioactivity) is not to be identified.

The presence of naturally occurring metabolites may interfere with concentrations released from man-made products and thus requires a more detailed analysis on a case-by-case basis.

Taking into account that mobile substances are considered as rather hydrophilic and resulting metabolites will also be water soluble, theory would suggest that the likelihood of NER formation can be low. However, NER formation may depend on the functional groups in the metabolite molecule and composition of the environmental matrix. Nonetheless, formation of NER is a significant process which limits translocation of chemical substances through soils and sediments. Furthermore, taking into account that 0.1 µg/L has been set as the threshold for drinking water, this will also consider possible releases from NERs into porewater, and the measured concentrations already provide a worst case.

**Knowledge Gaps and Research Needs:**

In addition to the needs indicated within Chapters 3, 4 and 5

- Consensus on definition of a relevant metabolite – at what % of applied dose a transformation product becomes relevant?
- Structural alerts to identify moieties likely to form significant levels of NER
- Development of tools to concentrate, separate and detect low metabolite concentrations.

# 7. APPROPRIATENESS OF THE ADDITIONAL T CRITERIA IN THE PMT CONCEPT AND RELEVANCE TO A RISK ASSESSMENT APPROACH

## 7.1 Summary

The UBA proposal on PMT (Neumann and Schliebner, 2019) has defined additional criteria, beyond those already established by the PBT/vPvB assessment under the REACH Regulation ((EC) No 1907/2006; EC, 2006b), for the toxicity (T) criteria. The justifications for these additional criteria are not clear.

In this Chapter the additional criteria are described and evaluated against existing regulatory requirements. This analysis indicates that current approaches are already conservative and protective. Inclusion of environmental hazards in the T criteria of PMT seems unjustified when the protection goal is human health via potential drinking water contamination. There appears to be no scientific justification or evidence that any additional criteria over and above those set out in Annex XIII of REACH (Criteria for identification of PBT/vPvB substances) will increase protection specifically related to drinking water resources.

## 7.2 Introduction

The German UBA states that although REACH has established PBT criteria it lacks similar criteria for the intrinsic substance properties that may indicate a potential drinking water contaminant of concern (Neumann and Schliebner, 2019). Therefore, UBA considered it necessary to develop T criteria for a PMT concept proposed for implementation under REACH. This would create additional criteria for the T element of PMT compared with the T criteria firmly established under the PBT assessment. Thus, this creates a discrepancy between the two assessments.

The scientific justification for this deviation is unclear. Including additional T criteria for PMT assessment does not make any significant contribution to further enhancing the safety of drinking water, as the suggested additional criteria are largely covered and would be identified through the application of existing definitions and criteria used to identify T properties.

Furthermore, the authors of this report believe the focus of the T criteria should only be on human health aspects, as aligned with the protection goal. Therefore, the ecotoxicity T criteria are excluded and not discussed further in detail but mentioned in the context for endocrine disruption (Section 7.5.4).

In this section of the report the additional T criteria are described and their value assessed by an analysis of existing T classification data.

## 7.3 The T criteria in PBT and PMT

As set out in Annex XIII 1.1.3 of REACH: a substance fulfils the toxicity criterion (T) in any of the following situations:

a) the long-term no-observed effect concentration (NOEC) or Effect concentration 10% ($EC_{10}$; concentration that effects 10% of a population) for marine or freshwater organisms 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 (EC, 2008c);

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 (EC, 2008c).

The additional T criteria as defined by UBA are as follows (Box 7.1):

**Box 7.1: Additional T criteria as defined by UBA (Neumann and Schliebner, 2019)**

‘Beyond these T criteria already now set out in Annex XIII, 1.1.3 of REACH there might be cases, where it is necessary to identify persistent and mobile substances with other hazardous properties posing a risk to human health and the environment. These substances will be addressed as a separate category. In such cases it is proposed to demonstrate according to Art. 57 (f) an overall concern which is equivalent to Art. 57 (a) - (e). Aspects to be considered are comparable to the SVHC-identification for respiratory sensitizers:

- 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, societal concern.

Evidence (so called indicators) for significant risk to human health and the environment for persistent and mobile substances may arise in any of the following situations and need assessment to demonstrate fulfilling the equivalent level of concern of Art. 57 (f).

These indicators are:

(d) the substance meets the criteria for classification as carcinogenic (category 2), or germ cell mutagenic (category 2) according to 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 following Annex I;

(g) the substance acts as an endocrine disruptor in humans and/or wildlife species according to the WHO/IPCS definition of an endocrine disruptor.'

## 7.4 Scientific and regulatory justification

The UBA report (Neumann and Schliebner, 2019) refers to scientific research and consultation that justifies the additional T criteria. However, the report itself does not contain any scientific justification for their addition.

It states, 'Beyond the T criteria set out in Annex XIII, 1.1.3 of REACH there might be cases, where it is necessary to identify persistent and mobile substances with other hazardous properties posing a risk to human health and the environment.' and refers to Matthies *et al.* (2016) for supporting evidence.

The publication by Matthies *et al.* (2016), is a review that describes the development of PBT criteria. Concerning the T criteria, the following is included (Box 7.2):

**Box 7.2: Development of PBT criteria (Matthies *et al.*, 2016)**

'During the development of the first set of criteria under the TGD 2003 revision (EC, 2003a), the EU system was extensively developed regarding human health, while the ecotoxicology scheme was under further development, particularly regarding aquatic chronic hazards and the terrestrial compartment.

Consequently, the T criteria were initially defined through three complementary sub-criteria, covering ecotoxicological studies, identification of chronic toxicity from mammalian studies using the classification and labelling scheme, and a 'safety net' covering endocrine disrupters and other evidence for long-term effects.

A case-by-case assessment was proposed for substances classified as CLP carcinogenic category 2 or mutagenic category 2 to decide whether the evidence is sufficient for the substance to be considered as toxic, in the context of this PBT assessment, or whether further information is needed to clarify this potential concern.

The 'safety net' provision was applied "when there is substantiated evidence of long-term toxicity".

Endocrine disrupting effects could be considered as an example of long-term toxicity even though the short-term exposure during a critical period of development resulted in latent effects. Such evidence should be considered on a case-by-case basis for each substance under review.'

Therefore, this reference provides no actual scientific justification for the proposed new criteria. Furthermore, the criteria are covered by guidance, as discussed by Matthies *et al.* (2016), as recommendations proposed on a case-by-case basis and not a regulatory required element of the T assessment. Adding these additional criteria in the current form would go beyond the safety net already provided (EC, 2003a) without a clear scientific justification.

## 7.5 Additional T criteria - Added value to risk assessment and risk management?

This section considers the additional T criteria as proposed by UBA (Neumann and Schliebner, 2019) and as set out in Box 1 of Section 7.3 (d-g).

### 7.5.1 (d) the substance meets the criteria for classification as carcinogenic (category 2), or germ cell mutagenic (category 2) according to Regulation EC No 1272/2008

The substances classified as category 2 carcinogens or mutagens do not fulfil the criteria to be considered a substance of very high concern (SVHC) under the REACH Regulation (Article 57). Furthermore, substances with a category 2 classification as a carcinogen and/or mutagen can be approved as active substances under the Biocidal Products Regulation (EC, 2012) and Plant Protection Products Regulation (EC, 2009). Substances classified as category 2 carcinogens or mutagens do fall outside the scope of the Carcinogens and Mutagens Directive (EC, 2014d) and are also allowed in consumer applications. Based on the hazard statements in the CLP (Classification, Labelling and Packaging) Regulation ((EC) No. 1272/2008; EC, 2008c), i.e., 'H351: Suspected of causing cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard' and 'H341: Suspected of causing genetic defects (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)', these substances are 'suspected'. In certain cases, such substances may undergo a higher tier assessment before a final conclusion about their use is reached. In other cases (e.g., industrial use) a standard risk assessment is performed for category 2 carcinogens or mutagens.

It is also relevant to note that the assignment of T is based on the hazard classification of a substance and it does not consider the potency of the substance or the mechanism of action (MoA). For example, a substance may be classified as a category 2 carcinogen because tumours may have been found at very high dose levels, while the tumours may be secondary to a specific target organ (e.g., liver) toxicity. These carcinogenic effects with a threshold and observed at a very high dose level may be irrelevant for a drinking water risk assessment when humans are exposed to a very low amount of a substance.

To propose that category 2 carcinogens or mutagens are T is considered by the authors of this report to be not justified. It would be premature to include these substances in the T category by default without performing an expert assessment on a case-by-case basis that considers elements such as potency, type of effect and relevance for humans. When humans are exposed to substances via drinking water the long-term toxicity should be considered when assessing the risks for humans. Substances which could raise a concern in this case are substances which are classified for CMR (carcinogenic, mutagenic or toxic to reproduction) category 1A or category 1B and substances which are classified with STOT RE (specific target organ toxicity - repeat exposure). This is in agreement with the current T criteria for PBT substances under REACH.

### 7.5.2 (e) the substance meets the criteria for classification as additional category for "effects on or via lactation", according to Regulation EC No 1272/2008

For this additional criterion the impact was assessed by identifying how many substances are classified for ‘effects on or via lactation’ without also a classification as reproductive toxicant in category 1A, 1B or 2 or STOT RE 1 or 2 (which are T criteria under PBT).

The criteria for the assignment of the hazard category for effects on or via lactation, with associated hazard statement ‘H362 (May cause harm to breast-fed children)’, under CLP are as follows (Box 3):

**Box 3: Criteria for the assignment of H362 (May cause harm to breast-fed children) under CLP**

‘Effects on or via lactation are allocated to a separate single category. It is recognised that for many substances there is no information on the potential to cause adverse effects on the offspring via lactation.

However, substances which are absorbed by women and have been shown to interfere with lactation, or which may be present (including metabolites) in breast milk in amounts sufficient to cause concern for the health of a breastfed child, shall be classified and labelled to indicate this property hazardous to breastfed babies.

This classification can be assigned on the:

(a) human evidence indicating a hazard to babies during the lactation period; and/or

(b) results of one or two generation studies in animals which provide clear evidence of adverse effect in the offspring due to transfer in the milk or adverse effect on the quality of the milk; and/or

(c) absorption, metabolism, distribution and excretion studies that indicate the likelihood that the substance is present in potentially toxic levels in breast milk.’

Based on available harmonised classifications (Annex VI to the CLP Regulation[23]) the number of substances classified for 'effects on or via lactation' without also a classification as reproductive toxicant in category 1A, 1B or 2 or STOT RE 1 or 2 is three (out of twenty-five). For one of these three substances the classification is not justified; the other two substances are pesticides:

- For the first one, the data in the REACH dossier shows that the **harmonised classification for 'effects via lactation' is not warranted** (See REACH disseminated dossier Section 'toxicity for reproduction, endpoint summary'[24]).

- The second substance **is the insecticide etofenprox**. The background for proposing the harmonised classification and labelling can be found in the Committee for Risk Assessment (RAC) Opinion[25]. This opinion notes the following points:

    - 'The effects seen in rat offspring indicate a need for classification but given their onset (mainly in the 3rd week of lactation or thereafter), classification for developmental toxicity seems not warranted. A classification for effects via lactation might be more appropriate.'

    - 'In conclusion, there is high transfer of etofenprox into the milk, with clear effects on or via lactation at a dose level considered too high for classification (5000 mg/kg bw/d). There is still evidence, albeit weak, for effects on or via lactation at the next lower dose levels tested (up to approximately 350 mg/kg bw/d). Although no doses between 350 and 5000 mg/kg bw/d have been tested, RAC [the ECHA Committee for Risk Assessment] considered it not unlikely that more severe lactational effects could have occurred at dose levels higher than 350 mg/kg bw/d that are still relevant for classification (up to 1000 mg/kg bw/d). RAC therefore considers classification with Lact. – H362 (CLP) justified. The labelling with R64 is applicable, as the required additional classification for etofenprox under DSD [the EU Dangerous Substances Directive] (Annex VI of DSD, 3.2.8) is present (namely for environmental effects). RAC noted that EFSA [the European Food Safety Authority] in their peer review of etofenprox in 2008 also proposed R64, but no classification for developmental toxicity.'

- The third substance **is the insecticide flufenoxuron.** The background for the harmonised classification and labelling can be found in the RAC Opinion[26]. This opinion notes the following points:

    - The effects on pup survival during the lactation and the presence of flufenoxuron in the milk fulfil the criteria set in CLP.

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[23] https://echa.europa.eu/information-on-chemicals/cl-inventory-database

[24] https://echa.europa.eu/nl/registration-dossier/-/registered-dossier/15252/7/9/1

[25] https://echa.europa.eu/documents/10162/161a383e-75f1-b25e-9e16-0ebd45489e8e

[26] https://echa.europa.eu/documents/10162/73cc3030-7a2f-b4d6-d076-c6e69e10cb47

- ‘decrease of viability and lower pup body weights were observed during lactation in the 2-generation study. The cross-fostering study failed to demonstrate that effect was due to an *in utero* exposure only. The preliminary study failed to demonstrate that effect was due to exposure during gestation and lactation without long pre-gestational exposure of dams. The toxico-kinetic profile of flufenoxuron and the observation of effects linked to Lactation (transfer of flufenoxuron through the milk and/or perturbation of the lactation) support that the effect is likely to be due to flufenoxuron in milk and that a long pre-exposure of dams to flufenoxuron is necessary to accumulate and lead to adverse effect via lactation.’

The Classification and Labelling inventory entries described above can be found using the webpage links in the table below (Table 7.1):

***Table 7.1: Classification and Labelling inventory entries for substances with a harmonised classification (Annex VI to the CLP Regulation) for ‘effects on or via lactation’ without also a classification as reproductive toxicant in category 1A, 1B or 2 or STOT RE 1 or 2***

| Index no | EC / List no | CAS no | Name | Link CLP |
|---|---|---|---|---|
| 602-095-00-X | 287-477-0 | 85535-85-9 | alkanes, C14-17, chloro | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/94445 |
| 604-091-00-3 | 407-980-2 | 80844-07-1 | etofenprox (ISO) | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/74008 |
| 616-206-00-4 | 417-680-3 | 101463-69-8 | flufenoxuron (ISO) | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/109842 |

It is further noted that based on self-classification [by industry] according to CLP the number of substances classified for ‘effects on or via lactation’ without also a classification as reproductive toxicant in category 1A, 1B or 2 or STOT RE 1 or 2 is sixty-five (out of 661). The background and data for these self-classifications is unknown and these 65 substances would require further review to conclude if the classification for ‘effects on or via lactation’ are warranted. For example, there may be multiple entries for one substance with conflicting classifications and labelling reported.

All the other substances harmonised- or self-classified for ‘effects on or via lactation’ are also classified as reproductive toxicant in category 1A, 1B or 2 or STOT RE 1 or 2. It was not evaluated for these substances if these would meet the P or M criteria.

Details of the analysis summarised above can be found in Appendix E.

Overall, the analysis indicates that the addition of the classification category for ‘effects on or via lactation’ to the current T criteria adds limited value to the risk assessment and risk management, since these substances will already be included following the current T criteria. It lends evidence that the T criteria currently in place are sufficient to also capture these substances.

### 7.5.3 (f) the Derived-No-Adverse-Effect-Level (DNEL) is ≤9 µg/kg body weight/d (oral, long term, general population), as derived following Annex I

This criterion is captured by the STOT RE 1 and RE 2 criterion that is part of the current T criteria. In this case, potency is considered since the classification for STOT RE includes, among other criteria, cut-off limits.

The UBA report (Neumann and Schliebner, 2019) notes that the DNEL cut-off within the PMT/vPvM assessment was proposed and justified by Kalberlah *et al.* (2014).

In the review by Kalberlah *et al.* (2014) the following is written:

> *'Substances with a DNEL of ≤9 µg/kg bw/ d (oral, long term, general population) will be regarded as toxic within the framework of this project.'*
>
> *'To keep the T-assessment in line with REACH PBT assessment in regard to human toxicity, compounds classified for STOT RE category 1 or 2 are also regarded as toxic within the framework of this project. Toxicity cut-offs for classification for STOT RE categories 1 and 2 approximately translate in DNEL-like values which are slightly below and above, respectively the cut-off value of 9 µg/kg bw/ d set for the DNEL.'*

The cut-off value of 9 µg/kg bw/d translates approximately to the cut-off limits of STOT RE categories 1 and 2 substances. With such a low DNEL, substances would already be classified in the STOT RE 1 and 2 categories. It is considered that adding this criterion would be of limited value since substances that have this level of potency would already be captured by the STOT RE 1 and RE 2 classification and labelling.

### 7.5.4 (g) the substance acts as an endocrine disruptor in humans according to the WHO/IPCS definition of an endocrine disruptor

The WHO (World Health Organisation)/IPCS (International Programme on Chemical Safety) definition of an endocrine disruptor is as follows:

> 'An exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.'

This definition is incorporated in regulatory frameworks worldwide. As such, it forms the basis for criteria to regulate endocrine disrupting properties under the Biocidal Products Regulation (EC, 2017a) and the Plant Protection Products Regulation (EC, 2018c). This is described in the accompanying ECHA/EFSA guidance document (ECHA & EFSA, 2009), which states the following:

> 'According to the ED criteria a substance shall be considered as having ED properties if it meets all of the following criteria:

> a) it shows an adverse effect in [an intact organism or its progeny]/[non-target organisms], which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;
>
> b) it has an endocrine mode of action, i.e., it alters the function(s) of the endocrine system;
>
> c) the adverse effect is a consequence of the endocrine mode of action.'

REACH regulates endocrine disruptors through the route of SVHC identification (REACH Article 57(f)). An ED expert group[27] has been established at ECHA to give non-binding scientific advice to the authorities supporting REACH. Currently, there is no explicit definition under REACH for endocrine disrupting properties.

As part of the hazard evaluation for REACH all available data must be evaluated in a single weight of evidence approach. If the available data indicates a concern for endocrine disrupting potential, further data generation may be requested. REACH does not currently include specific standard testing requirements for investigation of ED properties. However, many of the toxicological tests that are information requirements at the higher registration tonnage bands provide relevant data for a mammalian evaluation. However, discussions on the potential extension of the standard information requirements to address endocrine disrupting properties for human health and the environment are ongoing. In addition, hazard classes for classification of endocrine disruptors under CLP have been proposed. This will be managed under the auspices of the Competent Authorities for REACH and CLP (CARACAL) sub-group on endocrine disruptors (CASG-ED).

The OECD Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption (OECD, 2018b) advises which studies can be performed to evaluate the endocrine disrupting potential of a substance and investigate its MoA. Test guidelines are organised according to the OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupting Chemicals (OECD, 2018a). This framework consists of 5 levels.

Level 1: Existing data and existing or new non-test information.

Level 2: *In vitro* assays providing data about selected endocrine mechanism(s)/ pathway(s) (mammalian and non-mammalian methods).

Level 3: *In vivo* assays providing data about selected endocrine mechanism(s)/ pathway(s).

Level 4: *In vivo* assays providing data on **adverse effects** on endocrine-relevant endpoints.

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[27] https://echa.europa.eu/endocrine-disruptor-expert-group

Level 5: *In vivo* assays providing more comprehensive data on **adverse effects** on endocrine-relevant endpoints over more extensive parts of the life cycle of the organism.

The last two levels list studies that can be performed to assess if adverse effects occur. The recommended studies for mammalian toxicology are presented in Table 7.2.

***Table 7.2: Recommended studies for mammalian toxicology, listed at Levels 4 and 5 of the OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupting Chemicals (OECD, 2018a), to assess if adverse effects on endocrine-relevant endpoints occur***

| Level 4 | Level 5 |
|---|---|
| Repeated dose 28-day study (OECD TG 407)<br>Repeated dose 90-day study (OECD TG 408)<br>Pubertal development and thyroid function assay in peripubertal male rats (PP male assay) (US EPA TG OPPTS 890.1500)<br>Pubertal development and thyroid function assay in peripubertal female rats (PP female assay) (US EPA TG OPPTS 890.1450)<br>Prenatal developmental toxicity study (OECD TG 414)<br>Combined chronic toxicity and carcinogenicity studies (OECD TG 451-453)<br>Reproduction/developmental toxicity screening test (OECD TG 421)<br>Combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (OECD TG 422)<br>Developmental neurotoxicity study (OECD TG 426)<br>Repeated dose dermal toxicity: 21/28-day study (OECD TG 410)<br>Subchronic dermal toxicity: 90-day study (OECD TG 411)<br>28-day (subacute) inhalation toxicity study (OECD TG 412)<br>Subchronic inhalation toxicity: 90-day study (OECD TG 413)<br>Repeated dose 90-day oral toxicity study in non-rodents (OECD TG 409) | Extended one-generation reproductive toxicity study (EOGRTS) (OECD TG 443)<br>Two-generation reproduction toxicity study (OECD TG 416, most recent update) |

Most of these are the same OECD standard testing methods as required for hazard evaluation under REACH at Annex IX and above. Significant adverse effects observed in any of these studies would lead to a classification as reproductive toxicant category 1A, 1B or 2 and/or STOT RE 1 and RE 2 classification and labelling.

The ecotoxicological studies on endocrine disrupting potential of a substance are not specifically relevant to the protection of drinking water resources. Where these data are lacking, they can still be requested under the substance evaluation procedure via the Community Rolling Action Plan (CoRAP). Typically, these are requested to address concerns identified by the mode of action, findings in the toxicological database or peer reviewed literature.

In summary, according to the WHO/IPCS definition and available testing methodologies, when an adverse health effect is reported from these human health studies a substance would be classified as reproductive toxicant category 1A, 1B or 2 and/or STOT RE 1 and RE 2. Since these hazard classification categories are included in the T criteria currently, the explicit inclusion of Endocrine Disruption as an additional criterion does not add value from a risk management perspective since these effects would already be captured by the existing T criteria. For the environmental assessment additional information can be requested under substance evaluation.

## 7.6 Conclusion

The existing T criteria in Annex XIII of REACH (Criteria for identification of PBT/vPvB substances) cover a range of hazardous substances and include sufficient characterisation to be conservative from a regulatory perspective. Consequently, extending the elements to be considered for T in the PMT concept, as proposed by UBA, would require further justification to support departure from the established assessment.

To extend the T criteria is unnecessary since

- Classification based on hazard is already a conservative and health-protective approach
- The key human health classifications of carcinogenic (C), mutagenic (M) and toxic to reproduction (R) do not take into account any element of toxicological potency, reinforcing this conservatism
- The criteria for T as set out in Annex XIII, 1.1.3 of REACH already fulfil the protection goal to ensure a high level of human and environmental safety
- There is no scientific justification or evidence that any additional criteria over and above those set out in Annex XIII will increase protection specifically related to drinking water

It is further recommended that the focus of the T criteria in the PMT concept should be on human health aspects (the protection goal), excluding ecotoxicity criteria.

# 8. CONCLUSIONS AND RECOMMENDATIONS

Several EU water policies (Water Framework Directive, Ground Water Directive, Drinking Water Directive) aim for the protection of surface, ground, bathing and drinking water. Furthermore, EU chemical regulations for plant protection products, biocides, medicinal products and industrial chemicals (i.e., those registered under REACH) already cover, to a certain extent, groundwater exposure and/or risks to humans via consumption of drinking water, as part of the required risk assessment.

The current PMT/vPvM (persistent, mobile and toxic/very persistent and very mobile) concept developed by UBA relies on property-based criteria for the identification of potential drinking water contaminants. Evaluation of the proposed persistence (P) and mobility (M) criteria concluded that a joint consideration of degradation rates and ability to cross natural barriers (sediment, soil) is desirable to make a scientifically sound prediction of whether a chemical can reach drinking water sources or not. The simple criterion of a threshold $K_{oc}$ value is too simplistic and does not consider the complex sorption behaviour chemicals can undergo in soils and sediments or the loading or application rate of the chemicals. Alternative approaches to the simplistic mobility criterion of $K_{oc}$ such as leaching indices, exposure criteria, screening models and more sophisticated process-oriented leaching or groundwater models with appropriate scenarios should be considered in a tiered assessment.

A tiered approach has been developed by the Task Force. An initial Tier 0 screening level risk assessment, using tools such as the GUS index, SCI-GROW and GWWL, develops the UBA proposal further to include combined degradation and mobility along with an exposure element. In higher tiers, where more refined data are required, a modelling approach is recommended.

For hydrophilic and ionisable chemicals, the $K_{oc}$ model is unreliable, particularly (but not exclusively) for soils with low OC contents. Even for hydrophobic chemicals, the model is not satisfactory at low OC contents. Research is needed to develop suitable descriptors which take into account interactions between these types of chemicals and the soil/sediment matrix.

The current proposed tiered approach has its limitations since the transport of contaminants via bank filtration systems is not addressed in the higher tier models. The need to develop a model to predict the fate of surface water contaminants in river bank filtration has recently been identified as a Cefic LRI research project (ECO 54)[28].

A review and evaluation of existing groundwater and surface water monitoring data via case studies concluded that P and M criteria (as defined by the UBA and based on $K_{oc}$, $K_{ow}$ or $D_{ow}$) alone, are not sufficient for predicting

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[28] LRI ECO 54: DEVELOPING A TIERED MODELING FRAMEWORK IN SUPPORT OF RISK ASSESSMENT OF CHEMICAL SUBSTANCES ASSOCIATED WITH MOBILITY CONCERNS https://cefic-lri.org/projects/eco-54-developing-a-tiered-modeling-framework-in-support-of-risk-assessment-of-chemical-substances-associated-with-mobility-concerns/

surface water or groundwater contamination. Tonnages, use patterns and emissions as well as routes of exposures are considered as major factors affecting the observed concentration of substances in groundwater.

Consideration of metabolites in the context of the PMT/vPvM concept concludes that the threshold for the identification of metabolites should follow the 10% recommendation as set out within the OECD 307, 308 and 309 test guidelines. The proposed 0.1% threshold might not be achievable due to technical/analytical limitations. In contrast to hydrophobic (lipophilic) substances, hydrophilic substances present a technical challenge since existing analytical methods are only to a limited extent amenable to these substances. Research will be required to develop tools to concentrate, separate and detect such low metabolite concentrations.

The presence of naturally occurring metabolites has been considered since they may interfere with concentrations released from man-made products and thus requires a more detailed analysis on a case-by-case basis. The impact of NER formation on the PMT/vPvM concept was examined. NER formation is complex and may depend on the functional groups in the metabolite molecule and composition of the environmental matrix. The 0.1 µg/L threshold for drinking water and the measured concentrations in groundwater are considered to provide a worst-case assessment which accounted for NER formation.

The evaluation of the toxicity (T) criteria extension (i.e., beyond those of ANNEX XIII of REACH) showed that the existing criteria already fulfil the protection goal to ensure a high level of human and environmental safety. Furthermore, it is proposed that any T criteria should focus on human health aspects in order to align with the protection goal of safe drinking water for humans.

The knowledge gaps and research need highlighted within this report are summarised below:

**Knowledge Gaps and Research Needs relating to mobility:**

- Effect of low OC sub-surface soil and sediment on measurement of $K_{oc}$, $D_{ow}$
- Ionisable substances – validation of appropriate techniques for measurement of adsorption characteristics and differentiate between the effects of soil OC and mineral content
- Improved modelling techniques to determine adsorption characteristics of ionisable substances
- Aged sorption studies and realistic application scenarios for substances entering soils via indirect application.

**Knowledge Gaps and Research Needs relating to a risk-based approach to protecting water sources:**

- Improve comprehension of bank filtration processes with respect to transfer of contaminants to and from water bodies
- Integrate this knowledge of bank filtration into environmental distribution models, such as EUSES
- Review current practices in sludge management and refine default parameters supporting the exposure assessment of industrial chemicals finding their way into soils via sewage sludge application

- Establish set of assumptions and generic hazard and risk scenarios in “look-up” tables to permit higher-tier modelling to be performed on chemicals where higher-tier environmental fate studies are not available.
- Advance screening test methods and approaches for the mobility assessment of ionisable substances by combining elements of fate and partitioning.

**Knowledge Gaps and Research Needs relating to use of monitoring data:**

- Additional in-depth analysis of robust groundwater monitoring data with the aim of identifying principle influencing factors leading to detects under natural, environmental realistic conditions.

**Knowledge Gaps and Research Needs relating to consideration of metabolites:**

- Consensus on definition of a relevant metabolite – at what % of applied dose a transformation product becomes relevant?
- Structural alerts to identify moieties likely to form significant levels of NER
- Development of tools to concentrate, separate and detect low metabolite concentrations.

# ABBREVIATIONS

AA: Annual average

ADI: Acceptable daily intake

AOX: Adsorbable organic halogens

AR: Applied radioactivity

ARfD: Acute Reference Dose

BoA: ECHA Board of Appeal

BPA:  Bisphenol A

BPR: EU Biocidal Products Regulation

CARACAL: Competent Authorities for REACH and CLP

CAS: Chemical Abstracts Service

CASG-ED: CARACAL sub-group on endocrine disruptors

CEC: Cation exchange capacity

CEEP: European Centre of Employers and Enterprises providing Public Services and Services of general interest

Cefic: European chemical industry council

CHESAR: ECHA CHEmical Safety Assessment and Reporting tool

CHMP: EMA Committee for Medicinal Products for Human Use

CIS WG GW: EU Common Implementation Strategy Working Group Groundwater under the WFD

CLP: EU Classification, Labelling and Packaging Regulation

CMR: Carcinogenic, mutagenic or toxic to reproduction

$C_o$: Concentration in octanol

CoRAP: ECHA Community rolling action plan

CRD: UK Health & Safety Executive Chemicals Regulation Division

CRI: Characteristic Root Index

CVMP: EMA Committee for Medicinal Products for Veterinary Use

$C_w$: Concentration in water

DNEL: Derived no-effect level

DOC: Dissolved organic carbon

$D_{ow}$: n-octanol/water distribution coefficient

DROPLET: DRinkwater uit OPpervlaktewater- Landbouwkundig gebruik Evaluatie Tool

DSD: EU Dangerous Substances Directive

$DT_{50}$: Disappearance time 50 (time within which the concentration is reduced by 50%)

$DT_{50}bio_{water}$: Half-life for biodegradation in bulk surface water

DWD: EU Drinking Water Directive

EA: UK Environment Agency

Easy TRA: Easy Targeted Risk Assessment

EC: European Commission

$EC_{10}$: Effect concentration 10% (Concentration that effects 10% of a population)

ECETOC: European Centre for Ecotoxicology and Toxicology of Chemicals

ECETOC TRA: ECETOC Targeted Risk Assessment

ECHA: European Chemicals Agency

ED: Endocrine disruptor

EDQM: European Directorate for the Quality of Medicines

EEA: European Environment Agency

EF: Exceedance frequency

EFSA: European Food Safety Authority

Eh: Redox potential

EIA: Environmental impact assessment

EIC: Environmental introduction concentration

$Elocal_{WATER}$: EUSES local release rate to influent wastewater

EMA: European Medicines Agency

ENVI: Committee on the Environment, Public Health and Food Safety of the European Parliament

EPI Suite: Estimation Programs Interface Suite

EQS: Environmental quality standard

ERA: Environmental risk assessment

ERC: Environmental release category

EU: European Union

EUROSTAT: Statistical office of the European Union

EUSES: European Union System for the Evaluation of Substances

FASC: Federal Assembly of the Swiss Confederation

FFDCA: US Federal Food, Drug and Cosmetic Act

FIFRA: US Federal Insecticide, Fungicide, and Rodenticide Act

FOCUS: FOrum for Co-ordination of pesticide fate models and their Use (EU DG SANTE)

FOCUS GW: FOCUS Groundwater

FOCUS SW: FOCUS Surface Water

FOEN: Swiss Federal Office for the Environment

$f_{oc}$: Fraction of organic carbon

Fpen: Penetration factor

FQPA: US Food Quality Protection Act

Fst-st: Fraction of steady state

GDWQ: WHO Guidelines for drinking water quality

GUS: Groundwater ubiquity score

GV: Guideline value

GW: Groundwater

GWD: EU Groundwater Directive

GWWL: EU GWD Groundwater watch list

HPLC: High performance liquid chromatography

HMA: EU Heads of Medicines Agencies

IPCS: WHO International Programme on Chemical Safety

IPPC: EU Integrated Pollution Prevention and Control

JRC: EC Joint Research Centre

$K_{CEC}$: Adsorption coefficient normalised to cation exchange capacity

$K_{clay}$: Adsorption coefficient normalised to clay content

$K_d$: Soil-water distribution coefficient

$K_f$: Freundlich factor (sorption isotherm)

$K_{oc}$: Organic carbon normalised adsorption coefficient

$K_{ow}$: *n*-Octanol-water partition coefficient

$Kp_{soil}$: Partition coefficient solid-water in soil

LoD: Limit of detection

LoQ: Limit of quantification

LRI: Cefic Long-range Research Initiative

LSER: Linear solvation energy relationship

M: Mobile (or Mutagenic)

MAC: Maximum allowable concentrations

MACRO: Macropore flow model

MCI: Molecular connectivity index

MCL: Maximum contaminant level

MCLG: Maximum Contaminant Level Goal

MEC: Measured environmental concentration

mEq: Milliequivalents

MoA: Mechanism of action

$MTC_{dw}$: Maximum tolerable concentration in drinking water

MW: Molecular weight

NAQUA: Swiss National Groundwater Quality Monitoring Network

NCAs: EU National Competent Authorities

NER: Non-extractable residues

NOEC: No-observed effect concentration

NRB or nonRB: Non readily biodegradable

OC: Organic carbon

OECD: (Intergovernmental) Organisation for Economic Co-operation and Development

OPPTS: US EPA Office of Prevention, Pesticides and Toxic Substances

OPP: Office of Pesticide Programs

P: Persistent

PAH: Polyaromatic hydrocarbons

$pK_a$: Negative log of acid dissociation constant

PBT: Persistent, bioaccumulative and toxic

PEARL: Pesticide Emission Assessment at Regional and Local scales

PEC: Predicted environmental concentration

$PEC_{DW}$: Predicted environmental concentration in drinking water

$PEC_{GW}$: Predicted environmental concentration in groundwater

$PEC_{regional}$: Predicted environmental concentration in the region

$PEC_{soil}$: Predicted environmental concentration in soil

$PEC_{SW}$: Predicted environmental concentration in surface water

PELMO: Pesticide Leaching Model

pF: Water tension (log of height of water column in cm)

PFASs: Per- and polyfluoroalkyl substances

PHS: Priority hazardous substances

PMT: Persistent, mobile and toxic

PNEC: Predicted no-effect concentration

pnRB: Potentially non-readily biodegradable

POM: Programmes of measures

PPP: Plant protection products

PPPR: EU Plant protection products regulation

pRB: Potentially readily biodegradable

PRZM: Pesticide Root Zone Model

PRZM GW: Pesticide Root Zone Model for Ground Water

PS: EU WFD Priority Substances

$Q_{10}$: A measure of the rate of change of a biological or chemical system as a consequence of increasing the temperature by 10 °C

$QS_{dw, hh}$ : Quality standards for water abstracted for drinking water

QSAR: Quantitative structure-activity relationship

RAC: ECHA Committee for Risk Assessment

RB: Readily biodegradable

REFIT: Regulatory fitness and performance

RBSP: EU WFD River-basin specific pollutant

RBMP: EU WFD River basin management plan

REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals

$RQ_{groundwater}$: Groundwater risk quotient

SCI-GROW: Screening Concentration In GROund Water

SFC: Swiss Federal Council

SDWA: US Safe Drinking Water Act

SMILES: Simplified molecular-input line-entry system

SSD: Sewage Sludge Directive

STE: EU WFD (JRC) Spatial, temporal and extent of PNEC exceedances

STOT RE: Specific target organ toxicity – repeat exposure

SVHC: ECHA REACH Substance of very high concern

SW: Surface water

SWAT: Soil and Water Assessment Tool

$t_{1/2,\ soil}$: Degradation half-life in soil

T: Toxic

TDI: Tolerable daily intake

TGD: ECHA Technical Guidance Document

TGD-EQS: EC Technical Guidance for Deriving Environmental Quality Standards

UBA: Umweltbundesamt (German Environmental Agency)

US EPA: United States Environmental Protection Agency

UVCB: Unknown or Variable composition, Complex reaction products or of Biological materials

UWWTD: Urban Waste Water Treatment Directive

VEGA: Virtual models for property Evaluation of chemicals within a Global Architecture

VICH: Veterinary International Conference on Harmonization (EU-Japan-USA) vM: Very mobile

VMP: Veterinary medicinal product

VOX: Volatile organic halogens

vP: Very persistent

vPvB: Very persistent and very bioaccumulative

vPvM: Very persistent and very mobile

VVWM: Variable volume water model

WFD: EU Water Framework Directive

WHO: World Health Organisation

WHOPES: WHO Pesticide Evaluation Scheme

WL: EU WFD Watch list

WPA: Swiss Federal Act on the Protection of Waters

WPO: Swiss Waters Protection Ordinance

w/w: Weight by weight

WWTP: Wastewater treatment plant

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# APPENDIX A: DERIVATION OF LOCAL RELEASE RATE TO INFLUENT WASTEWATER (ELOCAL$_{WATER}$) FOR MODELLING IN SECTION 4.7

Similarities and differences between the EUSES, FOCUS and models used for the evaluation of PPPs is discussed in Section 4.7. All exposure assessment models require a release characterisation step, which differs between models supporting the assessment of plant protection products and those supporting the evaluation of industrial chemicals. The release of a PPP is aligned with the field application rate to soil, which is expressed in grams per hectare (g/ha). The release of an industrial chemical on soil depends on several factors, as the EUSES model includes direct and indirect release to soil. The typical release input for a given use are expressed as “Local daily release rate” as described in the ECHA guidance Chapter R.16.2 on the release assessment (ECHA, 2016a). In the assessment in Section 4.7, the exposure to soil was assumed to result exclusively from the application of sewage sludge to land, to which the chemical is adsorbed. The concentration in dry sludge is nevertheless not an input to the exposure assessment. The emission to the influent of sewage treatment plant (Elocal$_{WATER}$), which is a standard input to the EUSES model, was derived according to the approach outlined below:

| **Step 1: derivation of dosing to soil** | | | | |
|---|---|---|---|---|
| Dosing of PPP | | g/ha | 1000 | input |
| Dose of substance to soil (Csludge * APPLsludge) | | mg/m²/yr | rev | |
| Unit conversion g to mg | | | 1000 | - |
| Unit conversion ha to m² | | | 10000 | - |
| Dose of substance to soil= (Csludge * APPLsludge) | | mg/m²/yr | 100 | Calculated |
| Dry sludge application rate in agricultural soil | APPLsludge | kg/m²/yr | 0.5 | Table R.16-13 |
| Concentration in dry sludge | Csludge | mg/kg | 200 | Calc. R16-50 |

The local release rate to influent wastewater Elocal$_{WATER}$ was calculated using equation R.16-21 and default values outlined in the guidance. The partitioning to sludge was selected for a theoretical soluble substance of low volatility (1000 mg/L and 1.3 Pa) and a log $K_{ow}$ of 4, for which a 21% partitioning to sludge is assumed according to Appendix R.16-3.

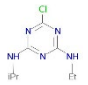
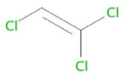
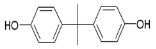
| **Step 2: derivation of emission in STP, assumption no degradation in STP** | | | | |
|---|---|---|---|---|
| Concentration in dry sludge | Csludge | mg/kg | 200 | Derived in Step 1 |
| Fraction of release directed to sludge by STP | Fstpsludge | - | 0.21 | Appendix R.16-2 |
| Concentration of suspended matter in STP influent | SUSPCONCinf | kg/m³ | 0.45 | Table R16-14 |
| Capacity of the STP | CAPACITYstp | eq | 10,000 | Table R16-14 |

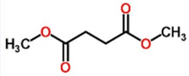
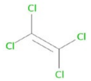
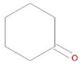
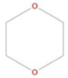
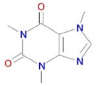
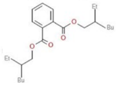
| **Step 2: derivation of emission in STP, assumption no degradation in STP** | | | | |
|---|---|---|---|---|
| Sewage flow per inhabitant | WASTEWinhab | $l.d^{-1}.eq^{-1}$ | 200 | Table R.16-14 |
| Effluent discharge rate of STP | EFFLUENTstp | $l.d^{-1}$ | 2000000 | Calculated R.16-18 |
| Surplus sludge per inhabitant equivalent | SURPLUSsludge | $kg.d^{-1}.eq^{-1}$ | 0.011 | Table R16-14 |
| Rate of sewage sludge production | Sludgerate | $kg.d^{-1}$ | 710 | Calculated R.16-21 |
| | Elocalwater | kg/d | 0.7 | Calculated R.16-20 |

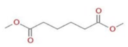
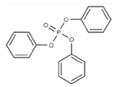
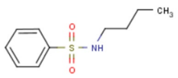
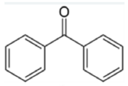
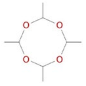
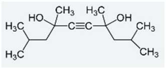
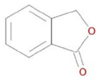
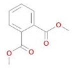
A fixed input value for $Elocal_{WATER}$ of 0.7 kg/d was subsequently used for all simulations. It is acknowledged that the amount released to soil is influenced in each simulation by assumptions on the partitioning in the wastewater treatment plant and in soil.

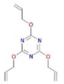
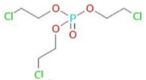
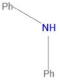
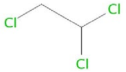
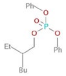
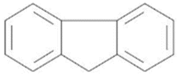
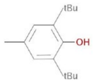
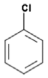
# APPENDIX B: 31 NON-IONISABLE REACH REGISTERED SUBSTANCES DETECTED IN UK GROUNDWATER ASSESSED AGAINST THE PROPOSED PMT/vPvM CRITERIA

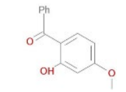
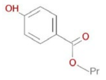
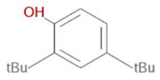
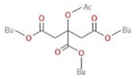
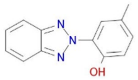
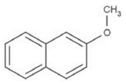
**Red = vP, vM or T; Orange = P or M; Green = not P, not M or not T**

| Analyte | CAS No. | EC No. | Reg type | P from dossier | M from dossier | T from dossier (no assessment of ED) | Conclusion | log $K_{ow}$ | Water solubility mg/L | Vapour pressure (Pa at 25°C) | Carbon Chain Length | Additional Functional Groups | Structure | Molecular Weight | Abraham parameter from ACD/labs |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Atrazine | 1912-24-9 | 217-617-8 | Intermediate | P may be vP | vM (log $K_{ow}$ = 2.59 at 20°C and pH 7.31-7.51) | T (STOT RE) | Could be vP/vM and /or PMT | 2.59 at 20°C and pH 7.31-7.51 | 32 mg/L at 20°C and pH 8.07-8.46 | 0 Pa at 25°C | 6-membered aromatic ring | N, Cl |  | 215.683 | A = 0.26, B = 0.97, B0 = 0.94, L =7.544, S = 1.12, E = 1.17, V = 1.6381 |
| Trichloroethene | 79-01-6 | 201-167-4 | 10,000-100,000 tpa | vP (and P) | vM (log $K_{ow}$ = 2.53 at 20°C) | T (Carcinogenic) | vP/vM and PMT | 2.53 at 20°C | 1,100 mg/L at 20°C | 9.9 kPa at 25°C | C2 | C=C, Cl |  | 131.388 | A = 0, B = 0.11, B0 = 0.11, L = 2.562, S = 0.64, E = 0.5, V = 0.7146 |
| Bisphenol A | 80-05-7 | 201-245-8 | 1,000,000-10,000,000 tpa | Not P | M (log $K_{ow}$ = 3.4 at 21.5°C) | T (Reproduction) | Not PMT | 3.4 at 21.5°C | 300 mg/L at 25°C | 0 Pa at 25°C | N/A | OH, 6-membered aromatic ring |  | 28.29 | A = 1, B = 0.79, B0 = 0.81, L = 8.894, S = 1.46, E = 1.59, V = 1.8643 |

| Analyte | CAS No. | EC No. | Reg type | P from dossier | M from dossier | T from dossier (no assessment of ED) | Conclusion | log $K_{ow}$ | Water solubility mg/L | Vapour pressure (Pa at 25°C) | Carbon Chain Length | Additional Functional Groups | Structure | Molecular Weight | Abraham parameter from ACD/labs |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dimethyl succinate | 106-65-0 | 203-419-9 | 1,000-10,000 tpa | Not P | vM (log $K_{ow}$ = 0.33 at 40°C and pH 7.1) | Not T | Not PMT | 0.33 at 40°C | 122,900 mg/L at 20°C and pH 4.4 | 23.5 Pa at 25°C | C4 | COOMe |  | 146.141 | A = 0, B = 0.7, B0 = 0.7, L = 3.957, S = 0.98, E = 0.13, V = 1.1028 |
| Tetrachloroethene | 127-18-4 | 204-825-9 | 100,000-1,000,000 tpa | P may be vP | vM (log $K_{ow}$ = 2.53 at 20°C) | T (Carcinogenic) | Could be vP/vM and /or PMT | 2.53 at 20°C | 150 mg/L at 25°C | 2.5 kPa at 25°C | C2 | C=C, Cl |  | 165.833 | |
| Cyclohexanone | 108-94-1 | 203-631-1 | 1,000,00-10,000,000 tpa | Not P | vM (log $K_{ow}$ = 0.86 at 25°C) | Not T | Not PMT | 0.86 at 25°C | 86,000 mg/L at 20°C | 7 hPa at 30°C | 6-membered ring | C=O, 6-membered ring |  | 98.143 | A = 0, B = 0.32, B0 = 0.32 , 3.723 , S = 0.77, E = 0.42, V = 0.8611 |
| 1,4-Dioxane | 123-91-1 | 204-661-8 | 1,000+ tpa | vP (and P) | vM (log $K_{ow}$ = -0.42 at 20°C) | T (Carcinogenic) | vP/vM and PMT | -0.42 at 20°C | 1,000,000 mg/L at 20°C | 42.8 hPa at 23°C | 6-membered ring | -O-, 6-membered ring |  | 88.105 | |
| Caffeine | 58-08-2 | 200-362-1 | 1,000-10,000 tpa | Not P | vM (log $K_{ow}$ = -0.091 at 23°C) | Not T | Not PMT | -0.091 at 23°C | 18700 mg/L at 16°C | No data | Fused 5 and 6 membered rings | N, C=O, rings |  | 194.191 | A = 0, B = 1.27, B0 = 1.27, L = 7.793, S = 1.9, E = 1.48, V = 1.3632 |
| Bis(2-ethylhexyl)phthalate (DEHP) | 117-81-7 | 204-211-0 | 10,000-100,000 tpa | P (not VP) | Not M (log $K_{ow}$ = 7.5) | T (Reproduction) | Not PMT | 7.5 | 0.03 mg/L at 20°C and pH 7 | 0 Pa at 20°C | Branched | 6-membered aromatic ring, COO |  | 390.556 | A = 0, B = 0.88, B0 = 0.88, L = 12.811, S = 1.41, E = 0.72, V = 3.4014 |

| Analyte | CAS No. | EC No. | Reg type | P from dossier | M from dossier | T from dossier (no assessment of ED) | Conclusion | log $K_{ow}$ | Water solubility mg/L | Vapour pressure (Pa at 25°C) | Carbon Chain Length | Additional Functional Groups | Structure | Molecular Weight | Abraham parameter from ACD/labs |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dimethyl adipate | 627-93-0 | 211-020-6 | 1,000-10,000 tpa | Not P | vM (log $K_{ow}$ = 1.4 at 22°C) | Not T | Not PMT | 1.4 at 22°C | 4,000 mg/L at 20°C | 2.5 Pa at 20°C | C6 | COOMe |  | 174.194 | |
| Triphenyl phosphate | 115-86-6 | 115-86-6 | 100-1,000 tpa | Not P | Not M (log $K_{ow}$ = 4.6 at 20°C) | Not T | Not PMT | 4.6 at 20°C | 1.9 mg/L at 20°C | 0.001 Pa at 25°C | 6-membered aromatic ring | Phosphate, 6-membered aromatic ring |  | 326.283 | A = 0, B= 1.48, B0= 1.5, L = 12.162, S = 2.07, E = 1.99, V = 2.3714 |
| N-butylbenzenesulphoneamide | 3622-84-2 | 222-823-6 | 1,000-10,000 tpa | P may be vP | vM (log $K_{ow}$ = 2.01 at 20°C) | T (STOT RE) | Could be vP/vM and /or PMT | 2.01 at 20°C | 450 mg/L at 20°C | 0 Pa at 20°C | C4 | 6-membered aromatic ring, N, S=O |  | 13.3 | |
| Benzophenone | 119-61-9 | 204-337-6 | 1,000-10,000 tpa | Not P | M (log $K_{ow}$ = 3.18 at 25°C) | T (STOT RE) | Not PMT | 3.18 at 25°C | 23.9 mg/L at 20°C | 0.003 hPa at 25°C | 6-membered aromatic ring | C=O, 6-membered aromatic ring |  | 182 | |
| Metaldehyde | 108-62-3 | 203-600-2 | Confidential | P may be vP | vM (log $K_{ow}$ = 0.12 at 20°C) | Not T | Could be vP/vM | 0.12 at 20°C | 222 mg/L at 21.5°C | 6.6 hPa at 25°C | N/A | -O- |  | 176.21 | |
| 2,4,7,9-Tetramethyl-5-decyne-4,7-diol | 126-86-3 | 204-809-1 | 1,000+ tpa | P may be vP | vM (log $K_{ow}$ = 2.8 at 20°C) | Not T | Could be vP/vM | 2.8 at 20°C | 1,700 mg/L at 20°C and pH 7.3-7.5 | 0.006 hPa at 20°C | C10 | C≡C, OH |  | 226 | |
| 1(3H)-Isobenzofuranone | 87-41-2 | 201-744-0 | 0-10 tpa | Not P | vM (log $K_{ow}$ = 0.5 at RT) | Not T | Not PMT | 0.5 at RT | < 1.5 mg/L at 20°C and pH 7.3 | 0.00072 Pa at 20°C | 6-membered aromatic ring | C=O, -O-, 6-membered aromatic ring |  | 134.132 | |
| Dimethyl phthalate | 131-11-3 | 205-011-6 | 1,000-10,000 tpa | Not P | vM (log $K_{ow}$ = 1.56) | Not T | Not PMT | 1.56 | 4,000 mg/L at 250°C | <0.01 mm Hg at 20°C | 6-membered aromatic ring | COOMe, 6-membered aromatic ring |  | 194.184 | |

| Analyte | CAS No. | EC No. | Reg type | P from dossier | M from dossier | T from dossier (no assessment of ED) | Conclusion | log $K_{ow}$ | Water solubility mg/L | Vapour pressure (Pa at 25°C) | Carbon Chain Length | Additional Functional Groups | Structure | Molecular Weight | Abraham parameter from ACD/labs |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2,4,6-Triallyloxy-1,3,5-triazine | 101-37-1 | 202-936-7 | 1,000-10,000 tpa | P may be vP | M (log $K_{ow}$ = 3.51 at 25°C) | Not T | Not PMT | 3.51 at 25°C | 328 mg/L at 20°C | 0.001 hPa at 20°C | 6-membered aromatic ring | N, -O-, C=C, 6-membered aromatic ring |  | 249.266 | |
| Tri-(2-chloroethyl) phosphate | 115-96-8 | 204-118-5 | 0-10 tpa | P may be vP | vM (log $K_{ow}$ = 1.56 at 20°C) | T (Carcinogenic, Reproduction) | Could be vP/vM and /or PMT | 1.56 at 20°C | 7,943 mg/L at 20°C | 0.061 mm Hg at 25°C | C2 | Phosphate, Cl |  | 285.49 | |
| Diphenylamine | 122-39-4 | 204-539-4 | 10-100 tpa | P may be vP | M (log $K_{ow}$ = 3.82 at 20.2°C) | T (STOT RE) | Could be vP/vM and /or PMT | 3.82 at 20.2°C | 40 mg/L at 25°C | 0.03 Pa at 293 K | 6-membered aromatic ring | N, 6-membered aromatic ring |  | 169.222 | |
| 1,1,2-Trichloroethane | 79-00-5 | 201-166-9 | Intermediate | P may be vP | vM (log $K_{ow}$ = 2.05-2.49 at 20°C and pH 7) | T (Carcinogenic) | Could be vP/vM and /or PMT | 2.05-2.49 at 20°C | 3,500 mg/L at 25°C and pH 7 | 22.25-25.35 hPa at 20°C | C2 | Cl |  | 133.404 | |
| 2-Ethylhexyl diphenyl phosphate | 1241-94-7 | 214-987-2 | 1,000-10,000 tpa | Not P | Not M (log $K_{ow}$ = 5.87 at 25°C) | Not T | Not PMT | 5.87 at 25°C | 0.0506 mg/L at 23.5°C | 26.7 Pa at 150°C | 6-membered aromatic ring | Phosphate, 6-membered aromatic ring |  | 362.4 | |
| Fluorene | 86-73-7 | 201-695-5 | Intermediate | No data | Not M (log $K_{ow}$ = 4.164) | Not T | Not PMT | 4.164 | No data | No data | Fused 5 and 6 membered rings | N/A |  | 56.219 | |
| Butylated hydroxytoluene | 128-37-0 | 204-881-4 | 10,000-100,000 tpa | P may be vP | Not M (log $K_{ow}$ = 5.1) | Not T | Not PMT | 5.1 | 0.4 mg/L at 20-25°C | 0.39 Pa at 25°C | 6-membered aromatic ring | OH, 6-membered aromatic ring |  | 220.35 | |
| Chlorobenzene | 108-90-7 | 203-628-5 | 10,000+ tpa | P may be vP | M (log $K_{ow}$ = 3 at 20°C) | Not T | Not PMT | 3 at 20°C | 538 mg/L at 20°C | 18.8 hPa at 25°C | 6-membered aromatic ring | Cl, 6-membered aromatic ring |  | 112.557 | |

| Analyte | CAS No. | EC No. | Reg type | P from dossier | M from dossier | T from dossier (no assessment of ED) | Conclusion | log $K_{ow}$ | Water solubility mg/L | Vapour pressure (Pa at 25°C) | Carbon Chain Length | Additional Functional Groups | Structure | Molecular Weight | Abraham parameter from ACD/labs |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Benzophenone-3 | 131-57-7 | 205-031-5 | 100- 1,000 tpa | P | M (log $K_{ow}$ = 3.45 at 40°C) | Not T | Not PMT | 3.45 at 40°C | 6 mg/L at 25°C | 0.001 Pa at 25°C | 6-membered aromatic ring | OH, C=O, -O-, 6-membered aromatic ring |  | 228.243 | |
| Propylparaben | 94-13-3 | 202-307-7 | 100- 1,000 tpa | Not P | vM (log $K_{ow}$ = 2.8 at 20°C) | Not T | Not PMT | 2.8 at 20°C | 500 mg/L at 25°C | 0 Pa at 20°C | 6-membered aromatic ring | OH, COO, 6-membered aromatic ring |  | 180.201 | |
| 2,4-Di-tert-butylphenol | 96-76-4 | 202-532-0 | 100-1,000 tpa | P may be vP | Not M (log $K_{ow}$ = 4.8 at 23°C) | Not T | Not PMT | 4.8 at 23°C | 33 mg/L at 25°C | 5 Pa at 38°C | 6-membered aromatic ring | OH |  | 206.324 | |
| Tributyl acetylcitrate | 77-90-7 | 201-067-0 | 10,000-100,000 tpa | Not P | Not M (log $K_{ow}$ = 4.86 at 40°C and pH 7.1) | Not T | Not PMT | 4.86 at 40°C | 4.49 mg/L at 20°C and pH 6.7-6.8 | 0 mm Hg at 25°C | C5 | COO |  | 402.479 | |
| Drometrizole | 2440-22-4 | 219-470-5 | 1,000-10,000 tpa | P may be vP | Not M (log $K_{ow}$ = 4.2 at 25°C) | T (Ecotox) | Not PMT | 4.2 at 25°C | 0.173 mg/L at 20°C | 0 Torr at 20°C | Fused 5 and 6 membered ring and 6 membered aromatic ring | N, OH, 6 membered aromatic ring and fused 5 and 6 membered rings |  | 225.246 | |
| 2-Methyoxynaphthalene | 93-04-9 | 202-213-6 | 1,000-10,000 tpa | P may be vP | M (log $K_{ow}$ = 3.318 at 25°C) | Not T | Not PMT | 3.318 at 25°C | 150 mg/L at 34°C | 1.097 Pa at 25°C | Fused 6 member aromatic rings | -O- |  | 158.199 | |

# APPENDIX C: BRITISH GEOGRAPHICAL SURVEY DATASET (INCLUDING 5600 SINGLE ANALYTICAL DETERMINATIONS) AND ASSOCIATED LOG $K_{OC}$ AND READY BIODEGRADABILITY DATA

| Substance | CAS number | Number of determinations | Log $K_{oc}$ (EPI SuiteTM KOCWIN – MCI model) | Ready Biodegradability (RB) | Source for RB | URL |
|---|---|---|---|---|---|---|
| 2,6-Dichlorobenzonitrile | 1194-65-6 | 20 | 2.4 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/12680 |
| 2-Ethylhexldiphenyl phosphate | 1241-94-7 | 78 | 4.5 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/2152 |
| Atrazine | 1912-24-9 | 125 | 2.4 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/10766 |
| Azoxystrobin | 131860-33-8 | 15 | 3.4 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1542 |
| Bentazone | 25057-89-0 | 70 | 1.0 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2015.4077 |
| Benzenesulfonamide, N-butyl | 3622-84-2 | 177 | 2.6 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/13402 |
| Benzophenone-3 | 131-57-7 | 27 | 3.0 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/5515 |
| Bis(2-ethylhexyl) adipate | 103-23-1 | 18 | 4.6 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15293 |
| bis(2-ethylhexyl)phthalate | 117-81-7 | 113 | 5.1 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15358 |
| Bisphenol A | 80-05-7 | 273 | 4.6 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15752 |
| Butyl benzyl phthalate | 85-68-7 | 40 | 3.9 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/12721 |
| Butylated hydroxytoluene | 128-37-0 | 72 | 4.2 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15975 |
| Caffeine | 58-08-2 | 465 | 1.0 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/10085 |

| **Substance** | **CAS number** | **Number of determinations** | **Log $K_{oc}$ (EPI SuiteTM KOCWIN – MCI model)** | **Ready Biodegradability (RB)** | **Source for RB** | **URL** |
|---|---|---|---|---|---|---|
| Carbamazepine | 298-46-4 | 276 | 3.1 | NRB | Internet | https://www.theseus.fi/bitstream/handle/10024/23236/Vankova%20Magdalena.pdf?sequence=1 |
| Chlorpropham | 101-21-3 | 20 | 2.5 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4903 |
| Clopyralid | 1702-17-6 | 14 | 1.3 | NRB | Internet | http://www.fmccrop.com.au/download/discontinued_FMC/MSDS/clopyralid_750_wg_herbicide_msds.pdf |
| Cocaine | 50-36-2 | 4 | 2.9 | NRB | Biowin | |
| Crotamiton | 483-63-6 | 228 | 2.6 | NRB | Biowin | |
| Cyprodinil | 121552-61-2 | 8 | 3.3 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2006.51r |
| Diethyl phthalate | 84-66-2 | 9 | 2.0 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/14869 |
| Diflufenican | 83164-33-4 | 44 | 4.4 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2008.122r |
| Dimethenamid | 87674-68-8 | 145 | 2.1 | NRB | Biowin | |
| Dimethoate | 60-51-5 | 2 | 1.1 | NRB | Biowin | |
| Dimethyl phthalate | 131-11-3 | 58 | 1.5 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/14997 |
| Di-n-butyl phthalate | 84-74-2 | 27 | 3.1 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/14862 |
| Ethofumesate | 26225-79-6 | 98 | 2.3 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2016.4374 |
| Flufenacet | 142459-58-3 | 143 | 3.4 | NRB | Internet | https://www.albaugh.eu/webres/File/Products/UK/LBL-SDS/UK_Fence_SDS.pdf |
| Flusilazol | 85509-19-9 | 19 | 4.9 | NRB | Biowin | |
| Flutriafol | 76674-21-0 | 23 | 3.6 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1868 |

| Substance | CAS number | Number of determinations | Log $K_{oc}$ (EPI SuiteTM KOCWIN – MCI model) | Ready Biodegradability (RB) | Source for RB | URL |
|---|---|---|---|---|---|---|
| Ibuprofen | 15687-27-1 | 18 | 2.6 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/1270 |
| Isopropyl myristate | 110-27-0 | 4 | 4.1 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/16077 |
| Isoproturon | 34123-59-6 | 42 | 2.3 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2015.4206 |
| Lenacil | 2164-08-1 | 0 | 2.1 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2009.1326 |
| Lidocaine | 137-58-6 | 19 | 2.6 | NRB | Internet | https://www.astrazeneca.com/content/dam/az/our-company/Sustainability/2017/Lidocaine.pdf |
| Linuron | 330-55-2 | 2 | 2.5 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2016.4518 |
| Metaldehyde | 108-62-3 | 356 | 1.0 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/24890 |
| Metazachlor | 67129-08-2 | 243 | 3.0 | NRB | Internet | https://products.basf.com/documents/pim;save/en/8810252937685.Shadow%C2%AE%20MSDS.PDF |
| Metribuzin | 21087-64-9 | 15 | 1.7 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2006.88r |
| N,N-Diethyl-m-toluamide | 134-62-3 | 409 | 2.1 | RB | Internet | https://circabc.europa.eu/sd/a/8445e206-41e2-407a-91f2-cc7dd2f99411/DEET%20Assessment%20Report.pdf |
| Oxadiazon | 19666-30-9 | 3 | 3.7 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1389 |
| Oxadixyl | 77732-09-3 | 79 | 2.0 | NRB | Biowin | |
| Paraldehyde | 123-63-7 | 15 | 0.2 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/11337 |
| Pendimethalin | 40487-42-1 | 25 | 3.7 | NRB | EFSA | https://www.efsa.europa.eu/fr/efsajournal/pub/4420 |
| Piperonyl butoxide | 51-03-6 | 3 | 2.8 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/6020 |
| Pirimicarb | 23103-98-2 | 8 | 1.7 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2005.43r |

| Substance | CAS number | Number of determinations | Log $K_{oc}$ (EPI SuiteTM KOCWIN – MCI model) | Ready Biodegradability (RB) | Source for RB | URL |
|---|---|---|---|---|---|---|
| Propiconazole | 60207-90-1 | 19 | 3.2 | NRB | Internet | https://cdn.nufarm.com/wp-content/uploads/sites/16/2017/08/06011042/Nufarm-Propiconazole_30367_SDS_E_21DEC2017.pdf |
| Propylparaben | 94-13-3 | 14 | 2.5 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/13890 |
| Propyzamide | 23950-58-5 | 289 | 2.6 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2016.4554 |
| Prosulfocarb | 52888-80-9 | 77 | 3.5 | NRB | Internet | https://www.syngenta.co.uk/file/12646/download?token=pwN0IQpf |
| Pyrazon | 1698-60-8 | 16 | 2.6 | NRB | Internet | https://www.agricentre.basf.co.uk/Documents/product_files_uk_files/safety_data_sheets_files/Takron_MSDS.pdf |
| Simazine | 122-34-9 | 115 | 2.2 | NRB | Internet | https://www.cropsmart.com.au/wp-content/uploads/2014/02/MSDS-Smart-Simazine-900-DF-1.pdf |
| Tebuconazole | 107534-96-3 | 36 | 3.2 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2014.3485 |
| Terbuthylazine | 5915-41-3 | 12 | 2.5 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.1969 |
| Terbutryn | 886-50-0 | 30 | 2.8 | NRB | Internet | http://www.fmccrop.com.au/download/discontinued_FMC/MSDS/terbutryn_500sc_sds_0214.pdf |
| Triacetin | 102-76-1 | 6 | 1.6 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15139 |
| Triallate | 2303-17-5 | 210 | 3.0 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2009.181r |
| Tributyl acetylcitrate | 77-90-7 | 12 | 4.9 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/14218 |
| Tributyl phosphate | 126-73-8 | 28 | 3.4 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/13548 |
| Triclosan | 3380-34-5 | 25 | 4.4 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/12675 |
| Trifluralin | 1582-09-8 | 16 | 4.2 | NRB | EFSA | https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2009.327r |
| Triphenyl phosphate | 115-86-6 | 132 | 4.0 | RB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/15972 |

| Substance | CAS number | Number of determinations | Log $K_{oc}$ (EPI SuiteTM KOCWIN – MCI model) | Ready Biodegradability (RB) | Source for RB | URL |
|---|---|---|---|---|---|---|
| Tris (1,3-dichloroisopropyl) phosphate | 13674-87-8 | 149 | 4.0 | NRB | ECHA | https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/14365 |

# APPENDIX D: COMMUNITY ROLLING ACTION PLAN (CORAP) AND BOARD OF APPEAL (BOA) DECISIONS ON SUBSTANCES WITH PBT/vPvB CONCERNS (STATUS 13.07.2020)

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| ECHA,07 Aug. 2017 | OECD 309 | Concentration level for the Identification metabolites/transformation products was not specified. | *[1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide* | 25155-25-3 | Netherlands |
| ECHA, 12 April 2018 | OECD 309 | Concentration level for the Identification metabolites/transformation products was not specified. | a mixture of: 4-(2,2,3-trimethylcyclopent-3-en-1-yl)-1-methyl-2-oxabicyclo[2.2.2]octane; 1-(2,2,3-trimethylcyclopent-3-en-1-yl)-5-methyl-6-oxabicyclo[3.2.1]octane; spiro[cyclohex-3-en-1-yl-[(4,5,6,6a-tetrahydro-3,6',6',6'a-tetramethyl)-1,3'(3'aH)-[2H]cyclopenta[b]furan]; spiro[cyclohex-3-en-1-yl-[4,5,6,6a-tetrahydro-4,6',6',6'a-tetramethyl)-1,3'(3'aH)-[2H]cyclopenta[b]]furan] | 426218-78-2 | Spain |
| ECHA 08 July 2019 | OECD 309 | Concentration level for the Identification metabolites/transformation products was not specified. | Bis(isopropyl)naphthalene | 38640-62-9 | Sweden |
| *ECHA,* 01 July 2019 | *OECD 309* | *p. 11. …transformation products must be identified and reasonable attempts must be made to quantify them down to 0.1% w/w.* | *O,O,O-triphenyl phosphorothioate* | 597-82-0 | Netherlands |
| ECHA, 15 Aug. 2019 | OECD 309 | …the identification of PBT/vPvB substances must also take into account the PBT/vPvB properties of relevant transformation products and/or degradation products. | quaternary ammonium compounds, tri-C8-10-alkylmethyl, chlorides | 63393-96-4 | Italy |
| ECHA 22 Mar 2018 | OECD | Concentration level for the Identification metabolites/transformation products was not specified. | Ethyl 3,5-dichloro-4-hexadecyloxycarbonyloxybenzoate | 115895-09-5 | Slovenia |
| ECHA, 17 April 2018 | OECD 309 | Concentration level for the Identification metabolites/transformation products was not specified. | Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene | 68411-46-1 | Germany |
| ECHA, 23 Feb. 2016 | *OECD 309* | *p. 3, 6. …and include the identification of transformation products* | 2,5-di-tert-pentylhydroquinone | 79-74-3 | Italy |

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| ECHA,<br>15 Feb. 2019 | OECD 309 | Thus, it is recommended to use a level of > 0.1% w/w, if technically feasible. If it is not technically possible, then it is recommended to explain the reasons in the study report | 6,6'-di-tert-butyl-4,4'-thiodi- m-cresol | 96-69-5 | Austria |
| BoA,<br>15 Jan. 2019 | OECD 308 | P 17, 118: … However, in the course of these appeal proceedings the Agency explicitly agreed that the 10 % threshold at paragraph 41 of the OECD TG 308 should be followed….The 10 % threshold for identification should be applied. | bis(2-ethylhexyl) 4,4’-(6-[4-tert-butylcarbamoyl)anilino]-1,3,5-triazine-2,4-diyldiimino)dibenzoate | 154702-15-5 | Germany |
| ECHA,<br>20 Dec. 2016 | | 1.1.3:… identification of transformation products relevant for PBT assessment (at a concentration of ≥ 0.1 % w/w unless it can be demonstrated that this is technically not possible). | | | |
| BoA,<br>8 Sep. 2017 | OECD 309 | p. 16, 122: The Board of Appeal finds that as the solubility of the Substance is at most 45 µg/l and the required concentration for the identification of major transformation products is greater than 100 µg/l, and sometimes greater than 1 mg/l, it is not realistic to expect the OECD TG 309 study to be suitable to identify the metabolites of the Substance that will be formed in the study.<br>p. 17, 125: The Board of Appeal notes however that according to the test guideline for OECD TG 309 studies ‘transformation products detected at ≥ 10% of the applied concentration at any sampling time should be identified unless reasonably justified otherwise. […] The need for quantification and identification of transformation products should be considered on a case by case basis, with justifications being provided in the report.’ The Appellants | l,4-Benzenediamine, N,Nt-mixed phenyl and tolyl derivatives (BENPAT | 68953-84-4 | Germany |

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| | | therefore must continue to make all reasonable efforts to identify and quantify the major transformation products during the conduct of the OECD TG 309 study and record these efforts in the study report accordingly | | | |
| ECHA,<br>1 Oct. 2015 | | Metabolites representing crucial steps in transformation pathways (key metabolites) shall be identified by use of QSAR. Standard solutions shall ensure that detection and quantification of these key metabolites is possible. | | | |
| BoA,<br>12 July 2016 | OECD 307 | P 9, 194:… transformation products of the Substance at levels lower than those foreseen in OECD TG 307 is conditional on technical feasibility and the making of 'reasonable attempts' to quantify transformation products of the Substance 'down to 0.1% (analytical sensitivity permitting)'. The Board of Appeal also notes that the transformation products identified between a LOD of 0.1% and 1% are potentially the most likely to have PBT/vPvB properties, and that the requested test is designed to clarify a concern that those transformation products may have PBT/vPvB properties | 1,1'-(ethane-1,2-diyl)bis[pentabromobenzene] | 84852-53-9 | Sweden |
| ECHA,<br>22 May 2014 | | …The focus should be the identification of transformation products formed at levels of 1% or more of the amount of test substance added, with reasonable attempts made to quantify these down to 0.1% (analytical sensitivity permitting). | | | |

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| ECHA,<br>16 June 2017 | OECD 307, 308, 309 | The simulation test should be performed at a temperature of 12°C and include analytical measurement of the registered substance and degradants/impurities including DIXD | reaction mass of O,O'-diisopropyl(pentathio)dithioformate and O,O'diisopropyl (trithio)dithioformate and O,O'-diisopropyl (tetrathio)dithioformate (ROBAC AS/100) | 137398-54-0 | Belgium |
| ECHA,<br>30 May 2017 | OECD 309 | Metabolites shall be identified and sufficiently quantified and characterized as regards their PBT properties (at a concentration of 0.1% w/w unless it can be demonstrated that this is technically not possible). | bis(a,a-dimethylbenzyl) peroxid | 80-43-3 | Norway |
| ECHA,<br>27 Mar. 2017 | OECD 308 | Sediment simulation testing; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24. / OECD 308 at a temperature of 12°C. | Dodecamethylpentasiloxane | 141-63-9 | Norway |
| ECHA,<br>27 Mar. 2017 | OECD 308 | Sediment simulation testing; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24. / OECD 308 at a temperature of 12 °C using the registered substance. | Octamethyltrisiloxane | 107-51-7 | Norway |
| ECHA,<br>23 Mar. 2017 | OECD 309/OECD 308 | Metabolites shall be identified and/or sufficiently quantified and characterized as regards their PBT properties (at a concentration of ≥ 0.1 % w/w unless it can be demonstrated that this is technically not possible) | 1-[4-(1,1-dimethylethyl)phenyl]-3-(4-methoxyphenyl)propane-1,3dione (BMDM) | 70356-09-1 | Germany |
| ECHA,<br>23 Mar. 2017 | OECD 307, 308, 309 | It is your duty to perform PBT assessments of all transformation products/metabolites formed in >0.1%, or to justify why this is not relevant. | 2,2 ‘6,6 ‘-tetrabromo-4-4 ‘isopropylidenediphenol | 79-94-7 | Denmark |
| ECHA,<br>23 Mar. 2017 | OECD 307 | Transformation products formed at levels of 1% or more of the test substance shall be | 2,2’,6,6’-tetra-tert-butyl-4,4’-methylenediphenol | 118-82-1 | Austria |

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| | | assed, with reasonable attempts made to quantify these down to 0.1%. | | | |
| ECHA,<br>7 Feb. 2017 | OECD 309 | The analytical techniques used shall have sufficient sensitivity to analyse and quantitate the monoesterified glycerol constituents (and other relevant constituents and/or transformation products) for the purposes of the tests. In practical terms, relevant constituents and transformation products need to be analysed to the extent technically possible. | Resin acids and Rosin acids, hydrogenated, esters with glycerol | 65997-13-9 | Finland |
| ECHA,<br>7 Feb. 2017 | OECD 309 | The concentrations of the test substance shall be analytically monitored during the test to verify the degradation. | Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol | 64365-17-9 | Finland |
| ECHA<br>19 Dec. 2016 | OECD 307, 309 | If transformation products are formed that meet the P criterion, their identity shall be determined by a substance specific analysis. If necessary to achieve a reliable determination of the chemical identity of stable transformation products an adapted execution of the study with higher test item concentrations shall be considered | S-(tricyclo[5.2.1.0 2,6]deca-3-en-8(or 9)-yl) O-(isopropyl or isobutyl or 2ethylhexyl) O-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioat | 255881-94-8 | Belgium |
| ECHA,<br>1 July 2016 | OECD 308, 309 | Simulation testing on ultimate degradation in surface water (test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309) at a temperature of 12 °C and Sediment simulation testing (test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24/OECD 308) at a temperature of 12 °C Soil simulation testing (test method: Aerobic and anaerobic transformation in soil, EU C.23/OECD 307) at a temperature of 12 °C. | Trixylyl phosphate | 25155-23-1 | Italy |

| Decision by/date | Information request | Justification | Substance | CAS | Evaluating Member State |
|---|---|---|---|---|---|
| ECHA,<br>23 Nov. 2015 | OECD 309 | Metabolites shall be identified and/or sufficiently quantified and characterized as regards their PET properties (at a concentration of 0.1 % w/w unless it can be demonstrated that this is technically not possible). | di-tert-butyl 3,3,5-trimethylcyclohexylidene diperoxide | 6731-36-8 | Germany |
| ECHA, 19 Sep. 2014 | OECD 309 | II.1.: … and the identification of transformation products relevant for PBT assessment (at a concentration of 0.1 % w/w unless it can be demonstrated that this is technically not possible). | Triclosan | 3380-34-5 | Netherlands |

# APPENDIX E: ANALYSIS OF T CLASSIFICATION DATA FOR THE CATEGORY 'EFFECTS ON OR VIA LACTATION'

Analysis details:

In Access the following analysis was performed of CLP data extracted from the ECHA website on 12th November 2019 (https://echa.europa.eu/information-on-chemicals/cl-inventory-database).

1. Only search from harmonised classification - ATP number: All

   - Health hazards: Only 'Lact' selected: 25 results - HarmonisedCLP-All laction.xlsx

   - Health hazards: Search operator OR: Repr.1A; Repr.1B; Repr.2; STOT RE1; STOT RE2: 863 results - HarmonisedCLP-All Repro&STOT-RE.xlsx

2. Complete CLP:

   - Health hazards: Only 'Lact' selected: 661 results - 661 results - FullCLP-All laction.xlsx

   - Health hazards: Search operator OR: Repr.1A; Repr.1B; Repr.2; STOT RE1; STOT RE2: 8065 results - FullCLP-All Repro&STOT-RE.xlsx

Import in database

QLact-CLPHarm

QFert-CLPHarm

In QLact-CLPHarm but NOT in QFert-CLPHarm: 3

QLact-CLPFull

QFert-CLPFull

QLact-CLPFull but NOT in QFert-CLPFull: 68 (Includes the three harmonised)

The table below contains the results from the comparison of all substances with lactation classification in complete CLP, but without a classification as Repr.1A, Repr.1B, Repr.2, STOT RE1, or STOT RE2: 68 CLP notified substances in total (of which 3 with harmonised classification)

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 10 | 602-095-00-X | 287-477-0 | 85535-85-9 | alkanes, C<sub>14-17</sub>, chloro | 94445 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/94445 |
| | 16 | 604-091-00-3 | 407-980-2 | 80844-07-1 | etofenprox (ISO) | 74008 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/74008 |
| | 33 | 616-206-00-4 | 417-680-3 | 101463-69-8 | flufenoxuron (ISO) | 109842 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/109842 |
| | 34 | | 207-420-5 | 469-62-5 | Dextropropoxyphene | 973 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/973 |
| | 51 | | 200-701-3 | 69-09-0 | Chlorpromazine hydrochloride | 7117 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/7117 |
| | 54 | | 292-460-6 | 90622-58-5 | Alkanes, C11-15-iso- | 9679 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/9679 |
| | 66 | | 613-980-5 | 66722-44-9 | 2-Propanol, 1-[4-[[2-(1-methylethoxy)ethoxy]methyl]phenoxy]-3-[(1-methylethyl)amino]- | 13478 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/13478 |
| | 67 | | 627-144-2 | 103577-45-3 | 2- [[[ 3- methyl- 4- (2,2,2 -trifluoroethoxy)- 2- piridinyl] methyl] sulfinyl]- 1Hbenzimidazole | 13725 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/13725 |
| | 74 | | 244-333-1 | 21324-39-0 | Sodium hexafluorophosphate | 15140 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/15140 |
| | 84 | | 603-392-7 | 130198-05-9 | 1-[2-amino-1-(4-methoxyphenyl)ethyl]cyclohexanol hydrochloride | 18996 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/18996 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 93 | | 619-449-4 | 99614-02-5 | 1,2,3,9-Tetrahydro-9-methyl-3-((2-methyl-1H-imidazol-1-yl)methyl)-4H-carbazol-4-one | 22886 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/22886 |
| | 94 | | 600-331-6 | 102625-70-7 | 1H-Benzimidazole, 6-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]- | 23317 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/23317 |
| | 107 | | 206-662-9 | 364-62-5 | Metoclopramide | 27682 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/27682 |
| | 121 | | 273-642-4 | 68991-50-4 | Alkanes, C14-17, arom.-free desulfurized | 33784 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/33784 |
| | 122 | | 260-770-0 | 57495-14-4 | Sodium 2-(3-benzoylphenyl)propionate | 33819 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/33819 |
| | 123 | | 204-717-1 | 124-90-3 | Oxycodone hydrochloride | 33912 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/33912 |
| | 131 | | 218-172-2 | 2062-84-2 | Benperidol | 36852 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/36852 |
| | 153 | | 242-209-1 | 18323-44-9 | Clindamycin | 42945 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/42945 |
| | 157 | | 227-551-1 | 5878-43-3 | 6-methylergoline-8β-carboxylic acid | 43755 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/43755 |
| | 162 | | 925-915-0 | | (4S,4aS,5aS,6S,12aS)-4,7-bis(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide di(4-chlorobenzenesulfonic acid) | 45157 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/45157 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 199 | | 251-980-3 | 34381-68-5 | (±)-N-[3-acetyl-4-[2-hydroxy-3-[(isopropyl)amino]propoxy]phenyl] butyramide monohydrochloride | 54387 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/54387 |
| | 207 | | 263-004-3 | 61788-76-9 | Alkanes, chloro | 58963 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/58963 |
| | 212 | | 207-596-3 | 483-63-6 | Crotamiton | 60432 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/60432 |
| | 215 | | 614-454-8 | 68410-99-1 | Alkenes, polymd., chlorinated | 61014 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/61014 |
| | 216 | | 247-409-2 | 26016-99-9 | Disodium (1R,2S)-(1,2-epoxypropyl)phosphonate | 61497 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/61497 |
| | 222 | | 253-539-0 | 37517-30-9 | Acebutolol | 63344 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/63344 |
| | 237 | | 281-527-5 | 83968-47-2 | (5α,6α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-yl (1S)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulphonate | 67524 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/67524 |
| | 248 | | 618-338-8 | 9002-86-2 | Ethene, chloro-, homopolymer | 69493 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/69493 |
| | 254 | | 232-015-5 | 7783-61-1 | Silicon tetrafluoride | 71896 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/71896 |
| | 268 | | 208-048-6 | 506-64-9 | Silver cyanide | 74486 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/74486 |
| | 272 | | 202-929-9 | 101-26-8 | Pyridostigmine bromide | 76014 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/76014 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 276 | | 216-683-5 | 1639-60-7 | Dextropropoxyphene hydrochloride | 77527 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/77527 |
| | 280 | | 245-549-9 | 23277-43-2 | (5α,6α)-17-(cyclobutylmethyl)-4,5-epoxymorphinan-3,6,14-triol hydrochloride | 79025 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/79025 |
| | 293 | | 206-462-1 | 345-78-8 | Pseudoephedrine hydrochloride | 83961 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/83961 |
| | 331 | | 200-109-5 | 51-60-5 | Neostigmine metilsulfate | 96922 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/96922 |
| | 354 | | 200-960-2 | 76-42-6 | Oxycodone | 104568 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/104568 |
| | 365 | | 601-269-2 | 113665-84-2 | Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (αS)- | 107290 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/107290 |
| | 375 | | 246-051-4 | 24168-96-5 | 1-[2-(2,4-dichlorophenyl)-2-[(2,6-dichlorophenyl)methoxy]ethyl]-1H-imidazolium nitrate | 108997 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/108997 |
| | 377 | | 228-768-4 | 6358-31-2 | 2-[(2-methoxy-4-nitrophenyl)azo]-N-(2-methoxyphenyl)-3-oxobutyramide | 109176 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/109176 |
| | 393 | | 917-355-0 | | (4S,4aS,5aR,12aR)-11a-halo-4-(dialkylamino)-3,10,12a-trihydroxy-1,11,12-trioxo-1,4,4a,5,5a,6,11,11a,12,12a-carbopolycyclyl-2-carboxamide hydrohalide | 113348 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/113348 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 395 | | 600-215-5 | 101463-69-8 | 1-(4-(2-cloro-α,α,α-p-trifluorotolyloxy)-2-fluorophenyl)-3-(2,6-difluorobenzolyl)urea | 113962 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/113962 |
| | 410 | | 615-347-9 | 7177-48-2 | (2S,5R,6R)-6-[[(2R)-2-Amino-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate. | 117869 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/117869 |
| | 466 | | 627-402-4 | 41372-20-7 | Apomorphine hydrochloride | 160452 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/160452 |
| | 468 | | 628-621-8 | 12022-46-7 | Lithium iron(III) oxide | 161564 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/161564 |
| | 475 | | 629-833-3 | 75438-57-2 | 4-chloro-N-(4,5-dihydro-1H-imidazol-2-yl)-6-methoxy-2-methylpyrimidin-5-amine | 162829 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/162829 |
| | 523 | | 663-705-8 | 107753-78-6 | 4-(5-Cyclopentyloxycarbonylamino-1-methylindol-3-ylmethyl)-3-methoxy-N-o-tolylsulphonylbenzamide | 194912 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/194912 |
| | 534 | | 682-158-6 | 144060-53-7 | 2-(3-Cyano-4-(2-methylpropoxy)phenyl)-4-methylthiazole-5-carboxylic acid | 212292 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/212292 |
| | 538 | | 682-334-2 | 70111-54-5 | [No public or meaningful name is available] | 212516 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/212516 |
| | 546 | | 682-750-4 | 191114-48-4 | 11,12-dideoxy-3-de((2,6-dideoxy-3-C-methyl-3-O-methyl-3-oxo-12,11-(oxycarbonyl(4-(4-(3-pyridinyl)-1H-imidazol-1-yl)butyl)imino))-erythromycin | 213200 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/213200 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 549 | | 684-191-1 | 25890-20-4 | Lithium-6Li2 carbonate | 214674 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/214674 |
| | 557 | | 686-116-8 | 302912-49-8 | Methyl-d3 salicylate-OD | 216843 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/216843 |
| | 559 | | 686-512-0 | 128420-71-3 | 2-naphtacenecarboxamide,4,7-bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-8,10,12,12a-tetrahydroxy-1,11-dioxo-,monohydrocloride | 217369 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/217369 |
| | 560 | | 687-621-6 | 81409-74-7 | (6aR,9R,10aR)-7-(prop-2-enyl)-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-fg]quinoline-carboxylic acid | 218737 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/218737 |
| | 561 | | 687-649-9 | 85329-86-8 | N-[3-(DiMethylamino)propyl]-6-(2-propen-1-yl)-(8β)-ergoline-8-carboxamide | 218832 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/218832 |
| | 562 | | 687-706-8 | 83602-43-1 | [No public or meaningful name is available] | 218998 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/218998 |
| | 573 | | 689-150-1 | 923604-59-5 | (1R,4R,6S,7Z,15R,17R)-N-(cyclopropanesulfonyl)-17-({7-methoxy-8-methyl-2-[4-(propan-2-yl)-1,3-thiazol-2-yl]quinolin-4-yl}oxy)-13-methyl-2,14-dioxo-3,13-diazatricyclo[13.3.0.0^(Arp & Hale, 2018)]octadec-7-ene-4-carboxamide | 221189 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/221189 |
| | 607 | | 801-825-6 | 199387-73-0 | 1H-Benzimidazole, 5-(difluoromethoxy)-2-(((3,4-dimethoxy-2- | 235129 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/235129 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | | | | | pyridinyl)methyl)sulfinyl)-, magnesium salt | | |
| | 613 | | 806-432-3 | 59787-61-0 | cyclosporin c | 241767 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/241767 |
| | 614 | | 806-433-9 | 63775-95-1 | cyclosporin b | 241768 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/241768 |
| | 615 | | 806-434-4 | 63775-96-2 | cyclosporin d | 241769 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/241769 |
| | 621 | | 806-473-7 | 59865-16-6 | Isocyclosporin A | 241847 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/241847 |
| | 622 | | 806-474-2 | 59865-15-5 | Dihydrocyclosporin A | 241848 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/241848 |
| | 648 | | 944-438-9 | | (2S,3S)-3-{[5-FLUORO-2-(5-FLUORO-1H-PYRROLO[2,3-B]PYRIDIN-3-YL)PYRIMIDIN-4-YL]AMINO}BICYCLO[2.2.2]OCTANE-2-CARBOXYLIC ACID | 253928 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/253928 |
| | 649 | | 945-869-5 | | 4-(5-Cyclopentyloxycarbonylamino-1-methylindol-3-ylmethyl)-3-methoxy-N-p-tolylsulphonylbenzamide | 256477 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/256477 |
| | 654 | | 701-210-1 | 1261931-56-9 | 4-((8-carbamoyl-5a-chloro-10-(dimethylamino)-4,6a,9-trihydroxy-5,6,7-trioxo-5,5a,6,6a,7,10,10a,11,11a,12-decahydrotetracen-1-yl)diazenyl)benzenesulfonic acid | 262330 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/262330 |

| QFert-CLPFull.Page ID | # | Index no | EC / List no | CAS no | Name | QLact-CLPFull.Page ID | Link |
|---|---|---|---|---|---|---|---|
| | 655 | | 821-186-7 | 1777721-66-0 | Bicyclo[2.2.2]octane-2-carboxylic acid, 3-[[5-fluoro-2-(5-fluoro-1H-pyrrolo[2,3-b]pyridin-3-yl)-4-pyrimidinyl]amino]-, (2R,3R)-rel-, | 263542 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/263542 |
| | 656 | | 947-351-4 | | Reaction mass of sodium chloride and potassium chloride and trisodium hexafluoroaluminate | 266357 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/266357 |
| | 658 | | 947-931-7 | | (4S,4aS,5aR,12aS)-4-(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide p-toluenesulfonate | 269115 | https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/269115 |

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www.ecetoc.org
D-2021-3001-264

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