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Review article

Risk characterisation of chemicals of emerging concern in real-life water reuse applications

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ABSTRACT

Water reuse is a viable option to address temporal or structural water shortages. However, the ubiquitous presence of chemicals of emerging concern (CECs) in natural systems, especially the aquatic environment, represents a significant obstacle to water reuse and the receiving environment. Therefore, an extensive literature review was performed to identify current water reuse practices at field scale, reported types and levels of CECs and their associated risks for human and environmental health. Treated wastewater was the primary reused water source, with agricultural reuse being the most frequently reported reuse application (28 %), followed by indirect-potable reuse (16 %). Contrary to potable reuse, it was observed that almost no studies applied additional treatment before water reuse for agricultural purposes. Based on calculated risk quotients, ecological risks were identified for perfluorooctanesulfonic acid, chlorpyrifos, triclocarban, and ethinylestradiol, and human health risks for perfluorooctanesulfonic acid and perfluorooctanoic acid. Environmental risks could be assessed for 77 % of detected CECs, while the human health risk assessment is limited to 28 %. For agricultural reuse, it was observed that CEC concentrations in produced crops were at acceptable levels. However, a thorough risk assessment of CECs during water reuse is currently limited due to a focus on a defined class of contaminants in the literature, i.e., pharmaceuticals, and falls short of per- and polyfluoroalkyl substances. Therefore, future water reuse studies should include a broader set of CECs and study additional mitigation options to decrease CEC concentrations before or during water reuse. Moreover, environmental harm caused by CECs during water reuse such as adverse effects on the microbial soil community or leaching to non-target sources has hardly been studied in the field and presents a knowledge gap.

1. Introduction

Clean and safe water is an essential good for society and its accessibility is closely related to human health. It is also vital for many industrial sectors and especially agriculture. However, global freshwater sources are under increased pressure due to population growth, urbanisation, and land-use changes, coupled with the growing impacts of climate change. Especially, arid to semi-arid regions are expected to experience increased water scarcity due to these changes (UN, 2020). For coastal communities, freshwater sources can also be affected by saltwater intrusion, impacting drinking and irrigation water sources, but also entire ecosystems (Tully et al., 2019). This also illustrates that water scarcity can be not only a quantity, but also a quality issue (Van Vliet et al., 2017). Moreover, freshwater demand and the number of people living in water-stressed areas are expected to increase in the future (UN, 2020).

Current water management systems must therefore adapt and prepare for future conditions, characterised by more frequent temporary shortages of available freshwater, to ensure a water supply of sufficient quality for the environment, public, industry, and agriculture. An option to fight water scarcity and alleviate the pressure on freshwater resources is the reuse of water that is normally discharged. Water reuse is in line with the sustainable development goals of the United Nations and with the ambitions of the European Green Deal to move to a circular economy (EC, 2021).

By using alternative water sources (AWSs), combined with various treatment techniques, water reuse can meet application-specific demands on the respective water quality. AWSs can be defined as

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water sources that are not surface or groundwater (Qin and Horvath, 2020). Extending the interpretation of this definition, they can also be defined as sources that alleviate freshwater demand through their reuse (US Energy Department, 2023). As such, AWSs include harvested rain- and stormwater, brackish (ground)water, domestic greywater, and treated wastewater (TWW) (Oppenheimer et al., 2017; Qin and Horvath, 2020).

The most prominent application of water reuse is for agricultural practices. As the global population continues to increase, agriculture must increase production. Thus, freshwater demand will increase and water reuse may provide a viable option to answer the demand. Additionally, multiple industries, such as the textile (Panda et al., 2022), the microelectronics (Ferella et al., 2021), and the food (Shrivastava et al., 2022) industries are investigating the benefits of water reuse, underlining its potential.

Globally, water reuse is already practiced in multiple countries. Pioneers in water reuse include Singapore (Seah et al., 2008), California (Olivieri et al., 2020), Australia (Leusch et al., 2014), and Israel (Ben Mordechay et al., 2021). In the European Union, as of 2018, about 2.4% of TWW is intentionally reused (Saliba et al., 2018). However, this number excludes unintentional or *de facto* water reuse, which is characterised by the unaccounted-for presence of TWW in a water source used for a specific application. Such *de facto* reuse might pose risks, that are not necessarily recognised. It is estimated that about 65% of the global croplands are irrigated by wastewater-affected streams (Thebo et al., 2017), and during dry seasons, when streams can predominantly consist of wastewater (Beard et al., 2019), the number of *de facto* wastewater-irrigated croplands will substantially increase.

Water reuse is associated with several complex and multifaceted challenges. Next to legal issues (Horne, 2016), economic boundaries (Dingemans et al., 2020), and public acceptance (Hurlimann and Dolnicar, 2010), there is currently a lack of international standardised regulations or monitoring practices (Angelakis et al., 2018; Paranychianakis et al., 2015).

Several EU countries such as Spain, France, Cyprus, Italy, Portugal, and Malta had already established regulations for water reuse prior to the adoption of EU Regulation 2020/741 for agricultural irrigation, which has led to a harmonised framework across all EU member states, ensuring that countries with previously lacking regulations, such as the Netherlands, drafted frameworks (Paranychianakis et al., 2015; Melchers, 2024). Furthermore, Australia and California (CSWRCB, 2024) have existing regulations and guidelines are also issued by the WHO and ISO (WHO, 2006, 2017; ISO, 2020). So far, the regulatory focus has been put on microbial contaminants such as *Escherichia coli*, and conventional water quality parameters such as the biological oxygen demand or turbidity.

Under EU Regulation 2020/741, water reuse operators have to apply for a permit after drafting a risk management plan that identifies potential risks for human and environmental health with a special focus on crops during reuse, including mitigation options. This also includes monitoring frequencies, and minimum water quality requirements that, in combination with irrigation techniques, define which crop categories (e.g., processed; raw consumed) may be irrigated (EU, 2020).

Currently, however, water reuse guidelines are not properly accounting for the risks posed by chemicals of emerging concern (CECs) such as pharmaceuticals or plant protection products. Especially, EU regulation 2020/741 has received criticism as human and environmental health may not be sufficiently protected against risks of CECs during water reuse (Rizzo et al., 2018; EFSA, 2017). This issue is exacerbated as chemical registration and authorisations (e.g., REACH) were not designed to account for the potential hazards of CECs in cyclic systems and are, therefore, insufficiently protective during water reuse (Deviller et al., 2020).

CECs are ubiquitously found in the aquatic environment due to inadequate removal by conventional water treatment plants (Alygizakis et al., 2020) and numerous entry pathways such as surface run-off. They are linked to several potential adverse effects on human and environmental health. For example, per- and polyfluoroalkyl substances (PFAS) have been found to interfere with vaccinations (Crawford et al., 2023), and estrogenic compounds can have devastating effects in the environment already at trace levels (i.e. $ng\,L^{-1}$) (Kidd et al., 2007). Additionally, CECs can be transported to drinking water sources when TWW reaches groundwater or when wastewater-affected surface water is used for drinking water production (Baken et al., 2018; Warner et al., 2019).

Multiple water treatment options are available for the removal of CECs from the water cycle. These include advanced treatments (e.g., sorption, oxidation, size-exclusion) or nature-based techniques (e.g., soil-retention filters, constructed wetlands). Nevertheless, not all treatments achieve the same treatment results. For example, a compound can be removed through adsorption to activated carbon, whereas ozonation degrades a compound (Hu et al., 2016). If degradation leads to complete mineralisation, the compound is fully removed. However, transformation products (TPs) are commonly generated through numerous abiotic and biotic processes during water treatment but also in the environment, such as photodegradation (Ellepola et al., 2022), hydrolysis (Bijlsma et al., 2013), microbial biodegradation (Li et al., 2022), or organism-specific metabolism (Ashauer et al., 2012). TPs complicate the chemical risk assessment as they are often unknown and can exhibit higher levels of toxicity or persistence than their precursors (Ellepola et al., 2022; Maculewicz et al., 2022), or can transform back to their precursor (Su et al., 2016).

Moreover, under specific circumstances, TPs can be present at higher concentrations than their precursors would indicate. In closed systems, the mass of a generated TP from a single precursor should not exceed its precursor's mass. However, closed systems are rarely observed in nature and there can be multiple sources of TPs. For example, for plant accumulation, internal TP concentrations are influenced by the aquatic and soil media as well as by plant metabolism (Bueno et al., 2022). Additionally, structurally similar chemicals can be metabolised into the same TP (Schollée et al., 2017; Rubirola et al., 2014).

As CECs and their TPs already pose a formidable challenge in conventional water systems, their fate and behaviour in water reuse systems must be thoroughly understood and managed before intentional water reuse can be implemented on a large scale to ensure acceptable risks. During water reuse practices, the potential for the accumulation of contaminants inherently increases (Fig. 1). Conventionally, TWW is discharged into surface waters where either intentional or *de facto* reuse can occur for non-potable reuse such as agriculture or indirect potable reuse. Thus, great care has to be taken to properly manage residual contaminants in TWW to ensure acceptable risks for the reuse application (Fig. 1).

Existing water reuse reviews have focused on topics such as conventional water parameters (Li et al., 2009), microbial risks (Nappier et al., 2018), social issues (Ricart and Rico, 2019), regulatory concerns (Jeffrey et al., 2022), or treatment and agricultural reuse specific questions (Narain-Ford et al., 2020; Christou et al., 2024). However, CECs and TPs are either not the focus of these reviews or are discussed in the context of a specific reuse case. This review complements previous efforts by focusing on the characterisation of risks posed by CECs and TPs during practiced intentional reuse applications at full scale, based on specific reuse applications, water sources, water treatment, and for specific chemicals.

2. Methods

2.1. Review process and selection criteria

Literature was retrieved from the SCOPUS database in August 2023 using various search strings and combinations, each consisting of two parts (Tab. S1). Firstly, they covered various terms relating to water reuse (e.g., reclaimed water) and secondly, they included different

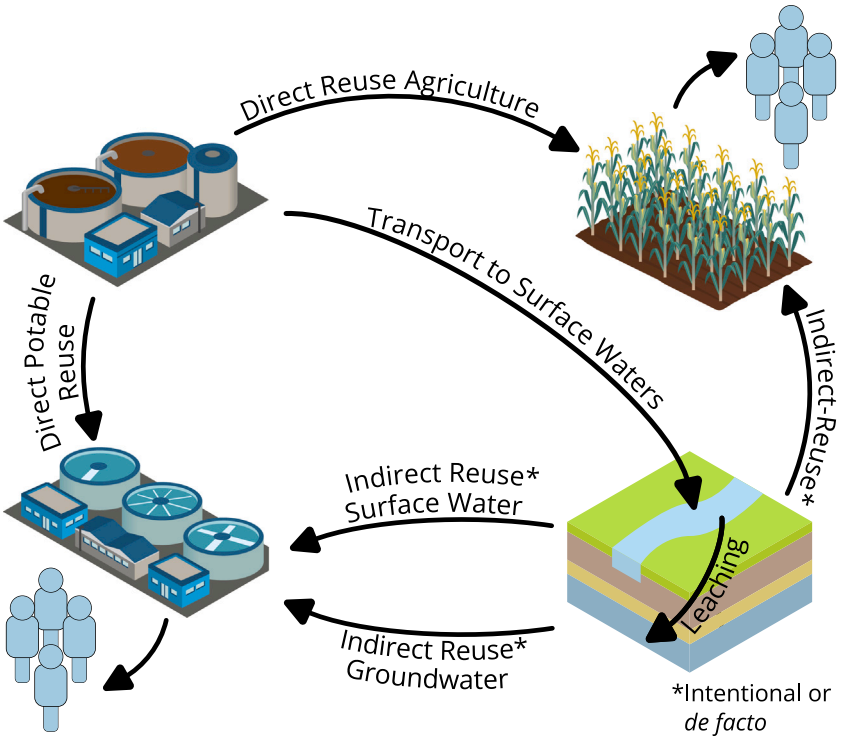

Fig. 1. Schematic water reuse cycle demonstrating intentional or *de facto* water reuse.

definitions for chemical contaminants (e.g., chemicals/contaminants of emerging concern). Literature was selected based on the following criteria: the study had to (i) practice water reuse, (ii) study CECs, and (iii) be performed at full scale. First, studies were filtered based on their abstract to determine if they met the relevant criteria and subsequently evaluated in detail.

2.2. Extracted literature data

From each paper, the reused water source, the reuse application, the water treatment technique and achieved removal efficiency, detected chemical concentrations, and targeted and detected chemicals were retrieved. Only reported numerical values were collected and no values were read from figures to avoid over- or underestimation. If not reported, removal was calculated per paper and per chemical based on reported values (Eq. (1)). Treatments were reported as indicated in the papers and were not categorised further.

$$Removal\ (\%) = 100 - \frac{CEC_i\ Concentration\ After\ Treatment}{CEC_i\ Concentration\ Before\ Treatment} * 100 \quad (1)$$

CECs were classified as detected if they were found at least once per study. The focus was exclusively on data that reported on water that was reused. For chemicals that were below the detection limit, (e.g., after treatment) the reported detection limit was used as a conservative worst-case scenario as well as half the detection limit (indicated in Tab. S2).

Reported water reuse applications were categorised firstly as *potable* or *non-potable* and subsequently to specific reuse applications (e.g., non-potable; agriculture). For the specific reuse applications, the studies were categorised as *landscape irrigation* if the reuse was practiced for green spaces such as city parks. If water reuse was practiced to restore or maintain a healthy water balance in ecosystems, it was categorised as *ecological restoration*. *Municipal reuse* was defined for general municipal purposes such as vehicle or street washing, excluding landscape irrigation, however. Reuse applied for industrial applications was defined as *industrial reuse*, with the general exception of producing drinking water, which was defined specifically as *potable reuse*. Studies that applied a form of soil-aquifer treatment were classified as *indirect potable reuse*.

For each reported chemical, physicochemical parameters were retrieved from PubChem or ChemSpider. These include the octanol-water partition coefficient (Log *P*, *or* Log K_{OW}), the pH-adjusted octanol-water partition coefficient (Log *D*), the organic carbon-water partition coefficient (Log K_{OC}), the bioconcentration factor (BCF), and the molecular weight (MW). Due to the number of collected chemicals, modelled data was preferred and data mining was carried out using the *R webchem* (Szöcs et al., 2020) and *RSelenium* packages (Harrison, 2022). Additionally, the OPERA readily biodegradable model (Version 2.9) was used to classify compounds for their general biodegradability (Mansouri et al., 2018).

The model is applicable to heterogeneous organic chemicals and is not restricted by a specific chemical class. Applicability of a given chemical to the model is evaluated by determining if it falls within the chemical space of the training set (binary outcome). Compounds outside the model's applicability domain were excluded from the analysis (Tab. S15).

2.3. Chemical classification

Three different approaches were chosen for the classification of chemicals, which were (i) a data-driven approach, (ii) their inclusion in the "Substitute It Now!" (SIN) list, and (iii) their registration under different frameworks.

For the data-driven approach, the median detection and analysis frequency of chemicals in the compiled dataset was set as a cut-off value. Chemicals exceeding this value were included in the analysis. Thus, the data were filtered on environmental relevance (i.e. detection) and their incorporation into monitoring lists (i.e. analysis). Every chemical was then classified into a respective class such as pharmaceuticals, plant protection products (PPP), personal care products (PcP), industrial chemicals, sweeteners, stimulants, illicit drugs, or ambiguous if no clear usage field could be retrieved. Additionally, distinct chemicals that exhibit increased potential hazards were classified separately including

PFAS, polycyclic aromatic hydrocarbon (PAH), and TPs which were grouped with disinfection byproducts. For the classification, publicly available databases or websites were used such as the NORMAN network, the website of the European Chemicals Agency (ECHA), or the Pesticide Properties DataBase (PPDB). If no clear classification could be found, expert knowledge was applied.

The second approach used the SIN list to enable a simple classification according to hazard and not according to application (SIN, 2024). A clear advantage of the SIN list is that it is specifically related to substances of very high concern such as very persistent, and very mobile substances, carcinogens, or endocrine disruptors.

As a third approach, chemicals were classified according to their presence in the work from Van Dijk et al. (2021). Van Dijk et al. assessed and evaluated five European chemical registration frameworks including pharmaceuticals (Directive 2001/83/EC), veterinary pharmaceuticals (Directive 2001/82/EC), pesticides (Reg no 1107/2009), biocides (Reg no 528/2012), and industrial chemicals (Reg no 1907/2006), and generated a list of chemicals, based on their CAS number, registered under each framework.

2.4. Risk assessment

The ecological and human health risks posed by CECs during water reuse were assessed by calculating their risk quotients (RQs) (Eq. (2)).

$$RQ_i = \frac{Concentration\ CEC_i}{Effect\ Concentration\ CEC_i} \quad (2)$$

Where the *Concentration* CEC_i is the reported concentration of an individual CEC and the *Effect Concentration* describes either the predicted no-effect concentration (PNEC) of an individual compound for the ecological risk assessment or a (preliminary) drinking water guideline value ((p)GLV) for human health risk assessment, respectively. For the RQ calculation, only the reported individual CEC concentrations were used. Furthermore, the RQ for the ecological risk assessment was also assessed to account for dilution effects, for which the *Effect Concentration* CEC_i (Eq. (2)) was divided by 10. Reported concentrations were filtered for chemicals with at least 10 available values to compensate for data availability.

Freshwater PNEC values were retrieved from the NORMAN database, (p)GLV from the available literature (Tab. S3), and selected for the lowest available value.

Furthermore, the threshold of toxicological concern (TTC) was applied as an additional approach to human health risk assessment. The distinct advantage of the TTC approach lies in its ability to assess compounds based on their structure, thus offering an alternative when guideline values are missing. For this, generic drinking water target levels for the Cramer classes were used as presented in Baken et al. (2018) and compared to the concentration of the reported CEC, similarly to Eq. (2). Cramer classes of the CECs, based on their canonical SMILES, were retrieved by Toxtree (Version 3.1.0.1851) with the "Cramer rules, with extensions" decision tree.

2.5. Simulation of CEC mass accumulation during water reuse practices

The theoretical CEC mass accumulation during water reuse practices for (agricultural) irrigation was simulated in a highly simplified, illustrative 4-year scenario: Water reuse with TWW was assumed to be practiced over three months (e.g., summer), followed by nine months of conventional water use with a clean water source. First-order degradation was assumed as degradation is likely concentration-limited and first-order kinetics are often assumed in environmental fate models (Boethling et al., 2009; Cousins et al., 2019). After three years of water reuse, a year without reuse but continued degradation was simulated. The initial mass, $m_{(t_0)}$, based on reported median CEC concentrations from selected studies, was assumed to be equal to the increase during reuse as a conservative assumption ($m_{(t_0)} = m_{increase}$). The general progress of the curve during the increase is, however, independent of this parameter. Changes during reuse and subsequent degradation were calculated using Eqs. (3) and (4), respectively, with t in days and k as the first-order rate constant derived from assumed half-life (DT_{50}) values of 30, 60, 90, and 120 days (Eq. (5)), covering the persistence criteria in REACH (EC, 1999). Furthermore, extreme scenarios were assumed with a DT_{50} of 200 and 2000, and for a non-degradable compound, k was set to 0 days (∞).

$$m_{t,i} = \left(m_{(t-i)} + m_{increase}\right) \cdot e^{-k} \quad (3)$$

$$m_{t,i} = m_{t-i} \cdot e^{-k} \quad (4)$$

$$DT_{50} = \frac{ln(2)}{k} \quad (5)$$

2.6. Data analysis

All analyses were performed with *R*, Version 4.4.1 (R Core Team, 2024) and RStudio, 2024.09.0 (RStudio Team, 2024).

3. Results & discussion

3.1. Collected literature data

The literature search yielded a total of 553 papers, with 87 (16%) tentatively classified as pilot studies and 113 (20%) as full-scale studies. The focus was put on the 113 full-scale studies, from which 48 (8%) were finally selected after reevaluating them. Multiple studies did not fulfil the required criteria, for example, by not applying water reuse. A complete overview can be found in the supplementary data (Tab. S4 - S6).

The number of papers published for selected and combined search strings between 1998 and 2023 increased steadily from 2013 onwards, with a steep increase after 2018 (Fig. 2 & Fig. S1). This may be explained by increased global awareness of water scarcity and more extreme weather events such as the severe European drought in 2018.

The 48 studies were carried out between 2003 and 2023 in 16 different countries: Spain (12), the United States (11), Australia (6), China (3), Germany (3), Israel (2), Brazil (1), Czech Republic (1), Cyprus (1), England (1), Italy (1), Jordan (1), Mexico (1), The Netherlands (1), Slovenia (1), Singapore (1), and Tunisia (1). Most of these countries are faced with natural water shortages due to their climate, geographical location, or dense populations that require increased freshwater supply.

3.1.1. Reused water sources

The reviewed papers most frequently studied the reuse of TWW (Table 1). About two-thirds of all studies reported using secondary or tertiary TWW, while the remaining third was made up mainly of different mixtures of water sources. These mixtures would conventionally be classified as surface water, but their specific composition was clearly influenced by TWW and should, therefore, be recognised as TWW reuse. This is especially important from a legal perspective. Under the EU regulation 2020/741, only “urban waste water resources” are allowed for reuse (EU, 2020), which are defined by Directive 91/271/EEC, as "domestic waste water or the mixture of domestic waste water with industrial waste water and/or run-off rain water" (EU, 2014). Therefore, it might be legally unclear whether the use of the mixtures shown in Table 1 would be considered water reuse, even though they are clearly defined as such from an environmental perspective. These ambiguities could hinder the implementation of water reuse applications. Hence, properly describing and defining water reuse sources, as well as recognising their composition, will help to avoid misunderstandings.

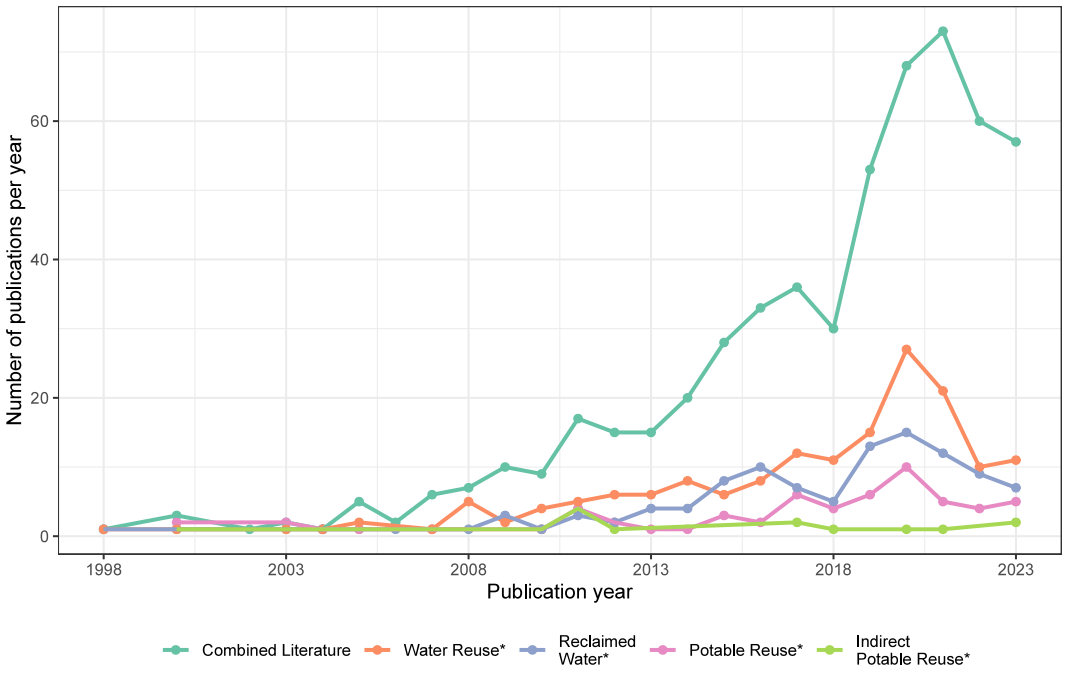

Fig. 2. Number of papers published yearly between 1998 and 2023 for selected search strings.
Only papers between 1998 and 2023 were included in the plot, one publication from 1978 was excluded. Search strings marked with an asterisk indicate combined search parameters (see Section 2.1). For example, "Water Reuse*" includes all literature collected using search parameters including the term "Water Reuse".

Table 1
Individual water reuse sources reported in the literature.

Specific water composition	Times reported (%)	Conventional classification
Secondary TWW	20/52 (38)	TWW
Tertiary TWW	14/52 (27)	TWW
TWW	5/52 (9)	TWW
TWW+SW	3/52 (5)	SW
Domestic WW	2/52 (3)	UWW
Primary TWW	1/52 (2)	TWW
Run-off from residential buildings	1/52 (2)	Unconventional
SW+Secondary TWW	1/52 (2)	SW
Stormwater	1/52 (2)	Unconventional
Stormwater + filter backwash drinking water treatment	1/52 (2)	Unconventional
Tertiary TWW+SW	1/52 (2)	SW
TWW+Stormwater	1/52 (2)	Unconventional
UWW+SW	1/52 (2)	SW

Specific water compositions are shown with their conventional classification. TWW = Treated wastewater; SW = Surface water; UWW = Untreated wastewater; WW = Wastewater. "Filter backwash drinking water treatment" was not further specified.

3.1.2. Water reuse applications

The 48 reviewed papers predominantly described non-potable reuse applications (Table 2), which was expected given the high quality requirements and legal boundaries for potable reuse. Overall, ten different reuse applications were reported, and two reuse cases were not further specified. Agricultural reuse is currently the focal point of water reuse studies, followed by indirect-potable reuse (Table 2). For industrial reuse, it was not specifically reported which industry sectors were applying reuse. No direct potable reuse cases were described in the literature based on the selected field studies.

3.1.3. Water treatment for reuse

Overall, 36% of the studies did not report tertiary or advanced treatment before water reuse (Table 3). Interestingly, these studies exclusively reused water for agriculture or green infrastructure irrigation. One study, however, reported treatment for agricultural reuse with managed aquifer recharge (Sunyer-Caldú et al., 2022). No single treatment stands out based on its occurrence in the literature. Contrastingly, treatment combinations are observed more frequently, combining oxidative, size-exclusion, or sorptive treatment processes. Exceptions are water reuse practices with a single treatment technique such as conventional treatment with activated sludge, soil-aquifer treatment, or ultra- and microfiltration.

3.1.4. Analysed chemicals during water reuse

Overall, 1051 different substances, verified by their respective CAS numbers (1007) or their names if CAS numbers were unavailable (44), were reported (Tab. S7). These chemicals were largely analysed by targeted analysis and only three studies applied non-target screening (McEachran et al., 2018; Alygizakis et al., 2020; Backe, 2021).

The top ten most frequently analysed and detected CECs are shown in Table 4 with a complete overview provided in the supplementary information (Tab. S8). All target compounds were frequently detected with rates of at least 75%, which underlines their ubiquity in water cycles.

Table 2
Water reuse cases in the literature, with reuse purpose and country of origin.

Specific reuse	Times reported (%)	General reuse	Countries
Agriculture	17/59 (29)	Non potable	ES(8), CY(1), IL(1), JO(1), MX(1), NL(1), SI(1), US(1)
Indirect-potable	9/59 (16)	Potable	US(5), ES(2), BR(1), SG(1)
Landscape irrigation	9/59 (16)	Non potable	US(3), CN(2), AU(1), ES(1), IL(1), IT(1)
Industrial	7/59 (12)	Non potable	AU(3), CN(1), DE(1), GB(1), US(1)
Ecological restoration	6/59 (10)	Non potable	CN(3), DE(1), ES(1), IL(1)
Reclamation/Resource Recovery	3/59 (5)	Non potable	AU(2), US(1)
Hydroponic	2/59 (3)	Non potable	DE(1), TN(1)
Unspecified irrigation	2/59 (3)	Non potable	DE(1), US(1)
Aquaponic	1/59 (2)	Non potable	CZ(1)
Domestical	1/59 (2)	Non potable	US(1)
Municipal	1/59 (2)	Non potable	US(1)
Unspecified	1/59 (2)	Unspecified	US(1)

(Indirect-)Potable = Water reuse to produce drinking water, indirectly via an environmental buffer; Landscape irrigation = Irrigation for green spaces or city parks; Industrial = Reuse for industrial applications, except drinking water production; Ecological restoration = Restoration or maintenance of a healthy water balance in ecosystems; Municipal reuse = Municipal purposes such as vehicle or street washing, excluding landscape irrigation.
Countries are indicated by their ISO 3166 A-2 country code. AU = Australia; BR = Brazil; CN = China; CY = Cyprus; CZ = Czech Republic, DE = Germany; ES = Spain; IL = Israel, IT = Italy; JO = Jordan; MX = Mexico; NL = Netherlands; SG = Singapore; SI = Slovenia; TN = Tunisia; US = United States of America

Table 3
Reported water treatments prior to reuse in the literature.

Treatment	Times reported (%)
Secondary Treatment	20 (36)
SAT	5 (9)
AS	2 (4)
Anaerobic-anoxic-oxic + MBR	2 (4)
MF + RO	2 (4)
O3 + BAC	2 (4)
Sand F. + UV + Chlor.	2 (4)
UF	2 (4)
Biological membrane rector	1 (2)
EGSB/SBR	1 (2)
EGSB/SBR/BACF	1 (2)
Green filters	1 (2)
MF	1 (2)
MF + RO + UV	1 (2)
MF/RO	1 (2)
Moving bed biofilm	1 (2)
NF/RO	1 (2)
O3	1 (2)
O3 + GAC	1 (2)
O3 + GAC + UF + RO	1 (2)
O3/BAF/GAC	1 (2)
RO	1 (2)
Sand F. + Chlor.	1 (2)
UF + RO + UV	1 (2)
UF + UV + GAC	1 (2)
rbMAR	1 (2)

SAT = Soil-Aquifer-Treatment; AS = Activated sludge; MBR = Membrane bioreactor; MF = Microfiltration; RO = Reverse Osmosis; O3 = Ozonation; BAC/GAC = Biologically/Granular activated carbon; Sand F. = Sand filtration; UV = ultraviolet irradiation; Chlor. = Chlorination; EGSB/SBR/BACF = Expanded Granular Sludge Bed Reactor/Sequencing Batch Reactor; NF = Nanofiltration; UF = Ultrafiltration; rbMAR = reactive barriers with managed aquifer recharge. Green filters were not further specified in the literature.

Regarding TPs, they are analysed less often but their detection frequency is comparable to that of precursor compounds (Table 4). Overall, the TPs of carbamazepine were analysed and detected most frequently. Further comparing Tables 4 and 5, it is noticeable that only one precursor, carbamazepine, of the analysed TPs is present in Table 4. As most CECs of Table 4 have identified TPs (e.g., 4'-hydroxydiclofenac, N4-acetylsulfamethoxazole, 3-hydroxyibuprofen), the TPs of commonly measured CECs should receive more attention in further research.

It is generally poorly understood which TPs are generated from which CEC, and due to their unknown properties, they represent both an environmental and regulatory blind spot. Especially TPs with high persistence merit increased attention for circular systems, as they may show significant accumulation. Additionally, TPs are often more polar than their precursors (Zahn et al., 2024), making them more mobile and increasing their potential to reach non-target sources (e.g., groundwater). This increased polarity also complicates their separation with conventional chromatographic techniques, presenting an analytical challenge. Combined with their typically low concentrations, this requires careful selection of appropriate enrichment methods (Zahn et al., 2024). Additionally, certain actively used chemicals can be both precursor and TP, which can hinder the identification of contamination sources. For example, salicylic acid is used against certain skin infections and is simultaneously a TP of aspirin. Similarly, benzophenone and its TPs (e.g., benzophenone-1, benzophenone-3) are used mainly as UV filters but also in fragrances. It is also important to carefully classify TPs based on their generation during water treatment (e.g., ozonation) or by naturally occurring processes (e.g., hydrolysis) (Löffler et al., 2023). Although these TP classes may overlap for certain processes (e.g., photodegradation), distinguishing them could help to ensure that appropriate TPs are analysed in a given matrix and context.

3.1.5. Classification of CECs

The applied approach, based on the selection of a chemical exceeding the median of detected and analysed chemicals, yielded 175 individual substances (Tab. S9), with 49% identified as pharmaceuticals and 20% as plant protection products (Table 6). Compared to the total number of reported chemicals (1051), only 16% were classified.

The relatively high percentage of TPs of the prioritised chemicals is noteworthy. Knowledge about the fate and behaviour of TPs water reuse systems is still limited, however, the reported data suggests that TPs are already receiving increased attention.

Moreover, only three different PFASs namely, perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), and perfluorobutanoic acid were analysed, which is consistent with PFAS-specific literature reviews which highlight that only a small fraction of PFASs are frequently studied (Gkika et al., 2023).

Of the 1051 reported compounds, 94 were classified as substances of very high concern on the SIN list (Tab. S11). Comparing the SIN list to the classified CECs and TPs (Table 6), 24 compounds are present in both (Tab. S12). This indicates that the CEC classification according to their area of application is not necessarily effective in identifying chemicals with potential adverse effects on humans and the environment. Therefore, databases such as the SIN list are of particular importance, as they enable the straightforward identification of substances of very

Table 4
Top ten most commonly detected and analysed CECs during water reuse practices.

Chemical	CAS	Times Detected/Analysed	Frequency of Detection [%]
Carbamazepine	298-46-4	37/39	95
Diclofenac	15307-86-5	29/31	94
Naproxen	22204-53-1	22/29	76
Caffeine	58-08-2	26/28	93
Sulfamethoxazole	723-46-6	26/28	93
Ibuprofen	15687-27-1	22/25	88
Atenolol	29122-68-7	23/25	92
Trimethoprim	738-70-5	25/25	100
Gemfibrozil	25812-30-0	22/24	92
Triclosan	3380-34-5	17/22	77

Times analysed and detected refer to the number of times a chemical was analysed and the times it was detected.

Table 5
Ten most commonly analysed TPs during water reuse practices with their precursors.

TP	CAS	Times Detected/Analysed	Frequency of Detection [%]	Precursor(s)
Salicylic Acid	69-72-7	6/9	67	Aspirin
Carbamazepine 10,11-Epoxide	36507-30-9	9/9	100	Carbamazepine
Cotinine	486-56-6	6/9	67	Nicotine
4-Acetamidoantipyrine	83-15-8	6/8	75	Metamizole
4-(Formylamino)Antipyrine	1672-58-8	8/8	100	Aminophenazone
Norcitalopram	62498-67-3	7/8	88	Citalopram
Chloroform	67-66-3	5/7	71	DBP
Dichlorobromomethane	75-27-4	5/7	71	DBP
Bromoform	75-25-2	6/7	86	DBP
N-Nitrosodimethylamine	62-75-9	7/7	100	DBP

Times analysed and detected refer to the number of times a chemical was analysed and the times it was detected. DBP = Disinfection by-product

Table 6
Classification of the 175 *prioritised* chemicals out of 1051 reported in the literature.

Classification	Observations	Percentage [%]
Pharmaceutical	85	49
Plant protection product	35	20
TP	21	12
Industrial chemical	12	7
Personal care product	11	6
PFAS	3	2
Illicit drug	2	1
PAH	2	1
Sweetener	2	1
Ambiguous	1	1
Stimulant	1	1

Displayed are, for each classification, the total number of observations and its corresponding percentage, rounded up for clarity.

Table 7
Classification of all 1051 chemicals reported in the literature based on their registration under different frameworks.

Classification	Legislation	Observations	Percentage [%]
Industrial chemical	Reg no 1907/2006	194	19
Pharmaceutical	Directive 2001/83/EC	80	8
Pesticide	Reg no 1107/2009	61	6
Biocides	Reg no 528/2012	31	3
Veterinary pharmaceutical	Directive 2001/82/EC	26	3
Multiple	NA	25	2

high concern. However, generally, only well-studied compounds are recognised as such and should not be used solely to identify harmful chemicals.

Chemicals classified according to their registration under different frameworks can be seen in Table 7 and Tab. S13. As opposed to Table 6, industrial chemicals dominate the classified compounds making up a fifth of the entire dataset, followed by pharmaceuticals as the second highest class. Overall, this approach was able to classify about 39% of the reported chemicals.

In general, each approach only classified a subset of the entire data set. Taking all approaches together, 47% of chemicals could be classified and 18 compounds are shared between the individual classifications. Classifying chemicals remains ambiguous and publicly available databases but also shifting towards a "one substance - one assessment" approach would help to avoid uncertainties and ease risk assessment (Van Dijk et al., 2021).

3.1.6. Physico-chemical parameters and biodegradability

The environmental transport processes of CECs are dictated by the physicochemical properties of the environmental media and the CECs. Knowing these properties helps to understand and predict their fate and behaviour in the environment. For example, the octanol-water partition coefficient K_{OW} describes the hydrophobicity and can serve as an indicator of a chemical's sorption to soil particles, sediments, activated sludge, or activated carbon.

The range of physicochemical parameters of all 1051 and the 175 frequently detected compounds in the selected literature can be found in Fig. 3 and Tab. S8 & S14. The reviewed literature focuses on compounds of relatively low molecular weight, classified, according to Neumann and Schliebner (2019), as mobile (Log $K_{OC} < 4$), and for the majority as very mobile chemicals (Log $K_{OC} < 3$). For compounds filtered based on their detection frequency, the clear majority is classified as very mobile. This shows that highly mobile compounds are expected to be present and frequently studied in a water reuse context and, therefore, often detected. Hence, compounds posing the highest likelihood of reaching groundwater sources due to their mobility are often studied.

For all compounds, the median Log K_{OW} value is 2.7. If the Log D value is used, for all values at pH = 7.4 in this section, the majority of the compounds could be classified as polar with a median Log D of 2.

Potential bioaccumulation in aquatic organisms was assessed by the BCF which indicates, according to the REACH criteria, that most compounds are not bioaccumulative (Log BCF > 3.3). For plant accumulation, however, Log D might be the better predictor to assess bioaccumulation potential (Maculewicz et al., 2022). Managing and

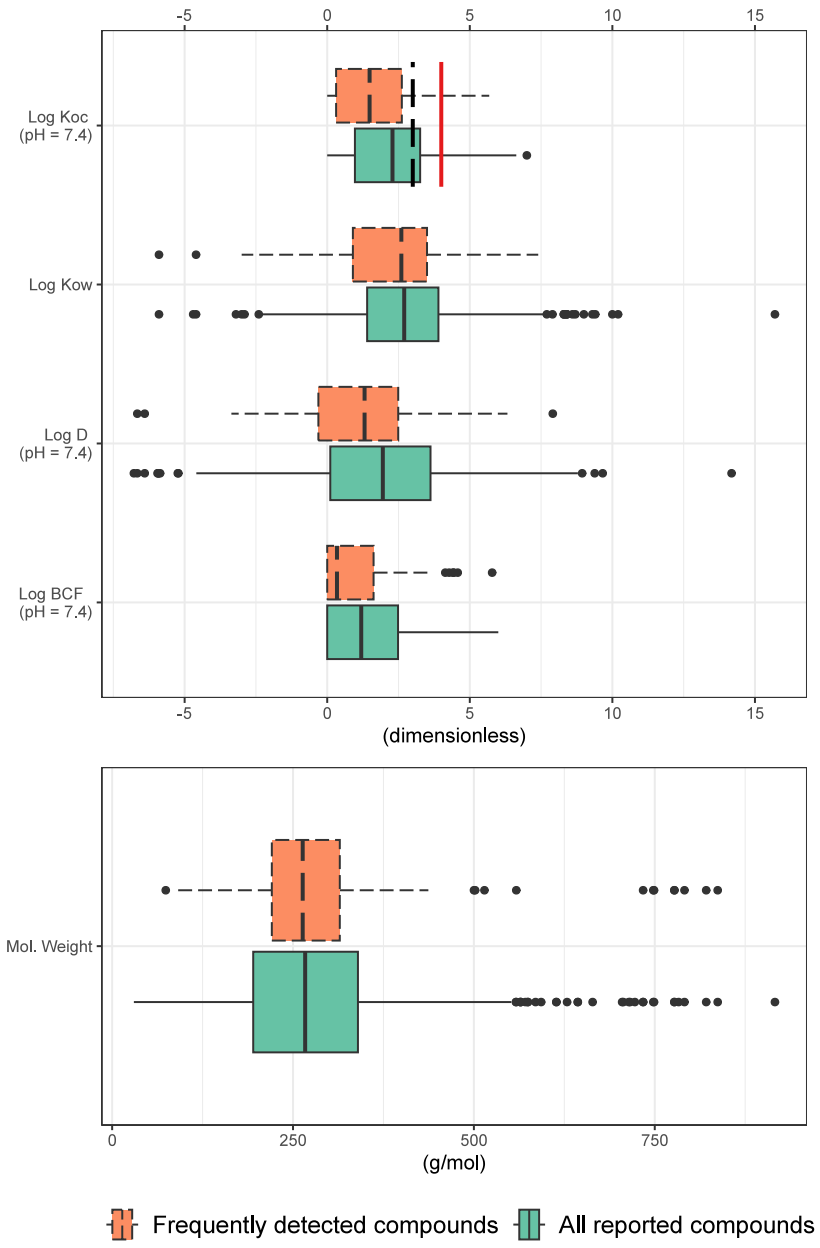

Fig. 3. Boxplots showing selected physicochemical parameters of all reported and the frequently 175 detected CECs.
Vertical black lines inside the boxes indicate the median, the box compromises the 25th and 75th percentile, and whiskers indicate the 5th and 95th percentile. Black dots denote outliers. Dashed black and solid red lines indicate thresholds for very mobile (Log Koc < 3) and mobile (Log Koc < 4) compounds according to Neumann and Schliebner (2019). Values for Log K_{OW} and the molecular weight were retrieved from PubChem, Log K_{OC}, Log *D*, and Log BCF from ChemSpider.

limiting the potential for CEC bioaccumulation in crops is vital to ensure consumer safety as it is likely that CECs are accumulated in crops, though to what extent is unclear. Identifying compounds with the highest crop accumulation potential could, therefore, aid in designing future strategies for agricultural water reuse.

The majority of all reported compounds and prioritised compounds that fell into the applicability domain are classified as non-biodegradable ($n_{reported}$ = 744, 83.3%; $n_{prioritised}$ = 101, 87.1%) (Tab. S15). This result is expected as more persistent compounds are likely to be detected more frequently in the environment.

Combining all studies, independent of the reuse type, the focus of the literature is on mobile, persistent, and polar compounds, which is in line with expectations as these are most relevant and most likely to be present in the aquatic environment.

3.1.7. Reported removal during water reuse

The removal rates and final CEC concentrations for the studied micropollutants, based on reported data (Tab. S2), are displayed in Fig. 4. It was not possible to calculate the removal rates for every treatment (Table 3), as the corresponding raw data were not always sufficiently provided. Technical treatment processes such as the MF/RO/UV AOP or MF double-pass RO achieve the highest CEC removal and lowest concentrations (Fig. 4). However, there is a clear unbalance in the data abundance for the various treatment methods from 6 to 410 data points per treatment or treatment combination.

It is noticeable that most of the treatments lead to CEC concentrations for reuse that are frequently found at trace levels between 0–100 $ng\,L^{-1}$ (Fig. 4, B). Consequently, relative removal should not be the decisive factor in the assessment of treatment efficacy for

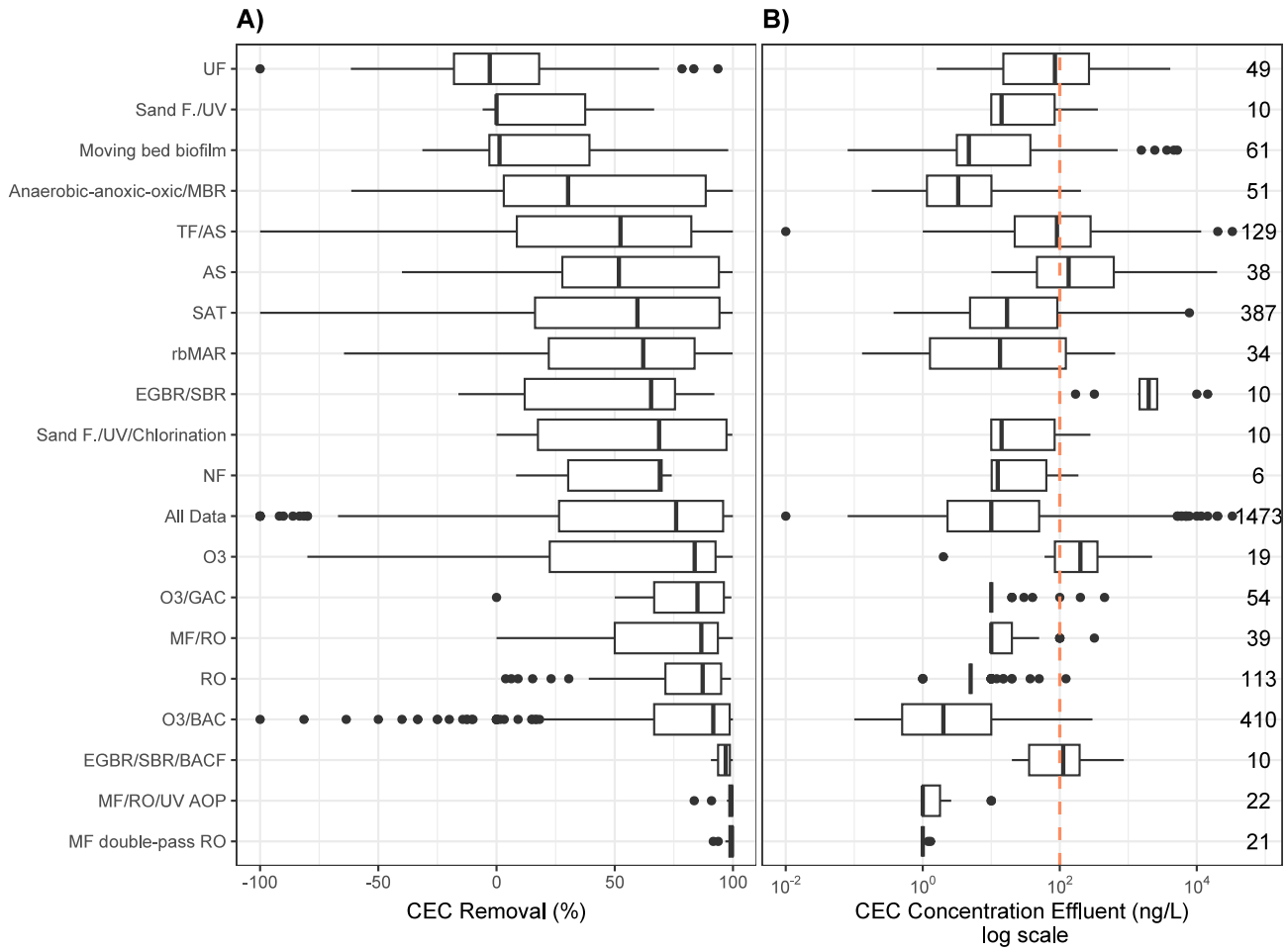

Fig. 4. Reported CEC removal rates (%) (A) and final CEC concentration per chemical after individual treatments for water reuse (B).
Vertical black lines inside the boxes indicate the median, the box compromises the 25th and 75th percentile, and whiskers indicate the 5th and 95th percentile. Black dots denote outliers and numbers, next to the whiskers (B), indicate the number of reported concentrations per group. The dashed red line (B) indicates the European Groundwater Directive precautionary threshold of 100 ng L^{-1} for pesticides with insufficient toxicity data.

water reuse. For example, SAT has a median CEC removal of 60%, suggesting moderate removal, but shows a median CEC concentration of 17 ng L^{-1}, which generally could be considered sufficiently low. As SAT is common for drinking water production, post-treatment would be likely and CEC concentrations could decrease further. Similarly, this divergence between removal efficiency and final CEC concentration can also be observed for the anaerobic-anoxic-oxic + MBR treatment or the moving bed biofilm treatment. Another example of why it is relevant to consider final effluent concentrations is the numerous observed outliers for O3/BAC indicating negative removal (Fig. 4, A). A closer look at the data reveals that these are influent and effluent concentrations between 0.1–12.4 ng L^{-1}. At these low concentrations, higher variability is to be expected as the treatment and analytical techniques may reach their limits. This also underlines the crucial role of detection and quantification limits in assessing CECs in TWW. These parameters are influenced by various factors, including sampling, sample processing, and analysis. However, there are no globally approved standardised methods for the detection of CECs in TWW, thus introducing considerable uncertainty into the assessment. Moreover, the potential production of TPs should be recognised when assessing treatment efficiency, especially for oxidative treatments, as a high removal of a precursor might lead to significant TP formation. Consequently, future studies should emphasise reporting both relative removal and absolute concentrations and include TPs in their assessment.

To put the data in a regulatory context, appropriate threshold values for the detected chemicals are essential but often unavailable. As a conservative alternative, the EU groundwater quality value for pesticides and their metabolites of 100 ng L^{-1}, could be applied ((EU) 2020/2184, 2020). Considering the entire data set, the majority (81%) falls below this value after treatment. Depending on the specific reuse, protection target, time frame, and especially the CEC, this threshold is, however, debatable and is most likely insufficiently protective of human and environmental health. Especially since the data cover a wider variety of chemicals than only pesticides and compounds below the threshold may still be relevant due their recalcitrant or toxicological properties, such as PFAS. The threshold value would also not be relevant for most TPs, which are normally characterised by low concentrations. Accordingly, the applied threshold of 100 ng L^{-1} should serve as an illustrative example that a single value is insufficiently protective but, simultaneously, general values are needed due to lacking toxicological data. Therefore, a way forward would be water reuse-specific threshold values, based on reuse applications and reused water sources, to ensure safe reuse.

3.2. Risk assessment of CECs & TPs for water reuse

Based on the reported CEC concentrations at the point of reuse (Tab. S2 & S3), ecological and human health risks were analysed that could stem from residual CECs and TPs and their RQs (Eq. (2)) were plotted as boxplots (Fig. 5, 6, S2, S3). For 77% of the detected CECs, PNECs were available on the NORMAN database and for 28% (p)GLV could be retrieved (Tab. S4). When considering no dilution, clear ecological risks were identified for PFOS, chlorpyrifos, triclocarban, and ethinylestradiol. Furthermore, ibuprofen and diazinon show increased risks with

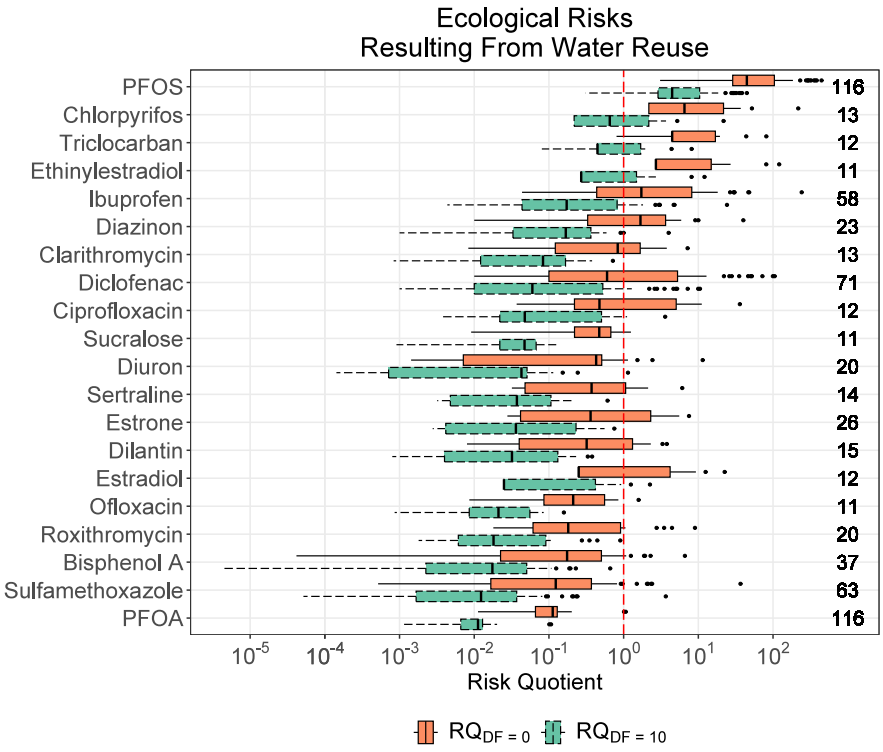

Fig. 5. The distribution of calculated risk quotients for the ecological risk assessment resulting from water reuse.
Only CECs with n > 10 reported values are shown and that exceed the RQ = 1 at least once. Red boxplots show resulting risks with a dilution factor (DF) of 0, green boxes resulting risk with a DF of 10. Vertical black lines inside the boxes indicate the median, the box compromises the 25th and 75th percentile, and whiskers indicate the 5th and 95th percentile. Black dots denote outliers and numbers, next to the whiskers, indicate the number of observations per CEC. The red line shows the threshold of RQ = 1. PFOS = Perfluorooctanesulfonic acid; PFOA = Perfluorooctanoic acid. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

median RQs > 1 (Fig. 5). However, the underlying NORMAN data uses a variety of assessment factors (AF). For example, the PNEC derivation of PFOS is based on the human health tolerable daily intake (AF = 200), and sucralose, ofloxacin, and roxithromycin are based on acute-toxicity data (AF = 1000). Therefore, uncertainty is introduced into the risk assessment and risks may differ if more robust PNEC values were available.

Considering a dilution factor (DF) of 10, only PFOS clearly exceeds the RQ of 1. However, DFs can significantly vary by region and during low-flow events, potentially falling below 10. (Rice and Westerhoff, 2017; Keller et al., 2014). Accordingly, the actual risks lie between a DF of 0 and 10. Therefore, resulting risks during droughts or direct reuse could be substantial, and proper risk mitigation methods should be implemented.

Human health risks resulting from potable reuse could be identified for PFOS and PFOA, which clearly exceeded the RQ of 1, together with PFHXs and PFNA, which exceeded the RQ but with a median RQ < 1 (Fig. 6). Considering half the detection limit (Fig. S3), the general distribution of RQs did not change considerably for the compounds presented in Fig. 6. Phenol, N-nitrosodimethylamine, 1,4-Dioxane, and dichloroacetic acid, exceeded the RQ of 1 but were characterised by poor data availability (n < 10). No other CECs exceeded the threshold, except for occasional outliers.

Ten compounds exceeded their TTC value, expressed as drinking water target level, of 4 $\mu g\,L^{-1}$ (Cramer class III) (Tab. S15). For the majority of these compounds, a p(GLV) was available and, accordingly, the TTC threshold was not applied. Ultimately, only allopurinol's TP, oxypurinol, was identified as an additional risk during potable reuse, but as only one value was reported, its relevance for potable reuse is limited. However, the literature suggests that oxypurinol is a ubiquitous aquatic contaminant due to its polarity and persistence (Funke et al., 2015).

The risk assessment considered only individual substances and not the resulting mixtures. Although mixture risk assessment is a promising approach, its technicalities are still the subject of debate and it was not performed in this study (Backhaus, 2024). Accordingly, further mixture effects cannot be excluded and risks are likely higher when accounting for mixtures. Future studies are therefore encouraged to use effect-based methods to assess mixture effects as they enable a comprehensive mixture assessment beyond known target compounds.

3.3. Risk characterisation during potable reuse

Potable reuse can be designed in two ways, direct or indirect (Fig. 7). In the latter case, an environmental buffer (e.g., aquifer, subsoil, river), serves as an intermediate storage or treatment step. *Vice versa* for direct potable reuse, there is no intermediate step and water is directly reused for drinking water production. Depending on direct or indirect reuse, different risks can be characterised.

3.3.1. Indirect-potable reuse and its potential risks

For indirect reuse, the possibility arises that the pollutant load entering the environmental buffer exceeds its natural removal capacity. A constant inflow of highly persistent compounds could be problematic in such a system. Therefore, the first treatment steps (Fig. 7, **1**) should be optimised to ensure sufficient removal but also sufficient protection of the environmental buffer (Fig. 7, **4**). This can, for example, be supported by appropriate residence times in the infiltration basin for aquifer treatment.

This approach not only allows dilution and renaturalization of the reused water but also offers additional removal processes including photo- and biodegradation and is implemented in Singapore's reuse

Fig. 6. The distribution of calculated risk quotients for human health resulting from potable water reuse.
Only CECs with n > 10 reported values are shown and that exceed the RQ = 1 at least once. Vertical black lines inside the boxes indicate the median, the box compromises the 25th and 75th percentile, and whiskers indicate the 5th and 95th percentile. Black dots denote outliers and numbers, next to the whiskers, indicate the number of observations per CEC. The red line shows the threshold of RQ = 1. PFOS = Perfluorooctanesulfonic acid; PFOA = Perfluorooctanoic acid; PFHxS = Perfluorohexanesulfonic acid; PFNA = Perfluorononanoic acid; 2,4-D = (2,4-Dichlorophenoxy)acetic acid; PFBS = Perfluorobutane sulfonate.

scheme, where TWW (i.e., MF, RO, UV) is stored in reservoirs before it is used for drinking water production (Seah et al., 2008). The positive influence of longer residence times was also observed for CEC removal and reduced bioactivity, albeit for non-potable reuse (Wang et al., 2021; Leusch et al., 2014). Leusch et al. reused TWW (conventional sedimentation, activated sludge, engineered anaerobic/aerobic lagoons) with residence times of 7 and 30 days. Wang et al. reused TWW after treatment with an anaerobic-anoxic-oxic and a membrane bioreactor and storing it for 14 days.

Nevertheless, water quality changes should be considered during storage time, for example by the generation of TPs. Since the combination of pre-treatment and environmental buffer is unlikely to offer optimal removal of all CECs, post-treatment must ensure potable water quality and effective CEC removal (Fig. 7, **9**). Nevertheless, the environmental buffer still offers a cost-effective nature-based treatment, with the advantage of storing water for periods of time.

3.3.2. Field scale studies applying indirect-potable reuse

Indirect potable reuse with SAT treatment was most frequently observed (Table 3) in the studies of Fajnorová et al. (2021), McEachran et al. (2018), Drewes et al. (2003), and Laws et al. (2011). One exception is the work of Munné et al. (2023) where indirect-potable reuse was achieved using surface water as an intermediate buffer.

Drewes et al. (2003), Fajnorová et al. (2021) and Laws et al. (2011) used a similar water source; secondary TWW with activated sludge followed by tertiary filtration with dual-media filtration. Similarly, Munné et al. (2023) used secondary TWW with activated sludge but subsequently applied a combination of flocculation, sedimentation, lamellar decanters, and disinfection by UV and optional chlorine. McEachran et al. (2018) only reported to have used secondary TWW. It is important to note that CEC and TP removal during water reuse will be significantly influenced by the applied wastewater treatment technologies and the overall water quality. These should, therefore, be reported as detailed as possible since, for example, ozonation or UV treatments can be affected by dissolved organic carbon, and the water pH can influence reverse osmosis' removal efficiency as it influences the charge of the membranes (Fischer et al., 2019).

In general, it was observed that longer travel times of 60 days (Laws et al., 2011), 180 days (Drewes et al., 2003), and 1 year (Fajnorová et al., 2021) improved CEC removal. While no travelling times were indicated, high removal rates were also reported over a 3-month sampling period by McEachran et al. (2018) of at least 68% for the majority of analysed CECs. Overall, the reported median CEC concentration of these studies was 59.2 $ng\,L^{-1}$ (IQR = 87.1 $ng\,L^{-1}$). These findings are also supported by Trussell et al. (2018) who performed an elaborate lab study simulating SAT over 4 years. However, compounds such as acesulfame, carbamazepine, hydrochlorothiazide, lidocaine, oxypurinol, phenytoin, primidone, simazine, sucralose, sulfamethoxazole, TCEP, valsartan acid, and 4-nonylphenol showed neglectable removal. Interestingly, McEachran et al. (2018) report a removal of 97% for carbamazepine indicating that site-specific factors during SAT can significantly affect CEC removal. Overall, this flags these compounds, as potential performance indicators for SAT as these can help to further elucidate which factors influence their removal. Except for 4-Nonylphenol, these compounds are classified as very mobile (Log K_{OC} < 3), potentially explaining their poor removal. Therefore, appropriate post-treatment steps must be in place to remove recalcitrant compounds or dilute the reused water source with an uncontaminated source (Fig. 7, **8**).

For indirect potable reuse using surface waters as an environmental buffer, it was reported that 1,4-dioxane proved to be problematic as it was consistently slightly below its human threshold (50 μg/L) and originated clearly from the TWW (Munné et al., 2023). Moreover, 10 compounds (Tab. S16) were identified that exceeded their environmental guideline values, which highlights that indirect potable reuse has to account for human and environmental health effects.

Consequently, SAT for indirect potable reuse with post-treatment can lead to acceptable removal rates where longer travel times of preferably up to one year during soil-aquifer treatment can lead to diminished CEC concentration, with observed median concentrations

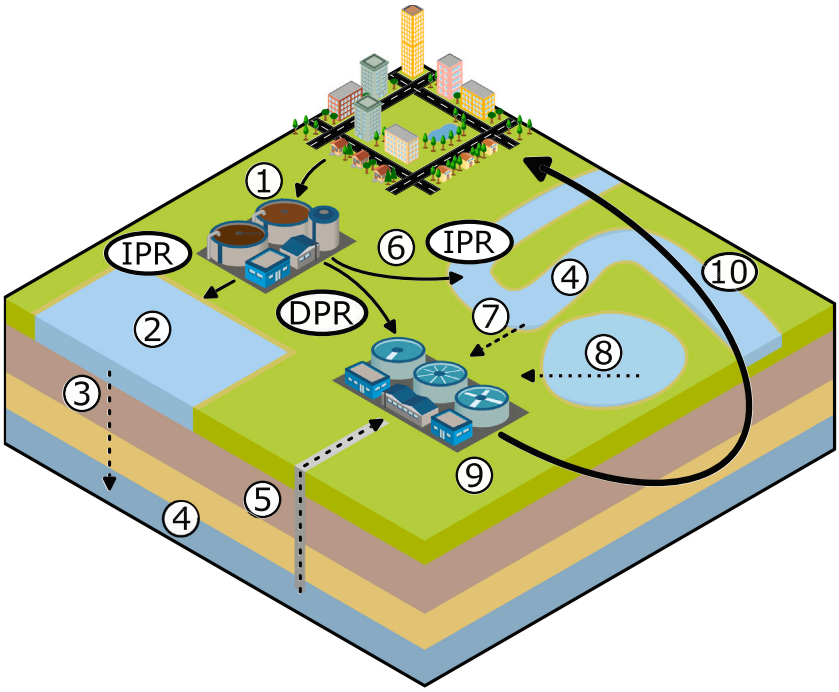

Fig. 7. Schematic design of indirect and direct potable reuse.
1 = First treatment, 2 = Infiltration Basin, 3 = Soil-aquifer treatment, 4 = Environmental buffer, 5 = Groundwater abstraction, 6 = Transport to surface water, 7 = Surface water abstraction, 8 = Clean water source for dilution, 9 = Post-treatment, 10 = Transport to consumers, IPR/DPR = Indirect/Direct Potable Reuse.

< 60 ng L^{-1} (Fajnorová et al., 2021; Laws et al., 2011; Trussell et al., 2018; McEachran et al., 2018; Drewes et al., 2003). Similarly, the indirect potable reuse using surface waters or reservoirs as intermediate buffer is also a viable option but may pose risks to the buffer (Munné et al., 2023; Seah et al., 2008). For both approaches the initial water source is strongly recommended to be of sufficient quality. This should be based on strict monitoring to ensure that the concentrations of CECs are low enough to guarantee sufficient removal, either during water treatment or in the environment.

3.4. Risk characterisation for non-potable reuses

For non-potable reuse, a larger variety of reuse applications is possible, each involving specific risks. As seen in Table 2, agricultural reuse was the most applied reuse practice and is the main focus of the following section.

3.4.1. Agricultural water reuse and its associated risks

Agricultural water reuse comes with a set of specific environmental risks, which include the transport of reused water to non-target sites, (bio)accumulation of CECs in soil and plants resulting in human health risks, and potential effects on the soil microbial community. Moreover, relevant environmental fate and degradation processes are dictated by the irrigation type such as sprinkler, drip, or sub-surface irrigation (see Fig. 8).

3.4.2. Field scale studies on agricultural reuse

Overall, 16 reuse cases were found in the literature that studied CECs during or for agricultural reuse (Tab. S6). The majority (9) of these studied reused secondary TWW, followed by mixed surface water and TWW, and tertiary TWW. The observed CEC concentrations for different water sources before irrigation show considerable disparity in the data (Table 8). Next to the difference in data availability, potential explanations include a focus on recalcitrant compounds or insufficient treatment efficiency.

It was generally observed that crops accumulated CECs but to varying levels which were below human health hazards (Ben Mordechay et al., 2021; Calderón-Preciado et al., 2011a; Riemenschneider et al., 2016; Meffe et al., 2021; Franklin et al., 2016; de Santiago-Martín et al., 2020; Calderón-Preciado et al., 2011b; Bueno et al., 2022; Christou et al., 2017; Kovačič et al., 2023). Especially the work by Ben Mordechay et al. (2023), who performed a large national field study on the fate of CECs in the soil-plant continuum, found that the human health risks through the dietary exposure of crops irrigated with TWW are generally acceptable. Only under an extreme exposure scenario, unacceptable risks for lamotrigine, carbamazepine, and 10,11-epoxycarbamazepine were observed. However, their set of analytes falls short of PFASs or endocrine disruptors, which can have grave health effects at very low concentrations. In contrast, Malchi et al. (2014) found that carrots and sweet potatoes irrigated with secondary TWW accumulated lamotrigine and 10,11-epoxycarbamazepine at levels exceeding their TTC under normal exposure conditions.

The general bioaccumulation pattern between different crops and CECs was found to be increased in leafy vegetables, followed by root vegetables and cereals, and lowest in fruits (Christou et al., 2019; Ben Mordechay et al., 2021). However, Bueno et al. (2022) found increased concentrations in tomatoes compared to the leaves, which could be due to crop- and contaminant-specific accumulation. Moreover, Sunyer-Caldú et al. (2022) found that sprinkler irrigation led to a decreased CEC bioaccumulation in lettuce as compared to drip irrigation. Applying soil amendments such as straw or biochar could

Table 8
Observed CEC concentration (ng L^{-1}) for reported reused water sources for agricultural reuse.

Water Source	Mean	SD	Median	IQR	n
Untreated WW+SW	10 320	29 536	748	1410	11
Tertiary TWW	762	1746	188	246	48
TWW+SW	291	656	63	320	122
Secondary TWW	172	565	18	83	426
All Data	440	4224	28	160	607

SD = standard deviation, IQR = interquartile range, n = Number of data points, (T)WW = (Treated) wastewater, SW = surface water.

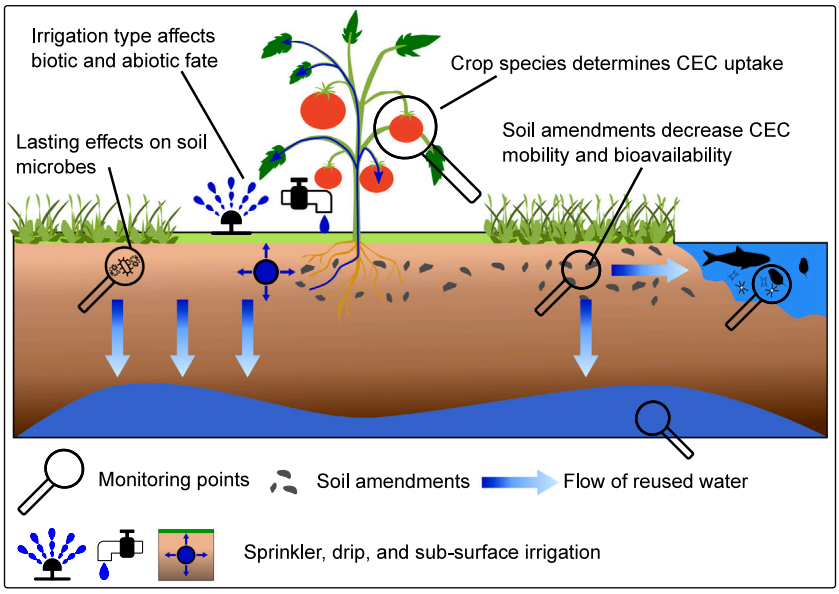

Fig. 8. Potential risks of wastewater reuse for agriculture.

help in this instance to not only enhance soil properties, and protect non-target sources through reduced leaching, but also reduce CEC crop bioaccumulation (Siedt et al., 2021).

Another option to limit CEC accumulation in the soil-plant continuum could be the alternation between conventional irrigation and water reuse (Shi et al., 2023; Ben Mordechay et al., 2023). However, this approach will not avoid CEC accumulation in the soil or protect non-target sources. While the shift from reusing water to conventional irrigation decreases the CEC concentration in the soil, and sufficient rainfall has been found to limit CEC accumulation (Narain-Ford et al., 2022), it does not eliminate them completely. Therefore, the irrigation history with TWW of agricultural land and local climatic conditions should be considered during water reuse practices (Ben Mordechay et al., 2023).

Studies investigating the effects of CECs during TWW irrigation on the soil microbial community seem to be limited. While a clear time-depending factor on the soil microbial community has been identified, CECs are not the focus point of these studies (Guedes et al., 2022; García-Orenes et al., 2015; Zolti et al., 2019). However, Bigott et al. (2022) could show that the TWW itself had a greater impact on the community structure than the CECs.

In conclusion, the CEC accumulation in fruity crops appears to be limited and generally does not exceed human health risks. Therefore, water reuse for agricultural reuse offers potentially acceptable human health risks. Still, risk mitigation options should be undertaken, which include appropriate irrigation methods, the application of soil amendments, and alternation between irrigation with TWW and conventional water sources. Furthermore, since agricultural reuse was carried out most frequently with secondary TWW, upgrading wastewater treatment plants with advanced treatment techniques would be an effective risk-reduction option.

3.5. Modelled CEC mass during water reuse

The results of the modelled mass load during water reuse over three years show that compounds with an increased half-life (DT_{50} > 200 days) would, as expected, accumulate during reuse (Fig. 9). More importantly, however, during reuse all compounds are present in the system and only a DT_{50} of 30 days would lead to a diminished mass lower than its initial mass of 17 ng during one reuse cycle (e.g., June–June).

Thus, during recurrent yearly reuse practices, compounds with increased persistence could be considered *reuse-persistent* as they are continuously reintroduced. Under REACH, a compound is only considered persistent with a DT_{50} > 120 days in soil, while the present analysis indicates that such an assumption would underestimate CEC persistence and accumulation during water reuse for irrigation. Especially when reuse periods are extended or the interval between reuse periods decreases. For direct potable reuse, however, this would not be a special case, as there is no *reuse-persistence* and pollutants would be correctly classified as persistent according to REACH with a DT_{50} > 40 days.

However, the approach neglects important processes such as dilution or wash-off by rainwater and is an oversimplification. Moreover, (bio)degradation is influenced by multiple factors and can vary widely between environmental media. 1,4-dioxane, for example, has an increased half-life in groundwater of 2 to 5 years, while in surface water of 56 days (Hale et al., 2020).

3.6. Recommendations for future water reuse studies

Future water reuse studies are recommended to include detailed descriptions of the reused water source including its origin (e.g., municipal, industrial TWW) and conventional water quality parameters (e.g., pH, DOC). This could help to understand how the water source and its quality relate to water treatment and CEC removal. Thus, improving the assessment of the fate and behaviour and the risk assessment of CECs during reuse.

Regarding specific CECs, pharmaceuticals are most frequently studied during water reuse. It is recommended to broaden the focus to CECs characterised by increased persistence such as PFASs.

Additionally, future studies should apply non-target screening to identify TPs. Compared to target screening, non-target screening is not confined by analytical standards or known compounds. Instead, it allows to analyse a sample without the need for *a priori* knowledge about the sample but identifies compounds based on their molecular mass, fragments, isotopic patterns, or retention times allowing unexpected compounds or unknown TPs to be identified (Hollender et al., 2023).

Chemical analysis should further be complemented with effect-based methods such as those applied in the water reuse studies of Leusch et al. (2014), Tang and Escher (2014), Reungoat et al. (2010), Escher et al. (2013, 2014). All these studies clearly showed improved water quality after treatment as the observed biological effects were

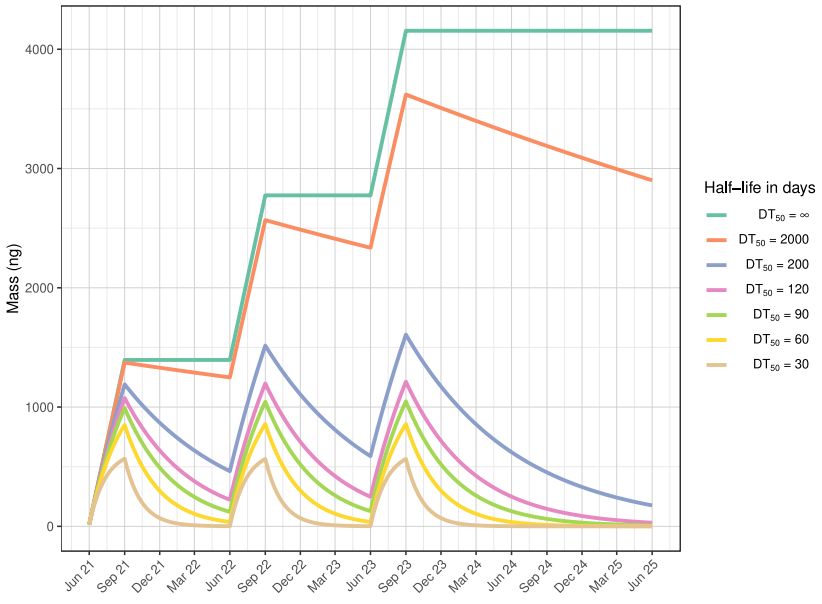

Fig. 9. Theoretical CEC mass over four years for a single CEC under the assumption of different DT_{50} values.

diminished. The distinct advantage of effect-based methods, lies in their ability to provide a risk-scaled toxicity assessment of the entire mixture without *a priori* knowledge about the sample chemical composition, similar to non-target screening, and thus overcome the lack of suitable indicator compounds for reuse applications or treatments. Furthermore, they could contribute to increased public confidence and acceptance of water reuse practices (Neale et al., 2023, 2022).

For agricultural reuse, it is recommended that future studies implement additional risk mitigation methods that aim at reducing the amount of chemicals that can accumulate in the soil-plant environment. This could either be achieved by additional water treatment, alternating between water reuse and conventional irrigation, irrigation techniques, or soil amendments.

Another critical point that was observed during the review was that the data reporting quality of the monitored chemicals failed the data principles of findability, accessibility, interoperability, and reusability (FAIR). While in general, all papers provided their data so that it was findable, data was frequently not accessible or interoperable, making data reusability significantly difficult and time-consuming. Especially in a developing field such as water reuse, where significant leverage on its implementation is held by policymakers and regulators, it is of the utmost importance that all data is reported in a way that eases its assessment. Therefore, further research should put special emphasis on:

- Providing specific chemical identifiers such as the CAS number, PubChem CID, SMILES, or the InChI key is crucial to avoid confusion about which CEC was studied. Only reporting trivial chemical names is not sufficient and abbreviations should be avoided in the reported raw data. Furthermore, CAS numbers are subject to change, often lacking for TPs, and providing at least two identifiers such as CAS + SMILES, or CAS + InChI key is recommended. With the aid of the *R webchem* package, such challenges can be handled with little effort.
- Reporting measured concentrations with at least a limit of detection and quantification for all monitored chemicals. Not detecting a chemical in the environment does not necessarily translate to the absence of a compound or a removal efficiency of 100%.
- Providing proper data formats and data files that are accessible to readers. Clear Excel or comma-separated files, accompanied by meta-data files, improve the reusability of the reported data. We strongly advise against providing raw data in Word or PDF files.

3.7. Conclusions

Water reuse practices can generally be tailored to achieve acceptable human and environmental health risks of CECs and TPs. However, certain CECs exhibit clear ecological (PFOS, chlorpyrifos, triclocarban, ethinylestradiol) and human health risks (PFOS, PFOA). Agricultural and indirect potable reuse with secondary TWW are currently the most frequently observed reuse practices and show low CEC concentrations in crops, groundwater, and surface water samples. Still, for agricultural reuse, it is recommended to irrigate crops with low bioaccumulation potential, particularly those where the consumed parts, such as fruits, accumulate in general less contaminants. However, additional treatment steps are recommended for both reuse applications to further reduce the number and concentrations of CECs reaching the environment.

Furthermore, more water reuse studies are needed to address important research questions, including studying the long-term effects posed by CECs and TPs in agricultural soil and potential adverse effects on soil organisms. This also includes the long-term effects of indirect potable reuse on the environmental buffer. There is a clear need to include more PFASs in water reuse studies as their data availability is currently limited for reuse practices, while their risks are potentially substantial. Moreover, more diverse data are needed regarding the initial reused water source. Almost all reviewed papers used TWW as their water source, but numerous additional options are available. In this regard, greater care should be given to characterise the water source as this will lead to an increased understanding of the relationship between water source, water treatment, reuse applications, and the risks posed by specific CECs and their mixtures.

Glossary

AF - Assessment factor; **AS -** Activated sludge; **AWS -** Alternative water source; **BAC/GAC -** Biologically/Granular activated carbon; **BCF -** Bioconcentration Factor; **CEC -** Chemical of emerging concern; **Chlor. -** Chlorination; **DF -** Dilution factor; **DT_{50} -** Half-life; **ECHA -** European chemicals agency; **EGSB/SBR/BACF -** Expanded Granular Sludge Bed Reactor/Sequencing Batch Reactor; **IQR -** Interquartile range; ***k*** **-** First-order rate constant; **Log *D*** **-** pH-adjusted octanol-water partition coefficient; **Log K_{OC} -** Organic carbon-water

partition coefficient; **Log P/Log K_{OW}** - Octanol-water partition coefficient; **MBR** - Membrane bioreactor; **MF** - Microfiltration; **MW** - Molecular weight; **NF** - Nanofiltration; **O_3** - Ozonation; **PAH** - Polycyclic aromatic hydrocarbon; **PcP** - Personal care product; **PFAS** - Per- and polyfluoroalkyl substances; **PFOA** - Perfluorooctanoic acid; **(p)GLV** - (preliminary) drinking water guideline value; **PNEC** - Predicted no-effect concentration; **PPDB** - Pesticide properties database; **PPP** - Plant protection product; **rbMAR** - reactive barriers with managed aquifer recharge; **RO** - Reverse Osmosis; **RQ** - Risk Quotient; **Sand F.** - Sand filtration; **SAT** - Soil-Aquifer-Treatment; **SD** - Standard deviation; **SIN** - Substitute it now; **SW** - Surface water; **TP** - Transformation product; **TTC** - Threshold of toxicological concern; **TWW** - Treated wastewater; **UF** - Ultrafiltration; **UV** - Ultraviolet irradiation; **UWW** - Untreated wastewater.

CRediT authorship contribution statement

Jan C. Specker: Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Antonia Praetorius:** Writing – review & editing, Supervision. **Milo L. de Baat:** Writing – review & editing, Supervision. **Nora B. Sutton:** Writing – review & editing, Supervision. **Annemarie P. van Wezel:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material associated with this article is available at https://doi.org/10.1016/j.envint.2024.109226 and on GitHub https://github.com/SpeckerJ/Review_Specker_et_al_2024.

Data availability

Supplementary material associated with this article is available in the online version.

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