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Mitigating risk in water reuse systems by enhancing biofiltration with sorptive media

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Abstract

The current wastewater treatment paradigm has remained relatively constant during the 20th and at the beginning of the 21st century, despite the fact that external factors acting upon it, such as population size and urbanization, climate, and treatment quality and quantity requirements have undergone massive changes. A shift towards more locally managed intentional water reuse projects could reduce future stress on local water sources and provide higher microbial and chemical water quality than current *de facto* reuse practices. Potable reuse systems, direct and indirect (IPR/DPR), employ tailored treatment trains which are focused on greater removal of chemicals and pathogens present in wastewater treatment plant (WWTP) effluents. Both DPR and IPR often include membrane filtration within their treatment train, which can have high associated energy and waste disposal costs. Hence, recent research in IPR treatment trains has focused more on naturally based unit processes. The SMART*plus* biofilter, an engineered unit process based on natural managed aquifer recharge (MAR), was established and investigated at pilot-scale in a concurrent doctoral dissertation. By providing controlled redox zonation and hydraulic conditions within a smaller footprint and at shorter hydraulic retention times (HRT) than conventional MAR systems, the SMART*plus* biofilter demonstrated similar to enhanced trace organic chemical (TOrC) and pathogen removal as MAR systems. This thesis was primarily focused on a) investigating how a SMART*plus* based IPR treatment train could mitigate risk from TOrCs and pathogens, and b) whether the use of alternative biofilter media could improve long-term TOrC removal.

Chemical and microbial risks were quantitatively evaluated. An initial literature review on quantitative microbial risk assessments (QMRA) for potable and non-potable reuse scenarios revealed that probability distribution functions (PDFs) are often used to describe pathogen concentrations in source water (stochastic), while log reduction values (LRVs) in unit treatments are rather described using point values (deterministic). However, when enough point value LRVs are known, a triangular distribution can be constructed to better describe the variability and uncertainty associated with the measurements and retain a stochastic description of removal. Additionally, using PDFs to describe removal facilitates a more comprehensive and nuanced assessment of final risk through the evaluation of various percentiles of final risk against health burden thresholds. Utilizing this knowledge, a screening level QMRA of the SMART*plus* based treatment train was conducted for three reference pathogens: norovirus, *Cryptosporidium*, and *Campylobacter*. Ambient removal in all unit treatment steps was described by LRVs obtained from literature, with the exception of norovirus removal in the SMART*plus* biofilter, which was described using experimental MS2 phage removal data. A Bayesian network (BN) was constructed to assess the probability of treatment train compliance with disease burden (10^{-6} disability adjusted life years (DALYs)) and annual risk of infection (10^{-4} infections per person per year) thresholds. The QMRA revealed that the treatment train successfully met both thresholds at the 95% percentile for all pathogens. A similar probabilistic BN was used to conduct a quantitative chemical risk assessment (QCRA) for TOrCs present in the Garching WWTP effluent in concentrations exceeding their health-based monitoring trigger levels (MTL). Concentrations of benzotriazole, gabapentin, diclofenac,

valsartan acid, and carbamazepine in the effluent of a sequential biofiltration (SBF), and their removals in subsequent GAC filtration and UV disinfection were modeled with PDFs. The TOrC concentrations in the UV disinfection effluent were evaluated as the point of compliance (POC). The BN revealed that most TOrCs were below their MTL at the POC, with the exception of valsartan acid, whose POC concentration had a 5-58% probability of exceeding the MTL.

To determine whether the initial and long-term removal of these TOrCs in the SMART*plus* biofilter could be improved by using adsorptive media instead of technical sand, parallel laboratory-scale column filters filled with technical sand and GAC were continuously operated with tertiary treated effluent over the course of 2 years. After a certain time and throughput, GAC filters amass a biofilm and become biologically activated carbon (BAC) filters. To determine the contributing of adsorption and biodegradation in a BAC filter, a rapid small-scale column test (RSSCT) was performed to quantify adsorption and compared to the removal observed in the BAC filter in an attempt to quantify adsorption and biodegradation removal contributions. The RSSCT TOrC breakthrough was observed through 40,000 bed volumes treated (BVTs). Adsorption overestimation due to the difference in particle size between the BAC filter and the RSSCT was corrected using a fouling index and breakthrough was modeled using a pore surface diffusion model (PSDM). This model fit the breakthrough of poorly to moderately adsorbable compounds (i.e. tramadol) better than for well adsorbable compounds (i.e. trimethoprim). However, the poor agreement between PSDM-modeled breakthrough and experimental BAC breakthrough of carbamazepine, venlafaxine and tramadol revealed that the modeling underpredicted the adsorption capacity of compounds. The initial high loading rate and short EBCT, as well as the fouling indices calculated for each compound, were identified as likely causes of the misfit. In the end, comparing RSSCT and BAC breakthroughs did not allow estimation of the biological removal contribution to cumulative BAC removal and its comparison with initial biodegradation in sand filters. TOrC removal over the long-term was studied in continuously-fed lab-scale filter experiments. Variable quality of feed water from the WWTP did not allow steady-state removal in the filters. However, high-resolution sampling after > 85,000 BVT and batch biodegradation tests using the media from long-term filters demonstrated similar removal of biodegradable and non-adsorptive compounds such as gabapentin, iopromide and antipyrine in sand and BAC after the adsorptive capacity of BAC had been exhausted. As no evidence of improved removal in BAC was observed, this demonstrates that technical sand is a suitable media for SMART*plus* and other biofiltration based unit treatment processes.

Zusammenfassung

Das derzeitige Paradigma der Abwasserbehandlung ist während des 20. und zu Beginn des 21. Jahrhunderts relativ konstant geblieben, trotz der Tatsache, dass Einflussfaktoren, wie Bevölkerungsgröße und Urbanisierung, klimatische Bedingungen sowie die Anforderungen an Qualität und Quantität der Abwasserbehandlung massive Veränderungen erfahren haben. Eine Verlagerung hin zu stärker dezentralen Behandlungsansätzen unter Einbeziehung von Konzepten zur geplanten Wasserwiederverwendung könnte in Zukunft die Belastung lokaler Wasserressourcen verringern und zugleich eine höhere mikrobielle und chemische Wasserqualität sicherstellen, als dies durch die derzeit weit verbreitete *de facto* Wiederverwendungspraxis der Fall ist. Bei der direkten und indirekten Wasserwiederverwendung (engl.: Direct Potable Reuse (DPR) und Indirect Potable Reuse (IPR) kommen Behandlungskombinationen zum Einsatz, die eine verbesserte Entfernung von Chemikalien und Krankheitserregern aus den Abwässern kommunaler Kläranlagen (engl.: Wastewater Treatment Plants (WWTP)) erreichen. Sowohl DPR- als auch IPR-Konzepte setzen häufig auf Membranfiltrationsschritte, was mit hohen Kosten für Energie und Entsorgung verbunden sein kann. Neuere Forschungsansätze im Bereich der IPR konzentrieren sich daher verstärkt auf weitergehende natürliche Aufbereitungsprozesse. Der SMART*plus*-Biofilter ist ein Prozess, der auf der künstlichen Grundwasseranreicherung (engl.: Managed Aquifer Recharge (MAR)) basiert. Das SMART*plus*-Biofilter wurde im Pilotmaßstab in einer begleitenden Doktorarbeit entwickelt und untersucht. Durch die Realisierung kontrollierter Redoxbedingungen und optimierter hydraulischer Bedingungen bei zugleich kleinerem Flächenbedarf und kürzeren hydraulischen Verweilzeiten, als bei herkömmlichen MAR-Systemen zeigte der SMART*plus*-Biofilter eine vergleichbare Entfernung von organischen Spurenstoffen und Krankheitserregern. Diese Arbeit konzentrierte sich in erster Linie darauf, a) zu untersuchen, wie ein auf dem SMART*plus*-Prozess basierendes IPR-Konzept das Risiko durch Spurenstoffe und Krankheitserreger mindern könnte, und b) ob die Verwendung alternativer Biofiltermedien die langfristige Spurenstoffentfernung verbessern könnte.

Chemische und mikrobielle Risiken wurden quantitativ bewertet. Eine Literaturrecherche zu quantitativer mikrobieller Risikobewertung (engl.: Quantitative Microbial Risk Assessment (QMRA)) für Wasserwiederverwendungsszenarien ergab, dass Wahrscheinlichkeitsverteilungsfunktionen (engl.: Probability Distribution Functions (PDFs)) häufig zur Beschreibung von Erregerkonzentrationen im Ausgangswasser verwendet werden (stochastisch), während logarithmische Reduktionswerte (engl.: Log Reduction values (LRVs)) für spezifische Prozesschritte eher durch Punktwerte beschrieben werden (deterministisch). Wenn die Reduktion jedoch ausreichend gut durch LRVs charakterisiert ist, kann eine Dreiecksverteilung konstruiert werden, um die Variabilität und Unsicherheit der Messungen besser zu beschreiben und eine stochastische Beschreibung der Entfernung beizubehalten. Darüber hinaus erleichtert die Verwendung von PDFs zur Beschreibung der Entfernung durch Darstellung verschiedener Perzentile eine umfassendere und nuanciertere Bewertung des Endrisikos. Auf Grundlage dieses Wissens wurde eine screening-level QMRA für den SMART*plus*-basierten Behandlungszug für

drei Referenzpathogene durchgeführt: Noroviren, *Cryptosporidium* und *Campylobacter*. Die Entfernung in allen Behandlungsschritten der Einheit wurde durch LRVs aus der Literatur beschrieben, mit Ausnahme der Norovirus-Entfernung im SMART*plus*-Biofilter, die anhand experimenteller Daten zur MS2-Phagenentfernung beschrieben wurde. Ein Bayes'sches Netzwerk (BN) wurde entwickelt, um die Wahrscheinlichkeit der Einhaltung gesundheitlicher Schwellenwerte für den Behandlungszug in Bezug auf die Krankheitslast (10^{-6} disability adjusted life years (DALYs)) und das jährliche Infektionsrisiko (10^{-4} Infektionen pro Person und Jahr) zu bewerten. Das Ergebnis der QMRA ergab, dass der Behandlungszug beide Schwellenwerte im 95%-Perzentil für alle Pathogene erfolgreich erreichte. Ein ähnliches probabilistisches BN wurde verwendet, um eine quantitative chemische Risikobewertung (engl.: Quantitative Chemical Risk Assessment (QCRA)) für organische Spurenstoffe durchzuführen, die im Abwasser der Kläranlage Garching in Konzentrationen vorhanden sind, die über den jeweiligen gesundheitsbasierten Monitoring Trigger Levels (MTL) liegen. Die Konzentrationen von Benzotriazol, Gabapentin, Diclofenac, Valsartansäure und Carbamazepin im Ablauf einer sequentiellen Biofiltrationsanlage (SBF) und ihre Entfernung während einer anschließenden Filtration über granulierte Aktivkohle (GAK) und einer UV-Desinfektion wurden mit PDFs modelliert. Die Spurenstoffkonzentrationen im Ablauf der UV-Desinfektion wurden als Point of Compliance (POC) definiert. Die Ergebnisse der BN-Simulationen ergaben, dass die Konzentrationen der meisten Spurenstoffe am POC unterhalb ihrer jeweiligen MTL lagen. Nur für den Stoff Valsartansäure wurde festgestellt, dass die POC-Konzentration mit einer Wahrscheinlichkeit von 5-58% die MTL überschritt.

Um zu ermitteln, ob die anfängliche und langfristige Entfernung dieser Spurenstoffe im SMART*plus*-Biofilter durch den Einsatz von Adsorptionsmedien anstelle von technischem Sand verbessert werden kann, wurden parallel dazu im Labormaßstab mit technischem Sand und GAK gefüllte Filtersäulen über einen Zeitraum von 2 Jahren kontinuierlich mit gereinigtem Abwasser betrieben. Nach einer bestimmten Zeit und einem bestimmten Durchsatz bildet sich in GAK-Filtern ein Biofilm, wodurch diese zu biologisch aktiven Aktivkohlefiltern (BAK) werden. Um den Beitrag von Adsorption und biologischem Abbau in einem BAK-Filter zu bestimmen, wurden Kleinsäulentests nach dem RSSCT- Konzept (engl.: Rapid Small Scale Column Tests) durchgeführt, um die Adsorptionskapazität bis zum Durchbruch zu quantifizieren, und mit der im BAK-Filter beobachteten Entfernung zu vergleichen. Der Durchbruch von Spurenstoffen in den RSSCT-Kleinsäulen wurde nach der Behandlung von etwa 40.000 Bettvolumina (BV) beobachtet. Die Überschätzung der Adsorptionskapazität aufgrund des Unterschieds in der Partikelgröße zwischen dem BAK-Filter und dem RSSCT wurde mit Hilfe eines Fouling-Indexes korrigiert und der Durchbruch wurde nach dem Porenoberflächendiffusionsmodell (engl.: Pore Surface Diffusion Model (PSDM)) modelliert. Dieses Modell passte für den Durchbruch von schlecht bis mäßig adsorbierbaren Verbindungen (z. B. Antipyrin) besser als für gut adsorbierbare Verbindungen (z. B. Trimethoprim). Die schlechte Übereinstimmung zwischen dem Durchbruch der Stoffe Carbamazepin, Venlafaxin und Tramadol nach dem PSDM-Modell und dem experimentellen Durchbruch bei der BAK zeigte jedoch, dass die Modellierung die Adsorptionskapazität der Aktivkohle für die Verbindungen

nicht ausreichend genau abbilden konnte. Die anfangs hohe Beladungsrate und die kurze Kontaktzeit sowie die für jede Verbindung berechneten Fouling-Indizes wurden als wahrscheinliche Ursachen für die ungenügende Anpassung angesehen. Der Vergleich der Durchbrüche in RSSCT- und BAK-Filtern erlaubte letztlich keine Abschätzung des Beitrags der biologischen Entfernung zur kumulativen Entfernung im BAK-Filter. Die langfristige Spurenstoffentfernung in Sand- und BAK-Filtern wurde in kontinuierlich betriebenen Filtersäulen im Labormaßstab untersucht. Die stark fluktuierende Beschaffenheit des Ablaufs der Kläranlage Garching erlaubte nicht die Einstellung einer stationären Entfernung in den Filtern. Hochauflösende Probenahmen nach > 85.000 BV und Batch-Versuche zum biologischen Abbaumit den Medien aus den Langzeitfiltern zeigten jedoch eine ähnliche Entfernung von biologisch abbaubaren und nicht-adsorbierenden Verbindungen wie Gabapentin, Iopromid und Antipyrin in Sand und BAK, nachdem die Adsorptionskapazität der BAK erschöpft war. Da kein Beweis für eine verbesserte Entfernung mit der BAK beobachtet wurde, zeigt dies, dass technischer Sand ein geeignetes Medium für SMART*plus*-Systeme und andere auf Biofiltration basierende Aufbereitungsprozesse ist.

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List of abbreviations

16S rRNA	16S ribosomal ribonucleic acid
ADI	Acceptable daily intake
AhR	Aryl hydrocarbon receptor
ATP	Adenosine triphosphate
AWT	Advanced water treatment
AOP	Advanced oxidation process
ARI	Annual risk of infection
BAC	Biologically active carbon
BDOC	Biodegradable dissolved organic carbon
BN	Bayesian network
BTP	Biodegradation transformation product
BVT	Bed volumes treated
CCP	Critical control point
CD	Constant diffusivity
CL_2	Chlorination
DALY	Disability adjusted life year
DO	Dissolved oxygen
DOC	Dissolved organic carbon
ΔDOC	Differential DOC
DOM	Dissolved organic matter
DNA	Deoxyribonucleic acid
DPR	Direct potable reuse
DWTP	Drinking water treatment plant
ETBE	Ethyl tert-butal ether
EBCT	Empty bed contact time
EfOM	Effluent organic matter
ER-α	Estrogen receptor-α
GAC	Granular activated carbon
GOW	Gesundheitlicher Orientierungswerte
GW	Groundwater

HAACP	Hazard analysis and critical control point
HQ	Hazard quotient
HRA	Health risk assessment
HRT	Hydraulic retention time
IPR	Indirect potable reuse
ISO	International Organization for Standardization
LC-HRMS	Liquid chromatography with high resolution mass spectrophotometry
LC-MS/MS	Liquid chromatography with tandem mass spectrophotometry
LFER	Linear free energy relationship
LOAEL	Lowest observed adverse effect level
LRV	Log removal values
MAR	Managed aquifer recharge
MEC	Mean effluent concentration
MF	Microfiltration
MTBE	Methyl tert-butyl ether
MTL	Monitoring trigger level
NDMA	N-Nitrosodimethylamine
NF	Nanofiltration
NMOR	N-nitrosomorpholine
NO(A)EL	No observed (adverse) effect level
NOM	Natural organic matter
O_3	Ozone
OECD	Organization for Economic Cooperation and Development
PAC	Powdered activated carbon
PD	Proportional diffusivity
PDF	Probability distribution function
PFOS	Perfluorooctanesulfonic acid
PFOA	Perfluorooctanoic acid
PNEC	Predicted No-Effect Concentration
POC	Point of compliance
PSDM	Pore surface diffusion model

PVDF	Polyvinylidene difluoride
QMRA	Quantitative microbial risk assessment
QCRA	Quantitative chemical risk assessment
qPCR	Quantitative polymerase chain reaction
QSPR/QSAR	Quantitative structure or activity relationship
RfD	Reference dose
RMSE	Root mean squared error
RO	Reverse osmosis
RSC	Relative source contribution
RSF	Rapid sand filter
RSSCT	Rapid small scale column tests
SBF	Sequential biofiltration
SMART	Sequential managed aquifer recharge technology
TDI	Tolerable daily intake
TOrC	Trace organic chemical
TTC	Threshold of toxicological concern
UF	Ultrafiltration
UV	Ultraviolet absorbance
UVA_{254}	Ultraviolet absorbance at 254 nm
UV AOP	Ultraviolet advanced oxidation process
WHO	World Health Organization
WRRMP	Water Reuse Risk Management Plan
WSP	Water Safety Plan
WWTP	Wastewater treatment plant

1. General introduction

The development of water supply and sanitation throughout history can be traced through public health impacts. Improper sanitation and increased pollution stemming from urban population growth during the Industrial Revolution caused outbreaks of waterborne diseases including cholera and typhoid (Smeets et al., 2006; Sinclair et al., 2015). The appearance of public water supply coupled with modern sewerage systems in the 19th century decreased the incidence of illness by transporting waste out of city centers to sewage farms or discharging it to surface waters (National Research Council, 2012). To further decrease waterborne illness spread to downstream settlements, cities built centralized wastewater treatment plants (WWTPs). These advancements led to an increase in life expectancy.

As the global population continued to increase throughout the 20th century, conventional WWTPs built in many cities removed pathogens, suspended solids and organic matter, and nutrients from sewage. Increasing pollution, greenhouse gas emissions, and the ever-expanding population consuming natural resources have induced climate change, which has had a cascade of negative effects on the availibility of water resources. The increased production of goods in various industries in the 20th century led to the greater usage of water in the manufacturing and many other industries.

Increased consumption of pharmaceuticals, personal care products, and a variety of other chemicals in the 20th and 21st centuries, coupled with advancements in analytical detection methods, revealed that removal of trace organic chemicals (TOrCs) in concentional WWTPs was insufficient. Incomplete removal results in the discharge of TOrCs in WWTP effluent to receiving surface water bodies, which affects not only the aquatic environment but also downstream drinking water treatement plants (DWTP), which abstract their raw water from the same water bodies, known as *de facto* reuse. Although pathogens are removed to a large extent in WWTPs, they can still also be found in groundwater and surface water in high-income and low-income countries alike. The current wastewater treatment paradigm has remained relatively constant, while the external factors acting upon it – population size and distribution, climate, treatment quality and quantity requirements, among others – have undergone massive changes in the 20th and 21st centuries.

In the 1980s, studies on quantitative microbial risk assessment (QMRA) began to quantify the risk from *de facto* reuse systems which sourced raw water for drinking water treatment from groundwater or surface water (Haas, 1983). Since then, significant advancement has been made in both pathogen detection and risk analysis methods for microbial pathogens, though outbreaks of waterborne disease due to improper water treatment or contamination still occur in high-income countries (MacKenzie et al., 1994). Risk assessment of threshold chemicals has identified safe concentration levels below which negligible human and environmental risk is expected, with specific chemicals regulated both in WWTP discharge and drinking water (World Health Organization, 2004).

However, conventional wastewater treatment or situations where *de facto* reuse occurs were not designed for sufficient removal of pathogens and TOrCs (Yang et al., 2017), which detrimentally affect aquatic life even at the ng/L-µg/L range (Reungoat et al., 2011; Jekel et al., 2013; Luo et al., 2014; aus der Beek et al., 2016). Therefore, many advanced water treatment (AWT) processes which focus on the removal of these and other contaminants have proposed to further mitigate these contaminants (Fischer et al., 2019). These employ a varity of removal mechanisms, such as size exclusion in membrane filtration (Snyder et al., 2007), oxidation during ozonation (Reungoat et al., 2011), biodegradation in biofilters (B. Ma et al., 2018), adsorption to sorptive media (Benstoem et al., 2017) or advanced oxidation processes (AOP) such as peroxide/UV irradiation (Miklos et al., 2018).

Intentional water reuse scenarios, such as direct and indirect potable reuse (DPR/IPR) have been introduced to combat the shortage of natural water sources in coastal as well as inland regions (World

Health Organization, 2017a). By selecting AWT unit processes capable of removing chemical and microbial contaminants present in the WWTP effluent, a final water quality can be tailored to the intended application, whether potable reuse for drinking water, or non-potable reuse for agricultural, urban or industrial uses. DPR involves the direct supply of advanced treated water to the DWTP or to drinking water distribution, and such systems have been around for more than 50 years, with one of the first DPR schemes in operation since 1968 in Namibia (Ander and Forss, 2011; World Health Organization, 2017a). IPR involves additional subsurface treatment via injection or introduction into an environmental buffer, such as surface or groundwater.

In an effort to move away from energy and resource intensive high-pressure membrane-based treatment systems, which also generated difficult to dispose of brine waste, further optimization of non-membrane based IPR systems have been the focus of recent research. Natural treatment systems such as managed aquifer recharge (MAR) have been shown to attenuate chemicals and pathogens via biodegradation, adsorption, and die-off processes occuring during subsurface transport (Drewes et al., 2015). The benefits of MAR treatment have been harnessed into sequential managed aquifer recharge technology (SMART) (Regnery et al., 2016; Hellauer et al., 2018a). Through enhanced control of redox and carbon conditions during subsurface treatment, and shorter hydraulic retention time resulting in a smaller physical footprint, enhanced removal of pathogens and chemicals can be achieved in engineered MAR treatment systems, such as sequential biofiltration (Müller et al., 2017). The SMART*plus* biofilter demonstrated this concept at pilot scale, investigating chemical and pathogenic contaminant removal in a technical sand biofilter operated with *in situ* aeration (Karakurt-Fischer et al., 2020a, 2020b, 2021).

A shift to more locally managed intentional water reuse projects can provide safer water quality from a microbial and chemical point of view than current *de facto* reuse (Chaudhry et al., 2017). Likewise, the reduction in energy costs and tailoring to local conditions and final desired effluent water quality increases the appeal of potable reuse systems.

This thesis will therefore investigate how a SMART*plus* based IPR system can mitigate risk from TOrCs and pathogens through two targeted objectives.

The first objective addresses microbial and chemical risk. By determining which assumptions are most scientifically sound for conducting quantitative chemical and microbial risk assessments (QMRA/QCRA) through screening peer-reviewed literature and interational guidelines, a probabilistic model to predict removals of chemicals and pathogens for each unit process of the SMART*plus* treatment trains can be constructed. The final results of these models, one each for chemicals and pathogens, will determine whether or not risk from the investigated treatment train complies with the respective guideline or threshold values.

The second objective addresses the possible short- and long-term benefits of utilizing activated carbon instead of technical sand in the SMART*plus* bioreactor as the substratum supporting biofilm growth. To accomplish this, two biofilter systems, one employing technical sand used in the SMART*plus* biofilter, and one using biological activated carbon (BAC), were operated in parallel. Both biofilter systems were fed with secondary effluent from the Garching WWTP to observe initial and long-term differences in TOrC removal. An extensive literature study of TOrC removal via biodegradation in various natural treatment systems determined compounds of interest showing high deviations in removal percentages for biofiltration systems. Long-term removal differences observed between the carbon and sand filters over 2+ years of operation were further quantified by performing batch biodegradation experiments to obtain decay rates for a kinetic removal comparison.

2. State-of-the-art

2.1 Risk assessment of water treatment

Risk assessment for environmental systems encompasses the following steps: hazards in an environment must first be identified, after which information on exposure and dose-response should be collected, and evaluated altogether to characterize, manage and mitigate risk. A handbook for conducting QMRAs was first released in 2000 and updated in 2014 to include new hazards and dose-response models (Haas et al., 2014). The handbook provides detailed information on how to conduct a QMRA and a comprehensive overview of mathematical and analytical methods which can be employed for assessment. Although there is no similar handbook for assessing chemical risk, numerous guideline values and approaches exist, which will be discussed in the subsequent sections.

2.1.1 Regulatory framework for quantitative risk assessment in water reuse

Human health risks from waterborne chemical or pathogen contaminations can vary depending on the intake route. The World Health Organization (WHO) has adopted the concept of disability adjusted life years (DALYs) to quantify risk, with the acceptable level of 1 DALY per 1 million people per year (10^{-6} DALYs pppy) (World Health Organization, 2004). While the DALYs concept can be applied to chemicals, it is more often used for quantifying microbial risk due to knowledge gaps in chemical risk (World Health Organization, 2017b). The WHO released a QMRA handbook of their own in 2016, which identifies reference pathogens, dose-response models, and provides numerous case studies of QMRA in water safety management (World Health Organization, 2016). This was followed by a potable reuse guideline and updates to the Guidelines for Drinking-water Quality (World Health Organization, 2017b, 2017a). Subsequent risk-based approaches for drinking water surveillance were also released recently (World Health Organization, 2019). However, the guidelines put forth by the WHO are suggestions: regulations must be set at the local, state/regional, national or international (EU) level.

Numerous countries have either adapted WHO guidelines or identified their own regulatory values for assessing risk of reclaimed water. Australia was one of the first countries to regulate reuse with their Guidelines for Water Recycling in 2006 (NRMMC–EPHC–AHMC, 2006), and their most recent update of the Drinking Water Guidelines (NHMRC-NRMMC, 2019). In the United States, where numerous federal guidelines specify contaminant concentrations limits in drinking water, surface water, and groundwater, no unified federal approach to water reuse exists (National Research Council, 2012), although progress towards such regulations is being made (US EPA, 2017). The Surface Water Treatment Rule proposed a maximum acceptable risk of less than 1 infection in 10,000 people per year (10^{-4} pppy) (US EPA, 2006), which has been adapted by frontrunners such as California, Texas, Arizona, Colorado, and Nevada in drafting state-specific reuse regulations (US EPA, 2019). Additionally, numerous ISO standards apply to water treatment, reuse, and risk assessment, including but not limited to ISO 20426, 20468, 20469, and 16075. A more comprehensive comparison of recommended reduction values and acceptable risk thresholds in the guidelines can be found in chapter 4.

2.1.2 European Union risk regulations

The recent EU regulation on minimum quality requirements for agricultural reuse was ratified on May 25, 2020 (EU Parliament, 2020). These regulations require that a water reuse risk management plan (WRRMP) for chemical and microbial contaminants is drafted for each location engaging in reclamation of wastewater, as well as additional requirements after the point of compliance (POC) to ensure the reuse system is safe. Although this plan is specific for reuse in irrigation, it provides a framework for expanding to other reuse applications in the future, and sets precedent for future amendments. Currently the regulations set validation monitoring log reduction values for the indicators *E. coli* (≥5 LRV),

coliphages (≥6 LRV), and *Clostridium perfrigens* or spore-forming sulfate reducing bacteria (4-≥5 LRV), and provide target log reductions for reference pathogens rotavirus (≥6 LRV), and *Campylobacter* and *Cryptosporidium* (≥5 LRV) as well, when starting from raw wastewater. Validation is only required for new reuse operations. Routine monitoring is required for *E. coli, Legionalla spp.* and helminth eggs, which do not encompass the full sensitivity of viruses, bacteria and protozoa to disinfection removal, or in the case of *Legionalla spp.*, do not focus on the most pathogenic strain, possibly resulting in an underestimation of risk (Dingemans et al., 2020). No regulation levels are set for chemicals: however, these can can be defined by Member States or site-specific thresholds can be set during the creation of the WRRMP.

2.1.3 Water (Reuse) Safety Plans and Hazard Analysis and Critical Control Point assessments

In 2009, the WHO officially adopted the concept of Water Safety Plans (WSP) which was already being utilized in many countries (Bartam et al., 2009; Tsitsifli and Tsoukalas, 2019). WSPs are designed to ensure the safety of final product water by assessing the boundaries of water production, from the watershed level down to the level of supply, in an effort to improve water quality, production, and reduce the likelihood of hazardous incidents (World Health Organization, 2004). This is accomplished through a series of 6 steps: team assembly, system analysis, operational monitoring, management and communication, review/approval/audit, and identification of future needs (Bartam et al., 2009; Tsitsifli and Tsoukalas, 2019).

Hazard Analysis and Critical Control Point (HACCP) assessments have been applied as a method for risk assessment in water utilities since the early 1990's (Havelaar, 1994). HACCP identifies hazards possibly contributing to unsafe final water quality which can be classified as biological, chemical, physical, and/or radiological (Tsitsifli and Tsoukalas, 2019), and corrective actions which can reduce the hazard by determining which locations in the treatment train are critical control points (CCPs) for monitoring to ensure appropriate final water quality. Additional benefits include a better understanding of the water network, which can be shared by multiple agencies or actors, increased consumer confidence, identification of appropriate corrective and preventative actions, and compliance with legislation (Tsitsifli and Tsoukalas, 2019).

Combining the HACCP with the WSP ensures that safe drinking water is produced through adequate risk assessment of unit processes, comprehensive evaluation of shortcomings, and interdisciplinary communication and collaboration. While Water Reuse Safety Plans were already proposed in the EU DEMOWARE project (Hochstrat et al., 2013), this framework was further adapted to explicitly include the feedback and periodic review of the plan in a WRRMP of the BMBF project 'TrinkWave' (Figure 2-1).

Another important factor to discuss in risk assessment is the engagement of stakeholders and the public. Although written into the WSP guidelines, engagement of stakeholders via public discussion or stakeholder meetings is often overlooked at the peril of many reuse projects, although public acceptance is critical for further promoting water reuse and reducing *de facto* reuse (Dingemans et al., 2020). Communicating scientific results to academic (Medema et al., 2020), legislative (Grevatt et al., 2020) and general public audiences (Global Water Research Coalition, 2020) must succinctly summarize the most relevant information using appropriate language. Clear communication of needs from all parties, including drinking water utilities, farmers/consumers, public health officials and government regulators, and engineers and consultants will result in proactive monitoring and implementation of best management practices (Bradford and Harvey, 2017). Whereas risk communication was only a part of risk characterization and management before the COVID-19 pandemic, it will surely attract more

attention in future water reuse projects. This specifically includes risk assessment of microbial and chemical risk, which can be done quantitatively.

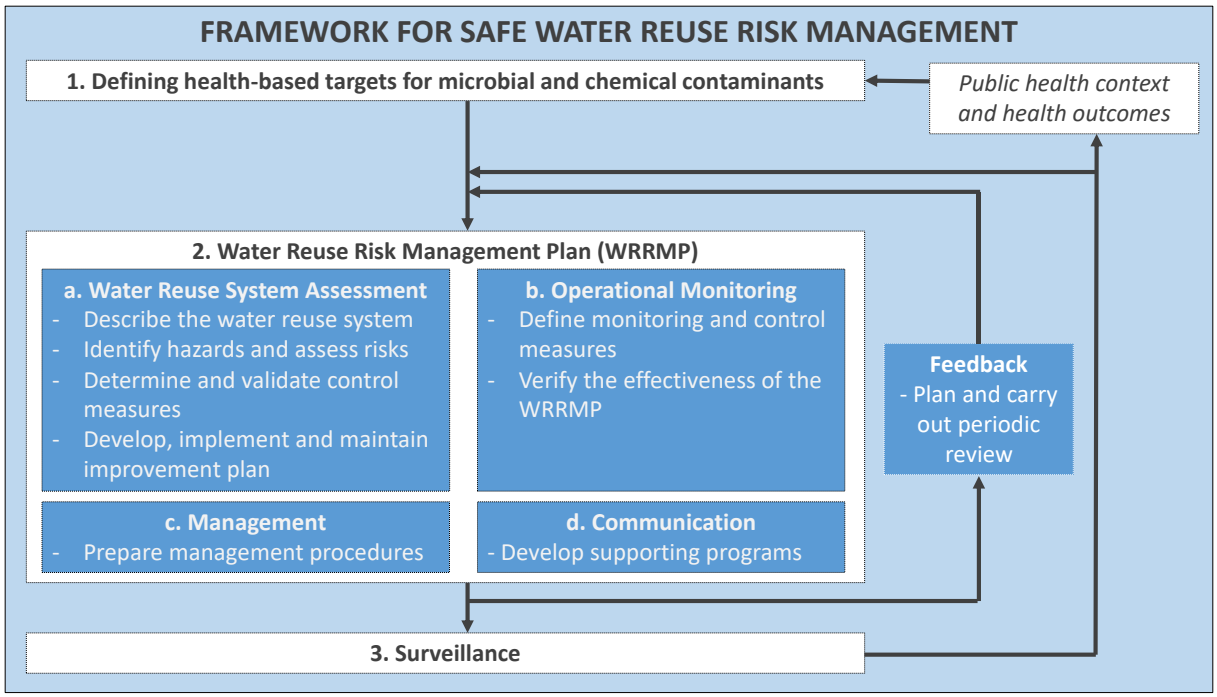

Figure 2-1: Water Reuse Risk Management Plan, adapted from TrinkWave project final report.

2.2 State of the art of QMRA

QMRAs are one method of assessing risk from pathogens in a water treatment system. Hunt and Johnson (2017) describe waterborne pathogen presence as an acute risk, with the single-hit theory describing the case where one organism can cause infection and illness, which is further compounded by the reproductive capability of pathogens leading to increased concentrations. QMRAs in the water industry improve the understanding of fate of pathogens within treatment trains and identify when more treatment is required to meet health burden thresholds. This can be done through quantifying removal of reference pathogens, such as norovirus, *Campylobacter*, and/or *Cryptosporidium*, through unit treatment processes (NSW Office of Water, 2015; World Health Organization, 2017a). If reference pathogens cannot be quantified, indicator or surrogate organisms, such as adenovirus, *Clostridium perfrigens*, *E. coli*, or bacteriophages, can increase knowledge of pathogen fate through unit treatment processes (World Health Organization, 2016, 2017a).

Although drinking water treatment scenarios have been extensively covered in recent QMRA literature (Elliott et al., 2019; Emelko et al., 2019; Tolouei et al., 2019; Owens et al., 2020; Paruch et al., 2020), reuse scenarios have not received the same attention. Owens et al. (2020) proposed a checklist for DWTPs conducting QMRAs to harmonize the information collected and reported so facilities could be more easily compared and evaluated, which could become standard for all QMRAs and a reporting requirement for WRRMPs.

Online tools for conducting QMRAs, such as the AquaNES QMRA tool, the Watershare QMRA Treatment Calculator, QMRAspot, and QMRAcatch are freely available (Schijven et al., 2011, 2015; AquaNES, 2016a; RIVM, 2016; Watershare, 2016a). Likewise, the Center for Advancing Microbial Risk Assessment has compiled a huge amount of information relevant for conducting a QMRA (CAMRA, 2020). A comprehensive discussion on QMRA steps, dose-response models, exposure assessment and methodology can be found in chapters 4 and 5.

2.2.1 Probabilistic QMRAs

Inclusion of probability into the assessment can better characterize the uncertainty and variability associated with individual assumptions and unit treatment processes (Smeets, 2008). Incorporation of unexpected risks into models predicting waterborne pathogen outbreaks in water reuse projects could help decision and policy makers make more informed risk- and evidence-based decisions (Bergion et al., 2020). To date, not many studies or applications have conducted probabilistic QMRAs. This can be done using a variety of methods including Bayesian networks (BNs). A more comprehensive discussion of probabilistic QMRAs can be found in chapter 5.

2.2.2 Emerging pathogens and indicators for unit processes and further improvements

As detection sensitivity and methods improve, it will be possible to analyze more pathogens and indicators within the framework of QMRA, such as Aichi virus or polyomaviruses (Momba et al., 2019). Non-enveloped viruses, such as adenovirus, Coxsackievirus, and hepatitis A virus, are of particular concern for potable reuse systems, as their small size and resistance to disinfection requires particular attention in reuse schemes (Rose et al., 2005; Nappier et al., 2018). Monitoring of norovirus and hepatitis A virus in wastewater treatment successfully predicted outbreaks in a population before the population showed symptoms of the virus (Hellmér et al., 2014), and more recent work supports that QMRA on coronaviruses could help identify possible risks in treatment and pre-empt public health protection before an outbreak occurs (Pecson et al., 2020). Additionally, although climate change effects on pathogen behavior are difficult to predict, studies have shown that correlations between numerous parameters including temperature, precipitation, humidity, and ultraviolet radiation with pathogens exist (EASAC, 2019). In this sense, probabilistic approaches are most suited to accommodating the multitude of variability and uncertainty associated with waterborne pathogenic risk.

2.3 State of the art of QCRA

Chemical presence in drinking water is regulated through risk-based approaches for chronic health risks, which build up over a lifetime of exposure. Chemical transport during treatment differs greatly from pathogen transport: this is especially notable in the subsurface, where pathogen transport is governed by colloid transport theory, whereas transport of conservative chemicals is governed mainly by advection and dispersion (Hunt and Johnson, 2017). Chemical risk assessments in water reuse have been conducted less extensively than pathogenic risk assessments, due to the lack of knowledge of exposure effects that lead to acute or chronic illnesses and the lack of data available to apply the DALY tolerable disease burden to chemicals (World Health Organization, 2017b). Potential long-term risk of chemical mixtures is also still unknown (Baken et al., 2018).

A comprehensive list of decision support tools for TOrC control strategies has been compiled in Fischer et al. (2017). Among these are numerous platforms for chemical risk assessments, such as AbatES within the Watershare network (Watershare, 2016b) and the QCRA tool produced within the AquaNES project (AquaNES, 2016b). However, as chemical variability and uncertainty is site-specific, risk assessments should ideally be conducted on experimental data, incorporation of which is limited in these tools. As per the WRRMP, a chemical monitoring and abatement plant should be specified for each site where reuse is being considered (EU Parliament, 2020).

2.3.1 Non-threshold vs threshold chemicals

Chemicals are generally classified as either threshold or non-threshold chemicals. If a chemical is believed to pose risk regardless of concentration or level of exposure, it is considered a non-threshold chemical. When a safe concentration of the chemical or exposure level below which no adverse effects are observed can be determined, it is deemed a threshold chemical. If a health relevant concentration

exists, such as a predicted no-effect concentration (PNEC), or a no observed adverse effect level (NOAEL), which are derived from toxicological studies on 3 trophic levels (algae, crustaceans and fish), these can be found for a range of chemicals in databases such as the NORMAN Ecotoxicology Database (EU Commission, 2003; Slobodnik, 2020). However, for pharmaceuticals, personal care products, and other TOrCs and transformation products, PNEC values can range widely, and as they are mostly determined through ecotoxicological analyses, are not directly relevant for human health. Databases of no or low observed adverse effect level (NOAEL/NOEL, LOAEL) concentrations exist for many threshold chemicals, and these levels of acute and/or chronic effects can be used to determine an acceptable or tolerable daily intake (ADI/TDI) for consumption, which can then be transformed into a guideline value (NRMMC-EPHC-NHMR, 2008).

If a pharmaceutical has not yet been classified as nonthreshold or threshold, the European Medicines Agency's Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use reveals that an environmental risk assessment must be performed for new pharmaceuticals if the predicted surface water concentration exceeds 10 ng/L, with exceptions made for highly lipophilic or potential endocrine-disrupting compounds as they may affect organisms below this concentration (European Medicines Agency, 2006; Oldenkamp, 2016). While pharmaceuticals are generally not addressed in the EU Water Framework Directive, the inclusion of three pharmaceuticals (diclofenac, 17α-ethinylestradiol and 17β-estradiol) into the EU list of priority substances has been proposed (Johnson et al., 2013). However, to date there is not enough sufficient evidence of the negative effects of TOrCs on human health and this does not warrant the calculation of a reference dose for TOrCs (World Health Organization, 2017a). Numerous risk assessments have determined that human health risk from TOrCs is negligible and that ecological risk is higher (Christensen, 1998; Jones et al., 2004; Schwab et al., 2005; Cunningham et al., 2009; Schriks et al., 2010). However, as many more chemicals can now be detected using improved analytical capabilities, improving treatment and removal of TOrCs prior to discharge into the environment and drinking water consumption is important (Reemtsma et al., 2016), particular in light of unknown toxicity stemming from mixing effects of chemicals (Tousova et al., 2017).

2.3.2 European guideline values for TOrC discharges

Individual EU member states have initiated their own regulations for pharmaceutical management (European Commission, 2019). Countries which have begun to regulate TOrC discharges have done so for environmental health (Sweden), protection of public health (Germany) or a combination of both reasons (the Netherlands). Sweden conducted an assessment of the degree of TOrC pollution from WWTPs and pinpointed which chemicals individual WWTPs should focus on (Swedish EPA, 2016; Golovko et al., 2020). The Netherlands drafted an implementation plan to remove TOrCs amid other pollutants for both environmental and human health by 2022 (Government of the Netherlands, 2018). While not part of the EU, Switzerland has a highly comprehensive approach to regulating micropollutants in discharge wastewater effluent for environmental health, and pinpointed which WWTPs should receive upgrades (Eggen et al., 2014; Swiss Federal Council, 2017).

While currently little toxicological data is available on the concentrations of threshold chemicals which lead to harm, this leads agencies such as the German Enviromental Agency to take more conservative approaches in setting precautionary values, which would be adapted when more information on toxicity is available (Gesundheitlicher Orientierungswerte, (GOW)) (Umweltbundesamt, 2019), in addition to more broad national groundwater and drinking water regulations (*Grundwasserverordnung*, 2010, *Trinkwasserverordnung*, 2018). Both of the latter regulations set limits for threshold chemicals (i.e. fluoride, copper) but do not mention TOrCs.

Improving the TOrC removal capacities of WWTPs and DWTPs should be done in conjuction with an overall reduction of pharmaceutical usage, and investments in WWTP upgrading should be done with potential trade-offs in mind (i.e. generation of byproducts, etc.) (OECD, 2019). Risk assessments for threshold chemicals could provide information for determining which treatment plants should be upgraded.

2.3.3 Threshold chemical risk assessment as a function of guideline value

Despite the low risk for human health, evaluating TOrC presence and removal in WWTPs is a priority for aquatic health, and certain guideline values and assessment methodologies have been proposed.

Chemicals for health relevance and process performance analysis have been compiled by the Science Advisory Panel of the California State Water Resources Control Board (Drewes et al., 2018). A monitoring trigger level (MTL) for each chemical was identified using the ADI and reference doses (RfD) from numerous international studies, the US EPA's contaminant candidate list and tap water regional screening lists, and GOW values, which were used only when no other value was found. Chemicals for which the ratio of measured effluent concentration (MEC) to MTL exceeded 1, which occurred for NDMA, NMOR, and 1,4-dioxane, were considered relevant for chemical risk assessment in the California setting in which the study was conducted.

These same chemicals were also recommended for monitoring by prior work in a European setting, using a similar threshold of toxicological concern (TTC) approach (Munro et al., 2008; Schriks et al., 2010). The study found that 1,4-dioxane, NDMA, benzene, MTBE, and ETBE encompassed the most risk, and recommended that PFOS and PFOA should also be monitored since they are persistent in the environment (Schriks et al., 2010). 1,4-dioxane presence in groundwater and surface water was confirmed by detection in the source water of DWTPs obtained from MAR applications (Karges et al., 2019). PFOS and PFOA have also been detected in drinking water by Thomaidi et al. (2020), who conducted a health risk assessment (HRA) according to EU and US EPA health advisory levels.

2.3.4 Probabilistic QCRAs

As the temporal and spatial separation between wastewater and drinking water can be reduced in potable reuse schemes, steps must be taken to predetermine and minimize any possible risk to human and environmental health. Due to notable variability associated with seasonality, demographics, WWTP unit processes employed, and sewer infrastructure, and in order to more accurately assess the uncertainty associated with analytical detection of trace concentrations, a probabilistic risk assessment can be conducted. Most studies focused on consequences of *de facto* reuse by assessing concentrations and risk stemming from surface or groundwater abstracted for drinking water production (Loos et al., 2013, 2015; Baken et al., 2018; Karges et al., 2019; Zhou et al., 2019).

However, to date few probabilistic risk assessments have been conducted which focus specifically on potable reuse systems (Khan, 2010) or on determining risk from a particular water reuse treatment train on a local level. Contributions of persistent and mobile compounds to aquifers are predicted to increase during wetter winters and decrease in drier summers, with an overall improved biodegradation due to climate change (Collins et al., 2019). This provides yet another reason for monitoring and modeling the behavior of chemicals on an annual basis using probabilistic methods.

Changing human patterns in response to climate change effects will increase exposure to many chemicals (EASAC, 2019). Reduced river flows combined with constant or even increasing discharges from point sources of pollution will lead to higher concentrations of chemicals in waters (Collins et al., 2019), on the order of 2-4 times higher in Germany (Sjerps et al., 2017). To account for this, a more health-based assessment is to integrate detection via mass spectrophotometry with toxicity assays to

prioritize which chemicals in drinking water should be investigated/regulated (Brunner et al., 2019, 2020), which has recently been explored in Sweden (Golovko et al., 2020). Or, if a drinking water utility has enough capital, conducting a large sampling campaign to prioritize chemicals for monitoring can also be undertaken (Sjerps et al., 2018). Simiarly, bioassays for broad screening of chemical affects applied in California regulations could be undertaken on a broader scale: the 2019 Recycled Water Regulations mandate that the estrogen receptor-α (ER-α) for 17-ß-estradiol and Aryl hydrocarbon receptor (AhR) for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) bioanalytical screenings be conducted against set monitoring trigger levels (3.5 and 0.5 ng/L) to determine the range of corrective responses depending on how much the bioassay risk exceeds MTL (CEPA, 2019). Uniform reporting of data will make comparison between screening-level assessments and evaluation of utilities much easier (Fischer et al., 2019).

2.4 Removal of TOrCs during porous media treatment

Porous media most often used in water treatment include technical sand, granular or powdered activated carbon, and anthracite. Research on TOrC detection and removal over the last 20 years has focused on occurrence, fate, operational conditions which dictate removal, removal mechanisms, innovative technologies for removal, and (co)metabolic removal pathways (Alvarino et al., 2018). The primary mechanisms of removal in porous media are biodegradation and adsorption (Yu et al., 2006).

2.4.1 Removal via biodegradation

Removal via biodegradation is an inherently complex mechanism sensitive to multiple factors. Microbial degradation in porous media treatment systems is dependent upon biodegradable dissolved organic carbon (BDOC) (Tran et al., 2013), dissolved oxygen (DO) concentrations which determine the predominant redox conditions (Massmann and Du, 2008; Baumgarten et al., 2011; Regnery et al., 2015), flow rate or empty bed contact time (EBCT) (Hermes et al., 2019; Müller et al., 2019d), and media type (Vignola et al., 2018b), among other factors. More detailed information on the biodegradability of TOrCs and these aforementioned factors can be found in chapter 8, which discusses removal in biofiltration-based systems. This section will focus more on the role of compound structure and kinetics during biotransformation.

In addition to operational and water quality parameters, compound structure determines susceptibility to biodegradation. Polar compounds have asymmetric distributions of electrons on their surfaces causing negative and positive dipoles, an excess of which results in an ionically charged compound, which are particularly water soluble (Reemtsma et al., 2016). The charge of the ionic compound will influence whether it partitions to organic surfaces, which are generally negatively charged, or stays in solution (Reemtsma et al., 2016). This partitioning can be quantified using a logD distribution coefficient, which is the pH dependent concentration of the ionized and deionized form of the species (Reemtsma et al., 2016). According to Tadkaew et al. (2011), a logD value >3.2 results in very good removal via adsorption, and when logD is ≤3.2 the removal mechanism switches to biodegradation. For compounds which are not present in ionic form in solution, a $\log K_{OW}$ distribution coefficient represents the compound's partitioning tendency to octanol or water (Nam et al., 2014; Tran et al., 2018). These coefficients can help estimate how a compound will behave in solution, but as compound interactions in complex matricies such as WWTP effluent are also influenced by other water constituents (Reemtsma et al., 2016), behavior cannot be predicted by these coefficients alone.

Generally speaking, simple aliphatic and monocyclic compounds (i.e. atenolol, diclofenac) are more readily degradable than polycyclic compounds (i.e. carbamazepine, primidone) (Tadkaew et al., 2011). Good degradation can be observed for compounds with electron donating groups, such as amine or hydroxy groups, as well as for compounds with both electron donating and withdrawing groups, such

as amide and carboxyl groups (Tadkaew et al., 2011). The coexistence of particular groups also determines biodegradation: amine and amide groups (i.e. atenolol and caffeine) result in good biodegradation, whereas amine and carboxylic groups (i.e. diclofenac) result in poorer biodegradation (Tadkaew et al., 2011).

Compound attenuation can be described by a removal rate, which requires observations of abatement over time. Determining removal kinetics can be done with or without measuring biomass, but kinetics are system-specific and dependent upon hydraulic retention time, temperature, and multiple other operational parameters. In the absence of biomass data, pseudo-first order kinetics have been proposed by Schmidt et al. (1985) and used in the recent work of Ma et al. (2018) in Equation 2-1,

$$k_{bio} = -\frac{1}{t} * ln\left(\frac{C_{eff}}{C_{inf}}\right) \qquad \textit{Equation 2-1}$$

where k_{bio} is the pseudo-first-order rate constant, t is hydraulic retention time, C_{eff} is effluent concentration and C_{inf} is influent concentration. Larger rate constants indicate faster decay. As pseudo-first order assumes removal is independent of substrate concentration, this approach is helpful for when experimental setup does not facilitate biomass sampling.

Biomass concentration is necessary for describe the decay rate using the Monod kinetic approach of Becker and Seagren (2009) depicted in Equation 2-2,

$$K_{B1} = \frac{q_{max}X}{K_S} \qquad \textit{Equation 2-2}$$

where $K_{B1}$is the lumped pseudo-first order decay coefficient, q_{max} is the maximum specific substrate utilization rate, X is the biomass concentration, and K_S is the substrate half-saturation constant. As microorganisms are responsible for degradation, determining kinetics based on the biomass concentration and the available substrate describes the complex conditions of biodegradation better than simple zero-, first-, or pseudo-first order decay (Mohamed and Hatfield, 2011).

2.4.1.1 **Biomass quantification**

A variety of methods for quantifying biomass on various types of media exist (Rauch and Drewes, 2005), with a few most common methods discussed in this section. Although sometimes overlooked in biofiltration experiments in favor of monitoring the removal of organic compounds, quantifying biomass is critical for determining removal kinetics and modeling removal (Vignola et al., 2018a). Methods for rapid estimation are of increasing research interest.

Phospholipid extraction estimates viable biomass by quantifying the phospholipid component of biological cell membranes (Rauch and Drewes, 2005). Useful for accounting for heterotrophic decay, nitrification, and denitrification, this method yields high extraction recovery and good reproducibility in sediment samples (Rauch and Drewes, 2005), and has also been applied to GAC. Difficulties with converting values between systems due to different levels of biodegradable substrate in the influent contribute to variations in cell numbers reported (Fonseca et al., 2001).

Culturable methods, such as heterotrophic plate counts, only detect the biomass which can be cultured (Çeçen and Aktaş, 2011). Molecular methods can provide a highly detailed assessment of biomass present, which can be normalized to the volume of sample taken. Quantitative polymerase chain reaction (qPCR) provides information about occurrence of organisms in water or media samples. 16S rRNA gene amplicon sequencing has shown that the type of media used will affect the types of communities establishing in biofilters (Vignola et al., 2018b). This method can reveal the diversity of the microbial

community, and is particularly useful to determine how additional factors, such as location, season, unit treatment process, and water quality affect the microbial population (D. Li et al., 2012; Gerrity et al., 2018). However, these methods are quite sensitive and not for all types of media, they can be expensive and have limitations in extraction efficiency, and are sensitive to interference from humic substances or extracellular DNA (Rauch and Drewes, 2005).

Flow through cytometry detects the total and intact cell count in a water sample, providing information about the amount of viable cells (Hammes et al., 2008; Vital et al., 2012; Prest et al., 2013). Very useful for water samples, this approach is more difficult for media samples as components of biofilm, such as exopolymeric substances, can interfere with the signal and give inaccurate measurements (Vignola et al., 2018a). However, flow through cytometry fingerprints, when paired with adenosine triphosphate (ATP) analysis, can help to explain variations in ATP values per media (Vital et al., 2012).

Quantifying ATP is among the fastest and least expensive methods for measuring biomass. ATP indicates overall microbial activity present in the sample, and correlates well with the number of viable biofilm cells and oxygen uptake rate (Simpson, 2008). ATP has often been used in quantifying the activity of drinking water biofilters (Pharand et al., 2014; B. Ma et al., 2018; Greenstein et al., 2018). A specific protocol for measuring the ATP activity of attached biomass on GAC surfaces was developed by Velten et al. (2007). As this method relies on luminescence measurements and is very time and temperature sensitive, recent upgrades to online ATP measurements have shown promise in standardizing measurement and analysis protocols (de Vera and Wert, 2019). The review of biofilter biomass of Pharand et al. (2014) did not observe a notable difference in ATP per bacterial cell ratios for WWTP effluent and drinking water treatment. However, only one study of WWTP effluent biofilters was mentioned and biomass measurements in WWTP biofilters are rarely found in literature (dos Santos and Daniel, 2019), therefore the sample size for such a conclusion is quite small and likely very site-specific.

Appropriate methodology should be selected based on the characteristics of the filter medium used: while certain methods have been adapted for *in situ* biomass quantification of adsorptive media (i.e., GAC) (Velten et al., 2007), care must be taken that the same adaptations are suitable for alternative filter media in experiments designed to compare removal efficiency.

2.4.1.2 **Biodegradation transformation products**

The microbial degradation of TOrCs can lead to the release or creation of biodegradation transformation products (BTPs). Usually present at lower concentrations than their parent TOrC compound, BTPs can be difficult to predict, although numerous prediction programs, such as Eawag's biocatalysis/biodegradation pathway prediction system (Eawag, 2017) and enviPath (Wicker et al., 2020), or databases listing known BTPs such as STOFF-IDENT (Bayrisches Landesamt für Umwelt, 2020), exist. Modeling techniques which further explore compound properties through the usage of quantitative structure property/activity relationships (QSPR/QSAR) can also help to predict BTP formation (Rücker and Kümmerer, 2012).

BTP detection using non-target screening with liquid chromatography- tandem mass spectrometry (LC-MS/MS) and/or liquid chromatography-high resolution mass spectrometry (LC-HRMS) (Schollee et al., 2015) is not yet widely applied, due to difficulty of structurally identifying unknown compounds and obtaining analytical grade reference standards for quantitative analysis. Data produced from non-target analysis requires bespoke software for peak picking and suspect and/or non-target screening, the results of which are then compared against databases such as the Chemistry Dashboard to identify which BTPs could be present in the water samples (Brunner et al., 2020).

As analytical methods improve, so does the detection and characterization of BTPs, mostly done in single-component biodegradation tests, among them the BTPs of diclofenac, iopromide, and trimethoprim (Schulz et al., 2008; Jewell et al., 2016b, 2016a; Hermes et al., 2019). However, questions about their possible toxicity and human and environmental health effects are still relevant (Hübner et al., 2014; Aymerich et al., 2016). Recent work has proposed a three pronged approach for BTP detection and toxicological analysis: by combining target analysis, non-target analysis, and bioassays, Brunner et al. (2020) provided a workflow for detecting TOrCs and their BTPs, as well as examining biological effects of the mixture of chemicals at a drinking water treatment plant.

2.4.2 Removal via adsorption

Adsorption affinity can be described using the compound specific adsorption coefficient K, which can be determined via single-solute isotherm experiments with powdered activated carbon (PAC) (Zietzschmann et al., 2016). Additional compound characteristics which dictate adsorption affinity include solubility, speciation, size, charge, and structure (Worch, 2012; Oberoi et al., 2019). While neutral chemicals are adsorbed by physical forces (van der Waals) and are sensitive to hydrophobicity, ionic compounds are more affected by electrostatic attractions (Anumol et al., 2015). More information on the adsorption of specific chemicals is discussed in chapter 7.

Although generally compounds with higher $\log D_{ow}/\log K_{ow}$ values and aromatic structures should adsorb better to carbon (Altmann et al., 2016), this may not be the case if compounds are present at very low concentrations (Yu et al., 2009; Rattier et al., 2012a). Preloading has been shown to significantly influence both adsorption capacity and mass transfer of compounds, and has been found to be more severe for hydrophilic or dissociated compounds (i.e. naproxen) (Yu et al., 2009). Likewise, film diffusion has been shown to be the primary mass transfer mechanism for compounds at very low concentrations (<1 μg/L), which can be miscalculated due to system hydrodynamics and GAC topography when using a correlation, and should rather be experimentally determined (Yu et al., 2009). Additional mass transfer mechanisms dictating removal are described in more detail in chapter 7. Physicochemical characteristics cannot always explain observed adsorption efficiency (Sbardella et al., 2018), which is particularly evident in adsorption of multi-solute mixtures containing compounds of different adsorption affinities (Altmann et al., 2016).

Various media can be used for adsorptive removal, but the most common adsorptive media in water treatment is GAC or PAC. GAC has a large surface area and can adsorb constituents directly onto itself (Sontheimer et al., 1988). Adsorption site competition between large and small organic compounds has been extensively debated in the literature, with the responsibility of pore blockage versus adsorption site competition based on pore size still contested. Prior studies have hypothesized that pore blockage is partially responsible for the dependence of fouling on particle size during GAC treatment, as blockages prevent the surface area available behind the blockage from contributing to adsorption of target compounds (Corwin and Summers, 2010). Smaller molecular weight compounds, such as TOrCs, are attracted to the high surface area of micropores (Kennedy and Summers, 2015). Large molecular weight compounds, which includes a portion of DOM, are limited by size exclusion from adsorbing to micropores, and instead adsorb to meso- and macropores and consequentially block the internal micropore area from adsorption (Corwin and Summers, 2010; Kennedy and Summers, 2015). Although crushed GAC has the same total surface area, cumulative pore volume, and pore size volume fractions as larger GAC (Patni et al., 2008; Corwin and Summers, 2010), smaller particles have more meso- and micropores open to bulk flow, but since larger molecular weight compounds do not block these pores due to size exclusion, the impact of pore blockage on fouling is reduced with the smaller particle size (Corwin and Summers, 2010).

When discussing the effects of site competition versus pore blocking in adsorption of DOM and TOrCs, GAC with a larger amount of micropores is associated with higher TOrC adsorption and pore blockage, while GAC with a greater variety of pore sizes is associated with higher DOM and higher TOrC adsorption, leading to adsorption site competition (Hu et al., 2016). However, when discussing adsorption of complex WWTP effluent matrices, the influence of pore blockage is still debated. Zietzschmann et al. (2014) found that for the removal of medium and weakly adsorbing TOrCs such as iopromide and sulfamethoxazole, competition for adsorption sites between TOrCs and low molecular weight DOM was more influential than pore blockage, while pore blockage was more influential for TOrC removal in the presence of high molecular weight DOM in PAC experiments. This was subsequently confirmed through testing on GAC (Hu et al., 2016). Guillossou et al. (2020) attributed the decreased TOrC removal capacity in GAC treating WWTP effluent in comparison to ultrapure water to pore blockage from higher DOM concentrations in WWTP effluents, with negatively charged TOrCs repelled by the adsorbed DOM on the carbon via electrostatic interactions.

Determining removal via adsorption onto GAC can be done using rapid small-scale column tests (RSSCTs), which are further described in chapter 7. Describing abiotic removal in biofilters (i.e. adsorption to biomass) can be done by employing sodium azide (Maeng et al., 2011) or autoclaving (Piai et al., 2020) to eliminate biological activity contribution to removal.

2.4.2.1 **Desorption**

Another mechanism can contribute to the mass balance of TOrC removal in biofilters: desorption of TOrCs or dissolved organic matter (DOM) when equilibrium concentrations at the liquid/solid interface change. Desorption processes are believed to be due to bacteria and exoenzymes transforming TOrCs into products with less adsorption affinity for the biofilm (Rattier et al., 2012), though they are also influenced by variable feed water concentrations. The desorbed compound is passed back into the biofilm, where it is either subject to further biodegradation or desorbed into the liquid phase (Simpson, 2008).

Desorption has been shown for naproxen and diclofenac in soil columns irrigated with reclaimed wastewater (Chefetz et al., 2008), as well as for sulfamethoxazole in BAC columns (Sundaram et al., 2020), and for DOC and other TOrCs (Reungoat et al., 2011; Sun et al., 2018). Aschermann et al. (2018) determined that micro- or mesoporous GAC should be used to avoid desorption in experiments fed with fluctuating DOM and TOrC concentrations. Adsorbed DOM blocks pores, preventing adsorbed TOrCs from desorbing, while in macroporous GAC, TOrCs can not only desorb, but can also be displaced by newly adsorbing DOM (Aschermann et al., 2018). Corwin and Summers (2011) showed that desorption occurs over the long-term and at low levels, after intermittent loading. Desorption of acesulfame in BAC was noted by Altmann et al. (2016), who reported greater than 100% breakthrough of acesulfame after complete breakthrough and initially explained this as desorption of acesulfame due to lower influent concentrations (Corwin and Summers, 2011) but then to displacement by better adsorbing compounds after acesulfame breakthrough in the long-term. Displacement could possibly be another mechanism contributing to compound removal.

As adsorption is a reversible process due to low physisorption binding energies (Aschermann et al., 2018), the interplay of adsorption and desorption could enhance the bioavailability of TOrCs at the BAC particle surface where biofilm is located. The combined effects of adsorption and desorption constantly refresh the adsorption capacity of the GAC (Corwin and Summers, 2011), which is governed by more mass transfer mechanisms than sand. This interplay makes TOrCs available for biodegradation again in a process termed bioregeneration (Çeçen and Aktaş, 2011), which could facilitate greater overall removal, as sites for biomass establishment and therefore biodegradation are renewed.

2.4.3 Removal via adsorption, desorption and biodegradation in biofilters

The combination of both removal mechanisms has short-term as well as potential long-term benefits. In the first stage of virgin GAC operation, adsorption sites are populated by effluent organic matter (EfOM) including TOrCs and DOC, while microorganisms are similarly occupying GAC adsorption sites, facilitating biodegradation via biofilm development. Initially, nutrients on the outer surface of the biofilm and the macropores of the GAC are degraded, while poorly-degradable DOC diffuses into the micropores (Sontheimer et al., 1988), where it is degraded by microbes in those pores. When the liquid phase concentration becomes lower than the adsorbed concentration, the partially degraded compounds will desorb and diffuse back towards the biofilm (Sontheimer et al., 1988), where they are again subject to degradation (Simpson, 2008). New compounds in the liquid phase follow the same path, where their partial degradation occurs first, followed by adsorption in the same concentration as the previous compound was present on the biofilm or GAC surface (Aktas and Cecen, 2007; Simpson, 2008). Therefore, greater initial GAC removal of adsorptive compounds is expected, which may also facilitate faster biofilm formation.

The GAC is then re-classified into a biologically active carbon (BAC) biofilter. The onset of biodegradation in filter media can vary, but when starting from virgin media, biodegradation has been observed after 40-70 days of operation (Maeng et al., 2011; Reaume et al., 2015; Sbardella et al., 2018; Sundaram et al., 2020). BAC biofilters are expected to enhance biofilm growth and improve long-term TOrC removal in comparison to technical sand due to the additional adsorption (Paredes et al., 2016; Shimabuku et al., 2019). BAC filters can successfully remove numerous TOrCs, though performance is dependent upon factors such as pretreatment, temperature, EBCT, influent matrix, and GAC characteristics (Worch, 2012; Chowdhury et al., 2013; Zhang et al., 2017). Lower organic loading rate in the form of lower DOC and greater EBCT may facilitate better adsorption (Simpson, 2008) as well as better biodegradation of certain compound classes (Sundaram and Pagilla, 2019). Previous studies demonstrated successful TOrC removal from WWTP effluent using BAC (Corwin and Summers, 2010; Reungoat et al., 2011, 2012; Lee et al., 2012), including adsorptive removal of poorly biodegradable compounds such as carbamazepine (Rattier et al., 2012). Even after adsorption sites are exhausted by DOC or other larger compounds, removal of TOrCs still continues (Urfer et al., 1997; Emelko et al., 2006; Reungoat et al., 2011; Rattier et al., 2012a).

Long-term removal due to adsorption and biodegradation in BAC filters can be investigated in a variety of ways. This has been done by inactivating the biomass on BAC through autoclaving (Piai et al., 2020) or adding biocides to a GAC filter and comparing removal differences with a BAC filter (Rattier et al., 2014). Modeling approaches, which require similar biomass parameters as in Equation 2-2, have also been used for differentiation: Oh et al. (2012) modeled both adsorption and biodegradation in separate equations, using Haldane kinetics instead of Monod kinetics to incorporate possible inhibitory effects of the substrate. Adsorption knowledge gained through RSSCTs can also be scaled up and compared with BAC removal.

After differentiating between adsorption and biodegradation, long-term removal differences in BAC and technical sand filters can be quantified. The increased adoption of ozone followed by biologically active filtration (BAF) in IPR/DPR schemes has provided multiple assessments of removal (Gerrity et al., 2011; Reungoat et al., 2011; Rattier et al., 2012b; Reaume et al., 2015; Zhu et al., 2015; Bourgin et al., 2018; Sun et al., 2018; Sundaram and Pagilla, 2019; Sundaram et al., 2020), which demonstrate a range of BVT and EBCT and prevent a direct comparison of overall removal (Table 2-1). Several of these studies indicate enhanced removal in BAC compared to sand/anthracite filtration (Reungoat et al., 2011; Zhu et al., 2015; Bourgin et al., 2018) but only one reported a BAC throughput, which was ~50,000 BVT in Bourgin et al. (2018), and acknowledged that adsorption capacity was not yet exhausted by the

end of the experiment. Consequently, the long-term removal of TOrCs in BAC and technical sand filters, after adsorption capacity has been exhausted and steady-state biodegradation removal has been reached, together with quantification of adsorption and biodegradation rates, has not yet been investigated.

Table 2-1: Previous BAC studies conducted with secondary treated effluent (S.E.) focusing on TOrC removal.

Study	Influent	BVTs	EBCT	Backwash	Media state at beginning of experiment	Comparison with sand?	Conclusion
Reungoat et al. (2011)	Ozonated S.E.	Not given	30, 60, 90, 120 min	No	Steady-state BAC	Yes	- Only 4 composite samples taken - Long-term monitoring confirmed that BAC is more effective than sand at both TOrC and DOC removal, even continued removal after 2 years of operation - Lower EBCT did not affect BAC DOC removal, but decreased removal of some TOrCs
Gerrity et al. (2011)	(Ozonated) S.E	30,136	30 min	Yes	BAC operated for 1.5 years prior to sampling	Sand used in BAC pretreatment	- ≥95% TOrC reductions achieved in BAC - Sand filtration not recommended for TOrC mitigation due to removal efficiency fluctuation
Rattier et al. (2012)	S.E.	0 & 35,000	Batch experiment – 5 days of contact time	No	Compared fresh GAC and BAC after 35,000 BVTs	No	- DOC removal in GAC (75%) higher than in BAC (30-40%) - BAC removed CBZ, CITA, DCF, SMX - Confirmed ATL, MTL, TRM, CITA, VFX adsorption onto BAC biofilm
Reungoat et al. (2012)	Ozonated S.E.	13,000-95,000	9, 18, 45 min	No	All BAC filters sampled were mature and adsorption was neglected	No	- Only 3 sets of grab samples taken - BAC removed some TOrCs left after ozonation by up to 99% - DOC removal not linearly related to EBCT - TOrC removal greater 18 minutes compared to 9 minutes, but no improvements observed when comparing 45 min to 18 mins - BAC adsorbes TOrCs even after DOC breakthrough
Reaume et al. (2015)	Ozonated S.E.	Sand = 10,400 BAC = 13,800	40 min	Yes	GAC pretreated with 3,400 BVT to facilitate BAC conditions	Yes, although overall BVTs different	- Steady state removal of DOC achieved in both BAC and sand after 40 days of operation (1,400 BVT) - BAC filter removed at least twice as much DOC and UVA_{254} as the sand filter
Zhu et al. (2015)	Ozonated S.E.	Not given	15 min	Not specified	Not specified	BAC and anthracite compared	- Turbidity well removed in BAC and anthracite (from 3 to 0.5 NTU)

							- No difference in UVA_{254} removal seen between BAC and anthracite - BAC showed better removal of atenolol, citalopram, metoprolol, and benzotriazole than anthracite
Paredes et al. (2016)	Aerobic & anaerobic synthetic S.E.	190 days / 106 days	0.2-3.2 days / 17-70 min	No	BAC and BAS fed with biomass from AS process	Yes	- For slowly biodegradable TOrCs, ↓ EBCT reduces removal: for medium/fast biodegradable TOrCs, removal improved with ↓ EBCT - DCF, CBZ = removed only via adsorption - TRI, SMX removed >90% in BAC due to higher EBCT - ↓ EBCT = higher biological activity through higher loading rate = increased cometabolism of certain TOrCs
Bourgin et al. (2018)	Ozonated S.E.	~50,000	18 min	No	BAC preloaded for 16,000 BVTs	Yes	- BAC removed TOrCs even after 50,000 bed volumes - BAC and GAC removed TOrCs better long term than sand biofilter
Sbardella et al. (2018)	Normal S.E. & 200 µm filtered S.E. nylon filter	13,800	50 min	Yes	Operated from virgin GAC to BAC	No	- Poor SMX removal in GAC attributed to short EBCT and low adsorption affinity, removed 35% more in BAC - TRI, MTL and ATL removed by adsorption, classified as non-biodegradable - CBZ and VFX removed via adsorption but also slight biodegradation - BAC reached steady biofilm state after 40 days of operation
Sun et al. (2018)	Ozonated S.E.	Operated for 12 months	23 min	Yes	GAC was in use for 3 years prior to study	No	- Removals: <10% DCF, <20% ANTI and PRI, <50% SMX, 50% CBZ, >80% ATL, TRI and CAF
Sundaram and Pagilla (2019)	Ozonated S.E.	60,000+	10 & 20 min	Yes	Not specified	No	- Carbamazepine, caffeine removed during ozonation - Atenolol and primidone persisted in BAC effluent at <100 ng/L - Exhausted media and higher loading rate results in ~20% TOC reduction - Non-exhausted media and lower loading rates results in 30-50% TOC reduction

3. Research significance and hypotheses

Due to the regulatory and scientific need for ensuring safe water quality is produced from potable reuse treatment trains, this thesis will investigate the microbial and chemical risk associated with the operation of a SMART*plus* based IPR treatment train, which features SMART*plus* treatment of tertiary WWTP effluent, followed by GAC adsorption, UV irradiation, and finally groundwater recharge. Additionally, mitigation methods for improved chemical removal through testing GAC as an alternative media to technical sand will also be discussed. As such, the objectives of the thesis are the following:

3.1 Objective 1: Evaluate microbial and chemicals risks to human health associated with the SMART*plus* potable reuse scheme

A literature review of approaches taken for conducting a QMRA in water reuse was conducted. This was done to obtain information on the assumptions, log removal values (LRVs) and if applicable, probability distribution functions (PDFs) used in studies which had conducted QMRAs on potable and non-potable reuse schemes. Once the approaches and assumptions were catalogued, the best practices could be applied to a QMRA for the SMART*plus* treatment scheme. Chapters 4-6 address objective 1.

To investigate objective 1, the following hypotheses were tested:

Hypothesis 1: Risk to human health from pathogens present in a potable reuse train employing SMART*plus* is below 10^{-6} DALYs

To test hypothesis 1, pathogenic removals including point LRVs and PDFs were obtained from published literature, and in the case of the SMART*plus*, empirical removal of norovirus. Removals in treatment steps were assigned a PDF. A Bayesian network capable of predicting whether pathogen concentrations at point of exposure (after DWT) would comply with the DALYs threshold was constructed in Netica. Chapters 4 and 5 address and test hypothesis 1.

To test chemical risk, monitoring trigger levels (MTLs) determined in the report of Drewes et al. (2018) were adopted as thresholds. Assuming a conservative removal within the SMART*plus* treatment based on unit treatment removal percentages obtained from empirical data, the following hypothesis was proposed:

Hypothesis 2: TOrC concentrations at the point of compliance of the potable reuse train employing SMART*plus* are above the corresponding MTL

To test hypothesis 2, TOrC removal data from sequential biofiltration and RSSCT experiments utilizing the same WWTP effluent as source water were obtained from Müller et al. (2017, 2019a). UV disinfection removal was similarly sources from previously conducted experiments at the same institute (Nihemaiti et al., 2018; Miklos et al., 2019b). All removals were assigned a probability distribution function. A Bayesian network capable of predicting whether chemical concentrations at the point of compliance (after UV disinfection) would comply with the appropriate MTL was constructed in GeNIe. Chapter 6 tests hypothesis 2.

3.2 Objective 2: Evaluate initial and long-term TOrC removal differences in activated carbon and technical sand

Assuming certain TOrCs would not be successfully removed in the SMART*plus* treatment train, the aim was to determine whether an alternative porous media would result in improved TOrC removal. Using the same influent water quality that the SMART*plus* bioreactor received, column studies investigating and comparing the removal of TOrCs in technical sand and BAC filters were carried out over 2+ years of operation. Chapters 7-9 address objective 2.

To evaluate objective 2, the following hypotheses were tested:

Hypothesis 3: Maturation time for biodegradation in BAC will be shorter than in technical sand

To test hypothesis 3, GAC and technical sand filters were operated from virgin state to determine how initial removal performance differed in both media. The breakthrough of a suite of environmentally relevant TOrCs was monitored. Although initial removal in the GAC filters is dominated by adsorption, sand does not have adsorptive capacity, therefore initial removal in sand would be negligible until the onset of biodegradation. Therefore, by focusing on the removal of non-adsorptive but biodegradable compounds such as gabapentin, the onset of removal via biodegradation could be identified in both the GAC and sand filters.

The removal due to adsorption in the GAC filter was tested in the following sub-hypothesis:

Hypothesis 3.1: Rapid small scale column tests (RSSCTs) can accurately differentiate between TOrC removal attributed specifically to biodegradation and to adsorption

To test hypothesis 3.1, the breakthrough prediction for persistent compounds was determined using an RSSCT. The RSSCT results were then compared with the BAC filter results to determine whether this method could elucidate the contribution of adsorption to the removal of TOrCs in the BAC filter. Chapter 7 addresses hypothesis 3.1.

Hypothesis 3.2: Biomass establishment will be faster in BAC than in technical sand

To test hypothesis 3.2, the measurement of active biomass would be used to elucidate information about how the establishment of microorganisms within the filters was progressing. This information could then be coupled with water quality parameters (DOC and DO concentrations, UVA_{254} absorbance) to present a holistic assessment of the biological activity. Sections 10.2.1 and 11.7 address hypothesis 3.2.

Hypothesis 3.3: TOrC biodegradation begins faster in BAC

To test hypothesis 3.3, initial biological TOrC removal in the BAC filter and in a technical sand filter was compared. Additionally, the onset of biodegradation was tested by identifying whether and which biodegradation transformation products were present in the influent and effluent of the filters. Sections 7.3.3 and 10.2.1 address hypothesis 3.3.

As the SMART*plus* bioreactor is meant to remove TOrCs via biodegradation in the long term without any replacement of media, the goal was to observe TOrC removal in the column experiments after biodegradation was stable and evident in the sand filter. Due to the adsorptive surface of the GAC, the concentration gradient of TOrCs in different phases, and the microbial community responsible for biodegradation, this complex environment could result in greater TOrC removal than in the sand filter. To this end, the column experiments were conducted from June 2017 – October 2019, during which time the breakthrough of chemicals and water quality parameters was monitored. This was tested in the following hypothesis:

Hypothesis 4: Long-term BAC filtration facilitates greater TOrC removal than technical sand

To test hypothesis 4, TOrCs exhibiting varying removal tendencies in biofiltration were identified through a comprehensive literature review. Cumulative TOrC removal in the BAC and sand filter would reveal which media was more successful in removing biodegradable compounds. To quantify how much better biodegradation would function in BAC than in technical sand, biodegradation rates obtained through batch experiments on the biologically active media at the end of the column experiments were compared. Chapters 8 and 9 address hypothesis 4. Figure 3-1 presents an overview of the layout of the dissertation, with all associated hypotheses, publications and chapters denoted.

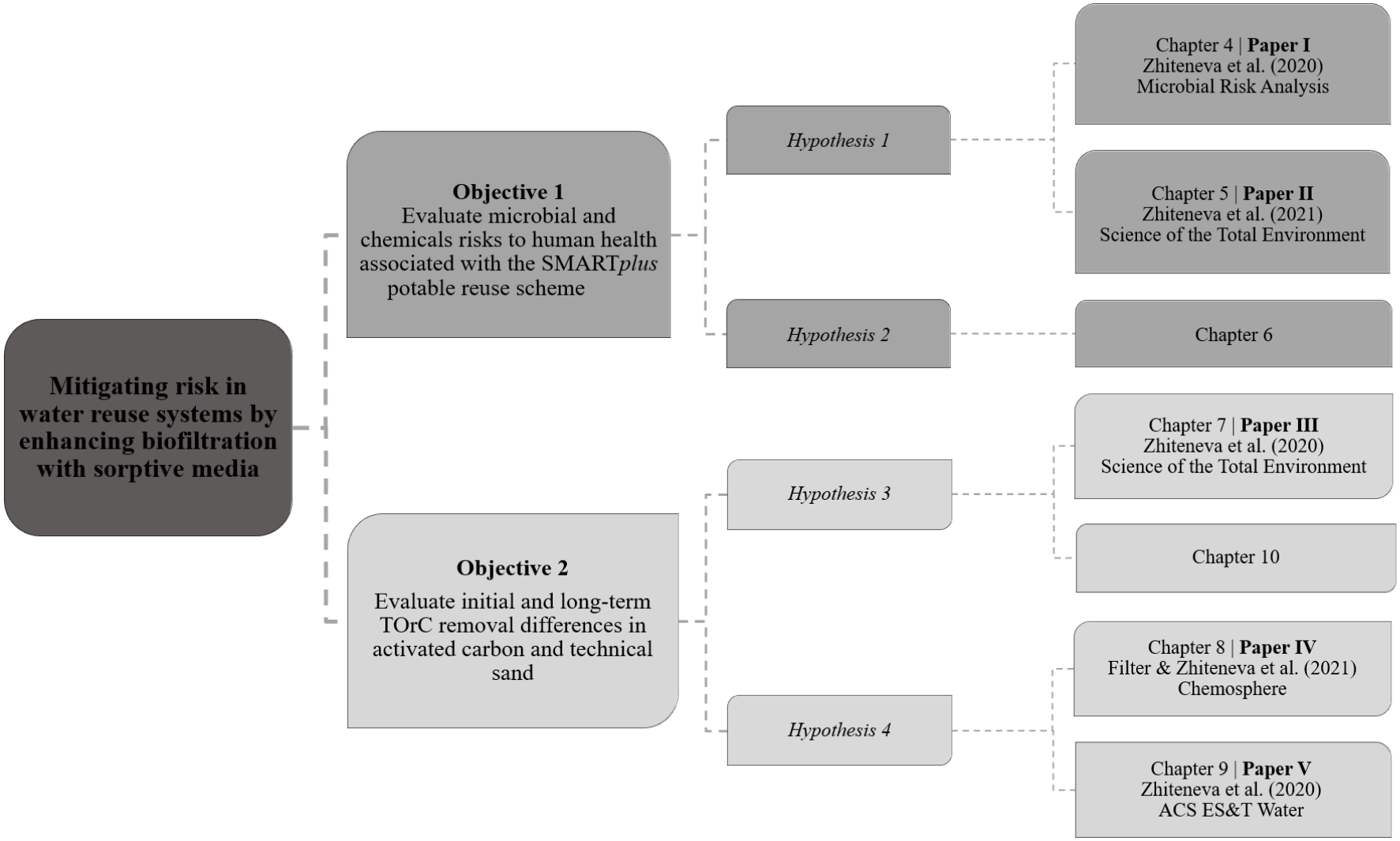

Figure 3-1: Graphical dissertation structure overview.

4. Trends in conducting quantitative microbial risk assessments for water reuse systems: a review

This chapter has been published with editorial changes as follows:

Zhiteneva, V., Hübner, U., Medema, G.J., Drewes, J.E. Trends in conducting quantitative microbial risk assessments for water reuse systems: a review. 2020. *Microbial Risk Analysis* 16, 100132. https://doi.org/10.1016/j.mran.2020.100132.

Abstract

As many regions seek to supplement traditional water sources with reclaimed water, there is also an increasing number of risk assessments conducted for these types of applications. The most comprehensive approach is to conduct a quantitative microbial risk assessment (QMRA) combining empirical and literature data, point value estimates, and probability distribution functions (PDFs) to estimate the final risk for human health from a treatment train in quantitative terms. The variability and uncertainty of reuse systems can be more adequately assessed by probabilistic methods instead of deterministic, point value estimates. This review summarizes common assumptions in PDF selection for source water and treatment steps and dose-response models for risk assessments applied to potable and non-potable reuse scenarios. The review revealed that source water pathogen concentrations were mainly modeled using PDFs, while log reduction values (LRVs) were often derived as point estimates to describe removal efficacy of individual treatment steps. When enough point value LRVs are known, a triangular distribution is recommended to retain the deterministic characteristics of the variable being modeled. Treatments steps with the least amount of experimental data included biological activated carbon, membrane bioreactors, and engineered storage buffers, among others. To circumvent such lack of experimental data, an open-source, anonymized database of concentrations and LRVs could be made available for future assessments. Numerous studies mentioned that testing multiple dose-response models can help determine how the dose-response choice affects final risk. Although sensitivity analyses to determine how variables in the assessment influence final risk were performed in most studies, how PDF selection affects the final risk was not consistently evaluated. Such a discussion could help to establish more informative and comprehensive risk assessment models in future studies as the water reuse field continues to grow.

Chapter 4: Trends in conducting quantitative microbial risk assessments for water reuse systems: a review

4.1 Introduction

To meet water demands in urban areas experiencing population increases and climate change stress, water utilities are increasingly considering water reuse (US EPA, 2017). Where surface water is used as raw water supply, water treatment schemes might utilize a source water that is partially impacted by upstream discharge of wastewater treatment plant (WWTP) effluents, referred to as *de facto* water reuse (Rice and Westerhoff, 2015; Karakurt et al., 2019). Intentional reuse schemes are designed to reduce risks from wastewater-derived microbial and chemical contaminants, increase water supplies, and provide fit-for-purpose water for potable and non-potable uses (urban, irrigation).

Potable reuse typically includes advanced water treatment (AWT) of secondary or tertiary effluent prior to augmentation of either a groundwater or surface water supply. Commonly utilized AWT steps during potable reuse considered in this review were ozonation (O_3), UV-based advanced oxidation processes (UV-AOP), biological activated carbon (BAC) filtration, biologically active filters (BAF), micro- and ultrafiltration (MF/UF), nanofiltration (NF), and reverse osmosis (RO). Disinfection processes considered were chlorination (Cl_2) and ultraviolet light (UV) irradiation. Potable reuse can either be direct by feeding into the drinking water treatment plant or the distribution system (direct potable reuse, DPR) or indirect by releasing first into an environmental buffer, such as surface water, groundwater, or a reservoir and then followed by conventional drinking water treatment (indirect potable reuse, IPR). Where *de facto* reuse is practiced, AWT processes are usually not employed, resulting in higher risk for *de facto* reuse than planned reuse (World Health Organization, 2016; Amoueyan et al., 2017, 2019a; Chaudhry et al., 2017; Lim et al., 2017; Nappier et al., 2018; Soller et al., 2019).

Non-potable irrigation reuse includes agricultural and urban landscape irrigation. As interest and necessity for reuse in agriculture increases, so does the need for effectively quantifying risks of such scenarios. Along with industrial reuse, the aforementioned categories make up the majority of current water reuse practices.

Potable water reuse schemes are scrutinized for possible risks associated with human consumption of reclaimed water. To predict and model possible high-risk exposure scenarios during various operational conditions of reuse practices, assess the safety of a reuse scheme, determine required treatment, or test alternative reuse treatment scenarios, quantitative microbial risk assessments (QMRA) are commonly performed. QMRA is a mathematical approach for estimating risk posed by pathogens to human health. However, in practice, data limitation requires many assumptions to be taken during this process. In an attempt to recommend log reduction targets, the World Health Organization (WHO) published detailed guidelines for conducting QMRAs for water safety (World Health Organization, 2016), although QMRA had already been mentioned in previous guidelines (World Health Organization, 2006). Despite the existence of these guidelines, the lack of a single approach, such as the use of QMRAspot in the Netherlands for drinking water assessment (Schijven et al., 2011; RIVM, 2016), on an international level is notable. This had led to varying results due to the range of approaches used to quantify risk, as well as debates on which risk threshold should be used for which final water usage (Haas et al., 1996; Mara, 2011). As QMRA is a very site-specific exercise, risk assessors should transparently communicate assumptions which can be done through following a newly proposed best practices checklist for reporting results, which includes such details as pathogen-surrogate and pathogen-indicator ratios, dose-response model and parameters, disease burden assumptions, and modelling approach, among other points (Owens et al., 2020).

The framework of risk assessment consists of four steps: 1) problem formulation, 2) exposure assessment, 3) health effects assessment, and 4) risk characterization (Figure 4-1).

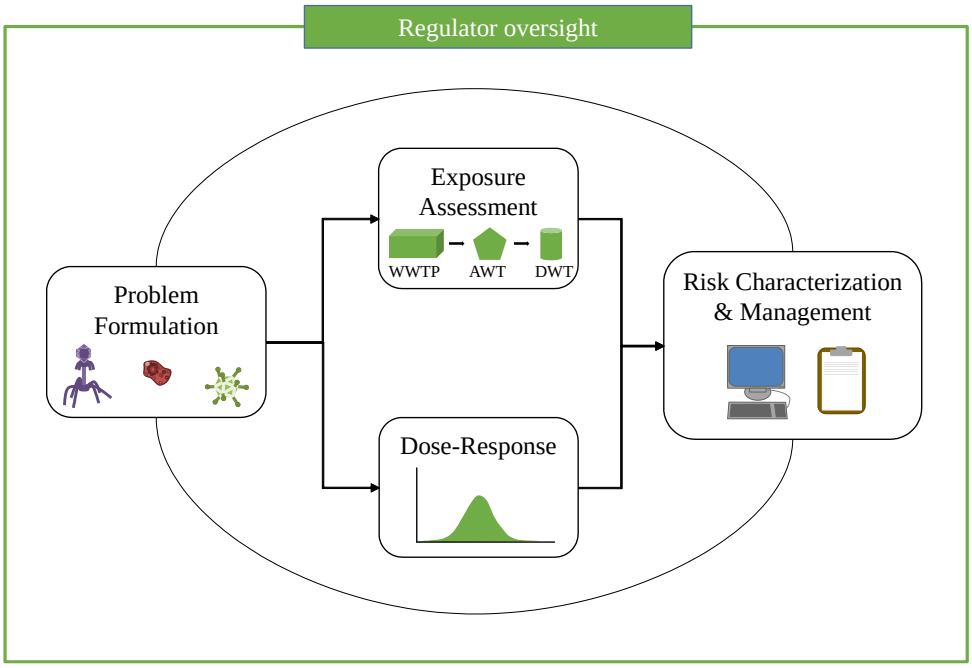

Figure 4-1: QMRA framework, where regulator oversight informs updates and additions to the process.

QMRA utilizes reference pathogens hazardous to public health, including bacteria, protozoa, and viruses. Reference pathogens are present at high concentrations in water which will be recycled, have high pathogenicity, are poorly removed during treatment and can survive at length in the environment, and reflect the risk from classes of pathogens of concern (NSW Office of Water, 2015). The WHO recommends conducting a risk assessment for at least one relevant pathogen from each group (World Health Organization, 2017a). However, pathogens even within one group can exhibit different raw wastewater concentrations/distributions, susceptibility to treatment, and dose response relationships, which may make evaluating multiple pathogens within a single group (i.e. norovirus vs. adenovirus vs. enterovirus) worthwhile. Improving databases of pathogen concentrations in raw wastewater is currently the focus of studies being conducted in California and by the WHO.

However, as pathogens are difficult and time intensive to detect, less harmful but more easily detectable indicator or surrogate organisms have been proposed (Table 4-1). Their behavior and removal in various treatment steps is used to fill in critical knowledge gaps related to treatment efficacy and environmental fate/transport of reference pathogens. As an example, while a culturable virus (i.e. adenovirus) can be used as a surrogate for norovirus or rotavirus, which are only detectable using molecular methods, norovirus or rotavirus are reference pathogens due to their observed adverse affects on human health. Reference pathogens should be deliberately selected to meet the aforementioned qualities (NSW Office of Water, 2015). Indicators or surrogates should only be used in a risk assessment either if a relationship or correlation between an indicator/surrogate and a reference pathogen has been previously established or the relationship can be assumed (World Health Organization, 2017a).

Table 4-1: Reference and indicator pathogens of interest for this review.

Pathogen	Type	Classification	Regulation/Guideline
Norovirus	Reference	Virus	(World Health Organization, 2016, 2017a, 2017b)
Rotavirus	Reference	Virus	(World Health Organization, 2016, 2017b)
Adenovirus	Reference/Surrogate	Virus	(World Health Organization, 2016, 2017a)
Enterovirus	Reference	Virus	(World Health Organization, 2016, 2017b)
Cryptosporidium spp.	Reference	Protozoa	(World Health Organization, 2016, 2017b)
Giardia	Reference	Protozoa	(World Health Organization, 2016, 2017b)
Campylobacter	Reference	Bacteria	(World Health Organization, 2016, 2017b)
Clostridium spp.	Indicator	Protozoa	(World Health Organization, 2016, 2017b)
E. coli	Indicator	Bacteria	(NHMRC-NRMMC-NHMR, 2011; World Health Organization, 2016, 2017a)
MS2	Indicator	Bacteriophage (virus)	(U.S. Environmental Protection Agency, 2015; World Health Organization, 2016, 2017a)
ΦX-174	Indicator	Bacteriophage (virus)	(U.S. Environmental Protection Agency, 2015)

4.1.1 Performance targets using log reduction values

Since pathogens are quantified using various concentration units and over several orders of magnitude, removal in treatment trains is commonly described using dimensionless log reduction values (LRVs). LRVs represent the base 10 logarithm of the ratio of pathogen concentrations in influent to effluent water and are useful to describe the efficacy of a treatment barrier.

To verify whether treatment targets are met, LRVs must be assigned to each individual process in a treatment train which maintains consistent operating conditions (Haas and Trussell, 1998; Olivieri et al., 1999). The LRVs can be determined for individual processes through routine monitoring of relevant (reference) pathogens and/or challenge tests, where higher concentrations of surrogate organisms are spiked to determine treatment efficacy. It helps if the processes have been identified as critical control points and validated as such, to ensure treatment efficacy is properly monitored and can be attuned when/if necessary. During operation, treatment efficacy can be monitored through the use of chemical or physical surrogates, such as total organic carbon, electrical conductivity, or turbidity, which correlate with LRV of reference pathogens for specific treatment processes. LRVs from each step are then summed up to provide a final cumulative removal for the overall treatment train. Point estimates, which are discrete in nature, are often used to describe the LRV and represent a deterministic approach, where the returned value of a treatment or parameter should always be the same. Deterministic methods assume the output of a system will always be the same if all boundary conditions, input variables, and parameters are kept constant (Rose et al., 2013).

Health outcome values or infection endpoints are typically used to determine recommended performance of treatment trains. These values describe the safety of consumed water by quantifying the tolerable disease burden, which is the maximum burden of health effects associated with waterborne diseases and is set to ensure illnesses stemming from treatment are maintained at an acceptable level (World Health Organization, 2017b). When conducting an assessment, health outcome values should ideally be identified prior to the commissioning of a treatment train, as they determine the acceptable level of water quality, performance, and technology targets.

The required removal is often defined by pathogen concentrations in the source water as well as the benchmark risk level. Two common risk levels are usually referenced. The World Health Organization recommends less than 1 in 1,000,000 disability adjusted life years (10^{-6} DALYs) (World Health Organization, 2004). The European Drinking Water Directive was adopted by the Dutch into a drinking water decree requiring less than 1 infection per 10,000 people per year (10^{-4} pppy) (Staatsblad, 2001; Smeets et al., 2009). This annual infection level, although not officially mandated by the US EPA (Sinclair et al., 2015), was also adopted in the United States, which requires mitigating water quality when mean source water *Cryptosporidium* concentrations correspond to ≥2 in 1,000 people per year (US EPA, 2006).

The 10^{-6} DALYs approach does not consider asymptomatic infections to pose any risk, which can lead to underpredicting risk from norovirus, deals with illnesses as opposed to infections (Emelko et al., 2019), and is more commonly used outside the United States. The 10^{-4} infections approach does not consider the severity of illness from one pathogen to be more harmful than another, therefore making it difficult to compare health risks between pathogens (Emelko et al., 2019). Future regulations may even shift to daily risk, as short-term failures and off-spec events have been shown to drive annual risk (Smeets et al., 2009; Soller et al., 2018b). Therefore, it makes sense to test both levels of risk to have a more comprehensive understanding of how a treatment train performs.

The WHO Potable Reuse Guidelines recommend setting removal targets based on individual monitoring data for pathogen concentrations in raw wastewater (World Health Organization, 2017a). If such data are not available, default performance targets of LRVs of 9.5/8.5/8.5 for enteric viruses, enteric bacteria, and enteric protozoa from untreated wastewater to drinking water quality are recommended (World Health Organization, 2017a). These LRVs do not serve as drinking water guideline values, but rather as performance targets for identifying suitable combinations of treatment processes. Additional guideline values used in the USA and Australia can be found in Table 4-2.

Table 4-2: Log reduction values suggested by various guidelines. To calculate these LRVs, the WHO guidelines use 10^{-6} DALYs, whereas US studies use the 10^{-4} infection target.

Range	Target type	Viruses	Bacteria	Protozoa	Guideline
From untreated wastewater to drinking water	Minimum performance targets LRVs	9.5 (enteric)	8.5 (enteric)	8.5 (enteric)	(World Health Organization, 2017a)
From untreated wastewater to drinking water	Minimum required LRVs	9.5 (enteric)	8.1 (Campylobacter)	8 (Cryptosporidium)	(NRMMC-EPHC-NHMR, 2008)
From untreated wastewater to drinking water	Performance targets LRVs	12	--	10/10 (Cryptosporidium/ Giardia)	(CDPH, 2014)

From untreated wastewater to drinking water	Performance targets LRVs	12	9, total coliform bacteria	10 (Cryptosporidium)	(National Water Research Institute, 2013)
From secondary treated wastewater to drinking water	Performance targets LRVs	8	--	5.5, 6 (Cryptosporidium, Giardia)	(Texas Water Development Board and Alan Plummer Associates, 2015)
Reclaimed water to unrestricted irrigation	Performance targets LRVs	6-7			(World Health Organization, 2006)

Recent studies have suggested that LRV thresholds and default pathogen concentrations described in various guidance documents could be updated (Gerba et al., 2017). Using average LRV point values has also been shown to underestimate end risk (Schmidt et al., 2020), and achievable risk based targets have been shown to vary depending on system size (Schoen et al., 2020). Pecson et al. (2017) found that to guarantee 12/10/10 LRVs (according to the California recycled water regulations) for 90-95% of operational lifetime, their investigated treatment train would need to achieve LRVs greater than 12/10/10 except for 5-10% of the time. Soller et al. (2018a) similarly determined that the target risk for their system (10^{-4}) was reached only by achieving 14/>11/>11 LRVs, which is attributed to the use of revised raw wastewater concentrations. Such varying results reveal that there is no consensus between studies on reporting estimates of the final risk, and which should fall under the health burden threshold – is it the average, the median, the 5^{th}, 75^{th}, 90^{th} or 95^{th} percentiles, any associated confidence intervals (Mara et al., 2007; Seidu et al., 2008; Page et al., 2010; Toze et al., 2010; Olivieri et al., 2014; Pecson et al., 2017), or other targets? Producing a point value estimate of final risk does not help in characterizing how the system performs in between point value estimates, which can be explored at higher resolution through the use of probability distribution or density functions (PDFs).

4.1.2 Probability distribution functions

QMRA can also provide insight into the variability of the estimated risk while noting uncertainties (Smeets et al., 2008). Although the usage of LRVs to determine which treatment steps are required is an established principle, probabilistic or stochastic methods, such as PDFs, assume variability and uncertainty are inherent to the system and provide varying final risk estimates (Vose, 2008). A PDF must be individually fit to each particular data set. Using a range of techniques, such as Monte Carlo or Latin Hypercube sampling, the amount of variability and uncertainty can be included in the QMRA. Models can also be dynamic or static, meaning that time is or is not considered a variable in the modeling (Soller and Eisenberg, 2008).

PDFs are not consistently employed in QMRA studies, usually due to lack of site-specific empirical data, especially when performing a screening level QMRA. However, improper PDF selection can lead to under or over estimation of final risk, which can have health, legislative, and financial consequences. Recent microbial risk assessments have begun to describe the implication of proper PDF selection in greater detail (Poma et al., 2019; Sylvestre et al., 2020).

Commonly used PDFs for characterizing various steps in a QMRA are illustrated in Figure 4-2. For theoretical background and recommended selection guidance for PDFs, readers are directed to prior literature and statistical studies (Walck, 2007; Mun, 2008; Vose, 2008; Dias, 2016). Risk assessors should take care that pathogen counts have been properly adjusted when dealing with empirical data (Owens et al., 2020), and that units are consistent for all data used.

The WHO guidelines do not identify or associate PDFs with certain pathogen presence, though they recommend testing multiple well-fitting PDFs to determine how the outcome is influenced to choose the best fit (World Health Organization, 2016). While some authors likely followed this recommendation prior to the WHO 2016 publication, most assessments before 2016 followed federal/state guidelines, and due to the site specific nature of QMRA and lack of specific directions in the WHO guidelines, future assessments will likely continue to apply different approaches.

However, why and on what basis certain PDFs are chosen (i.e., literature review, best fit, theory, etc.) is not always explained, leaving risk assessors to find information on their own. An open source database of pathogen concentrations and removals in various treatment steps common in water reuse schemes would be incredibly helpful. As this does not yet exist, a starting point is to catalog PDFs to determine which are the most utilized and suitable for the pathogens in treatment steps of interest in this review.

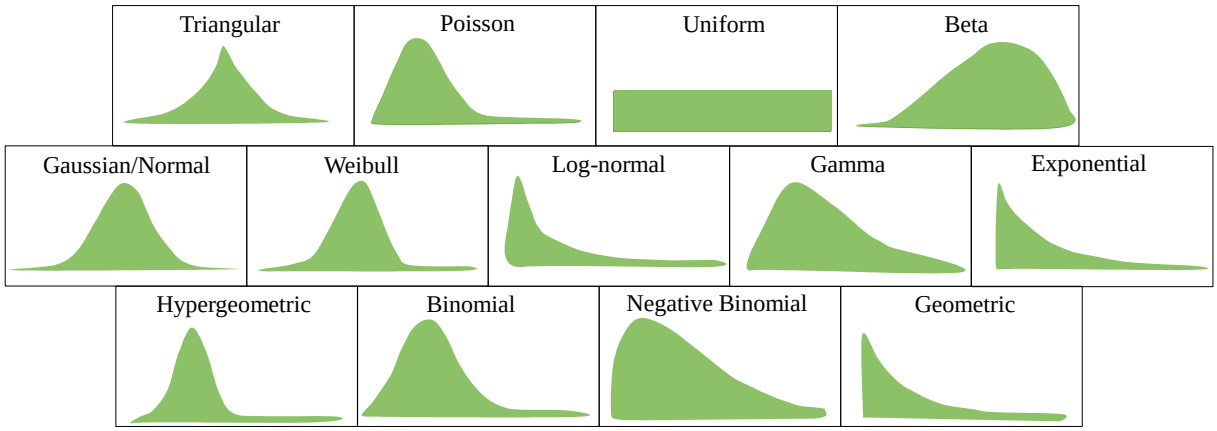

Figure 4-2: Most commonly used PDFs in QMRA studies for describing pathogen presence in water reuse systems, with frequency displayed on the x-axis and probability on the y-axis. PDFs can also be applied to other QMRA steps, such as dose-response.

A recent review of drinking water QMRAs identified numerous aspects of reporting assumptions, reductions and uncertainty which could be improved upon, and created a water supply reporting checklist to help standardize how case study details and results are communicated (Owens et al., 2020). However, this review focuses specifically on water reuse practices, which require other considerations. These include 1) characterizing pathogen density in source waters, 2) identifying distributions used to characterize pathogen reduction in treatment steps, 3) identifying which dose-response models are used, and 4) determining how PDF choice affects final risk. These points will be addressed in this review.

4.2 Search criteria

The pathogens of interest for this study included norovirus, rotavirus, adenovirus, enterovirus, *Cryptosporidium* spp., *Giardia*, *Campylobacter*, *Clostridium* spp., *E. coli*, MS2 and ΦX-174. A search for combinations of these 10 pathogens (excluding *Clostridium*) with various reuse related terms was conducted in Scopus or publications between 2000-2020 in February 2020 and resulted in 2,669 articles (for search string, see Supplemental Information (SI) Figure 11-1). Using the PRISMA approach, studies which did not have keywords in the abstract, title or keywords were omitted. A total of 117 full length peer-reviewed papers from database searching and expert knowledge and theses were screened. Forty-three papers were ultimately accepted for this review on the basis of whether they provided information in the following categories: probability distribution functions, intentional water reuse, and QMRA model assumptions. In the 43 studies taken from database searches, a total of 74 reuse scenarios were investigated, of which 20 were DPR, 10 were IPR, 6 were *de facto* reuse, and 38 were irrigation reuse.

Five studies investigated both DPR and IPR applications, 3 investigated both *de facto* and IPR, and 3 investigated both *de facto* and DPR.

Source waters and treatment trains utilized in the individual studies are presented in Table 11-2. Frequencies of pathogen appearance in treatment trains are summarized in Table 11-1. Over 30% of the studies (14/43) utilized indicator or surrogate organisms in some form. Certain studies established either explicit surrogate-reference ratios (Seidu et al., 2008; Barker-Reid et al., 2010) or implicit relationships (Mara et al., 2007; Pavione et al., 2013) , while others used surrogate for certain parts of the QMRA assessment, such as calculating decay rates (Petterson et al., 2001) or removals in certain treatment steps (Ander and Forss, 2011; Chaudhry et al., 2017; Soller et al., 2017). Nearly all studies mentioned that the usage of surrogate organisms is controversial and was done only because sufficient reference pathogen data was unavailable. For pathogens which cannot be cultured, the use of the molecular signal during treatment can be an unreliable performance predictor, therefore a surrogate should be used (for example, use of coliphage attenuation for indicating norovirus reduction during treatment).

The main difference in potable and non-potable studies was noticed in the volume of data available to conduct a QMRA, exposure and health outcome values. Data can be more difficult to obtain in the field which could prevent a probabilistic analysis, and while this limitation is acknowledged, Monte Carlo analyses have been conducted even with limited data (Mara et al., 2007). Exposure is associated with a high degree of uncertainty (Haas et al., 2014), and varies for field workers, market workers, and consumers. A discussion on the most appropriate health outcome value for agricultural reuse is included in section 4.3.3.2. Other differences between potable and non-potable studies are discussed where relevant.

4.3 Discussion of LRV characterization

Studies found that cumulative risk was driven by the highest pathogen concentrations, reinforcing the need to perform probabilistic risk assessments for individual trains, including numerous assumptions and variations, instead of assigning general LRVs (Soller et al., 2018a). This prompted a targeted evaluation of the studies for the following questions:

1. Were multiple PDFs tested to determine which provided the best fit?
2. Was the effect of PDF selection on final risk estimate discussed?
3. For treatment steps: in comparison to point values, how do PDFs affect the LRVs?
4. For treatment steps: can PDFs be recommended instead of point values to describe LRVs?

All LRVs and PDF parameters are summarized in a spreadsheet in the SI.

4.3.1 Pathogen presence in source water

For this review, source water was categorized as either raw wastewater, treated wastewater, or surface water (*de facto* reuse). For treated wastewater, only conventional wastewater treatment (mechanical and biological treatment) was considered. Mechanical treatment removes particles from sewage, whereas biological treatment refers to organic carbon degradation and nutrient removal. As the source water chosen dictates the total LRVs required, this is an important step to explicitly report, which was rather inconsistently done in studies. When considering each source water individually, results show that raw wastewater was dominated by lognormal PDFs and point values, treated wastewater was dominated by point values, and *de facto* source water was characterized by lognormal, gamma, and uniform PDFs (Figure 4-3).

Lognormal distributions depict the results of many random processes, are suitable for describing the concentration of pathogens in source water which are generally positively skewed to high concentrations

with low probability, and have been used for many years in pathogen characterization (Haas et al., 2014; World Health Organization, 2016). Gamma distributions are bounded at zero and positive, and have also often been used to characterize concentration in source waters (Mun, 2008; Dias, 2016; World Health Organization, 2016). Uniform distributions signify that all concentrations within the defined range have the same probability of occurring, which is an assumption that can be used when minimal or no pre-existing knowledge about the parameter is available (Haas et al., 2014). Uniform distributions minimize statistical bias when summing LRVs determined from multiple studies, where the raw data cannot be combined to fit a PDF due to, for example, differences in unit treatment operational parameters (i.e., fluence, hydraulic retention time, etc.). They are therefore often used when a minimum and maximum LRV is known. Thus, uniform distributions can be justified for generalized results from a class of facilities or for broad-scale regulations.

As there were many different units used to quantify pathogens, it is difficult to state which PDF is recommended, but some conclusions could be drawn: in raw wastewater, *Cryptosporidium*, norovirus, and rotavirus were mainly categorized using lognormal PDFs, while *Campylobacter* was categorized using uniform PDFs. The overall trend for raw wastewater concentrations from the studies aligns with the WHO recommended lognormal distributions for pathogen concentrations (World Health Organization, 2016). The importance of using PDFs instead of point values to describe raw wastewater pathogen concentrations was noted in numerous studies (18/43). This is supported by the twofold cumulative risk increase for a DPR system when updated norovirus raw wastewater density information was incorporated (Soller et al., 2018a). Ito et al. (2017) also raised the importance of accumulating more information on the probabilistic pathogen distributions in source water, especially in a multiple-barrier system. Gonzales-Gustavson et al. (2019) used maximum likelihood to determine best fitting PDF to raw wastewater concentrations.

Concentrations in treated wastewater were dominated by point values. Although empirical data should be collected when possible as pathogen concentrations are site specific, the prevalence of published point value concentrations could allow risk assessors to use either a uniform or a triangular distribution when a PDF is desired.

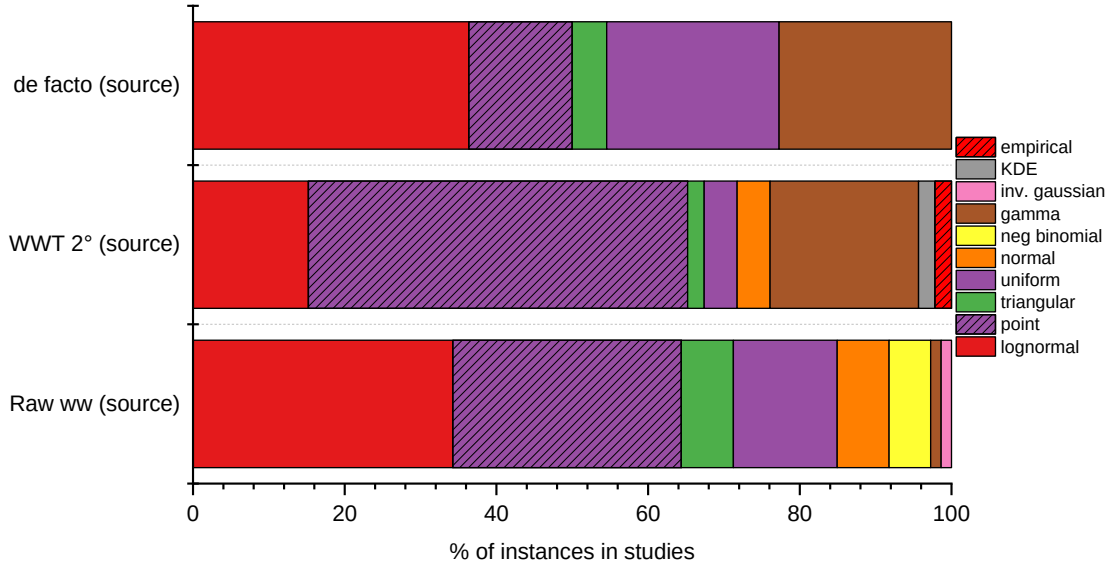

Figure 4-3: PDFs and point values used for pathogen characterization in each source water. KDE = kernel density estimator, inv. gaussian = inverse Gaussian, neg. binomial = negative binomial.

Pathogen concentrations in surface water were mainly characterized by lognormal, uniform, and gamma, PDFs. However, the close split between the 3 distributions reveals the need for better characterization of pathogen concentrations in *de facto* reuse scenarios, particularly as urban populations and wastewater volumes discharged to surface waters increase in many locations. Åström et al. (2007) and Sato et al. (2013) both used a maximum likelihood estimate to choose gamma as the appropriate distribution. Bergion et al. (2018) also suggested that using probabilistic modeling for log reductions in surface water quality would improve QMRA predictions for these scenarios, and when coupled with testing multiple PDFs, could give insight into how selection affects final risk.

Of all studies describing pathogen concentrations in source water, only one study (Petterson et al., 2001) tested multiple PDFs and discussed the effect on final risk.

An additional point worth discussing is how selection of source water is handled when distributions in both raw sewage and treated wastewater is available. Although Gerba et al., (2017) revealed that viruses are likely present in greater numbers than what most guideline documents have advised as average concentrations, not all detected units are infectious, which could potentially lead to overly conservative treatment requirements when using raw sewage as source water. Therefore, comparing presence determined via molecular detection with simultaneous detected surrogates would provide more reliable estimates.

Using secondary effluent could provide more reliable concentrations of pathogens (i.e., matrix interference in raw sewage) or more consistent concentrations due to equalization (i.e., not affected by temporal variability in raw sewage). Regardless of source water, reporting operational parameters of wastewater treatment is imperative.

4.3.2 Characterizing pathogen removal in different treatment processes

Removal in wastewater treatment, advanced water treatment, and drinking water treatment was characterized by point values and uniform distributions (Figure 4-4). The high frequency of uniform distributions used is likely explained by the fact that of the possible PDF options provided in Figure 4-2, uniform distributions are the closest distribution option to a minimum-maximum point value range. Using deterministic point estimate LRVs to describe removal in a particular treatment makes it more difficult to quantify uncertainty associated with the LRV variable. A uniform distribution, characterized by minimum and maximum point values, retains the stochastic nature of the variable by using a range as narrow or as wide as necessary while also providing some information on the uncertainty related to the variable.

Testing multiple PDFs for each pathogen in each treatment step was not commonly done in studies. However, one notable example is worth highlighting: Pecson et al. (2017) created a PDF using the empirical cumulative distribution function in R and compared this non-parametric distribution to several parametric ones, including normal, inverse Gaussian, Weibull, gamma and lognormal, to determine best fit. PDFs were then ranked using the Bayesian Information Criterion, which compares the likelihood of obtaining specific data with a particular PDF to determine which PDF fit best (Ito et al., 2017; Pecson et al., 2017). Such a method is possible when enough empirical data exists. Other studies used maximum likelihood estimates (Åström et al., 2007; Barker, 2013; Sato et al., 2013; Olivieri et al., 2014; Sales-Ortells et al., 2015; Gonzales-Gustavson et al., 2019), chi-squared goodness-of-fit (Barker, 2013; Bergion et al., 2018), Kolmogorov-Smirnov tests (Sales-Ortells et al., 2015; Bergion et al., 2018), the Akaike Information Criterion (Mok and Hamilton, 2014; Mok et al., 2014; Owusu-Ansah et al., 2017), or kernel density estimation (Petterson et al., 2001) to determine best fit.

4.3.2.1 Secondary/tertiary wastewater treatment

Point value LRVs were most popular, followed by uniform, triangular, and normal PDFs. The lack of specificity of treatment involved in the reporting of these distributions, especially in irrigation studies, led to the high usage of point values for all pathogen classes. Numerous studies also described concentrations in treated water instead of calculating LRVs. Accordingly, multiple PDFs were not tested and their effect on final risk was not mentioned. For secondary treatment, uniform and triangular PDFs had lower minimum and higher maximum values than those used for point value LRVs for *Campylobacter*, *Cryptosporidium*, and for tertiary treatment, the range of LRVs used for uniform PDFs was slightly greater than the range of point values for norovirus. However, if a PDF is desired, then adapting knowledge of point value LRVs to a uniform or triangular distribution could be suggested.

4.3.2.2 Advanced wastewater and drinking water treatment

Influent water qualities to AWT/DWT in QMRA studies varied greatly, ranging from raw wastewater used in theoretical/lab-scale assessments to identify how AWT would reduce risk (Barker et al., 2013; Pecson et al., 2017) to conventional mechanical and biological wastewater treatment with no disinfection (Page et al., 2010; Ander and Forss, 2011; Mok et al., 2014; Soller et al., 2017, 2018) to WWTP effluent blended with stormwater (Page et al., 2010). Most studies used point values, or uniform or lognormal PDFs based on literature data to describe pathogen removal (Figure 4-4). There was no discernable pattern between type of PDF used and pathogen class.

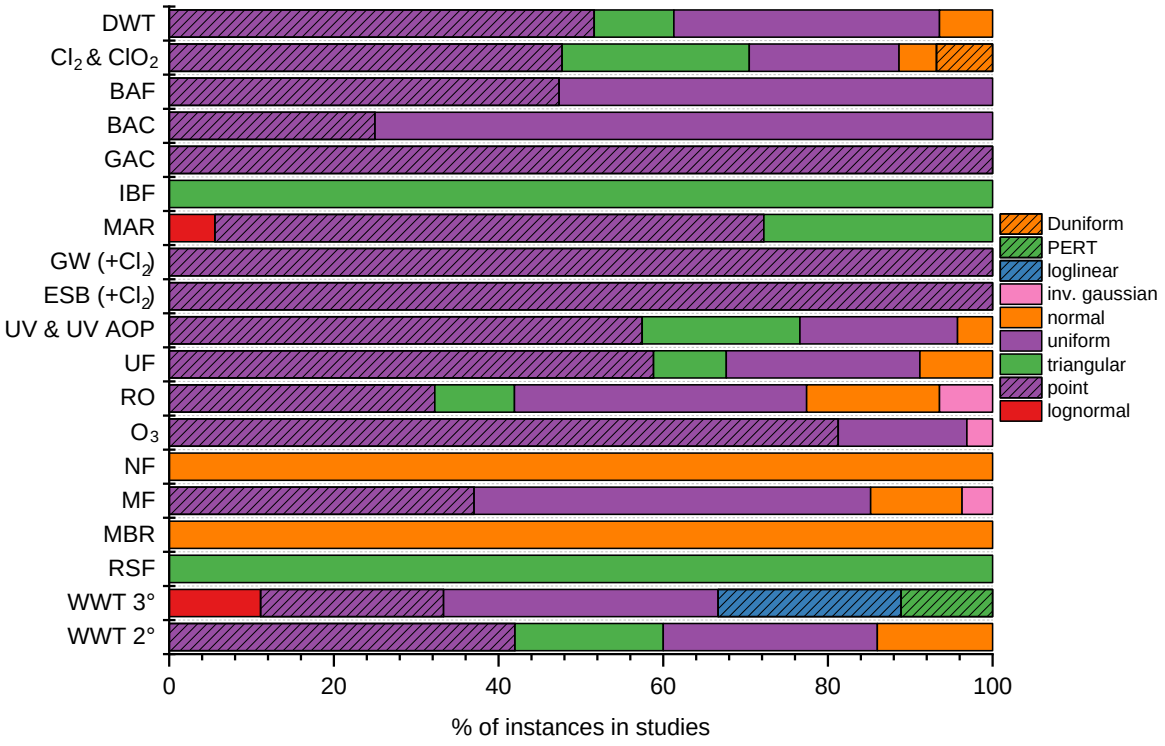

Figure 4-4: PDFs and LRVs used in characterizing pathogen removal in wastewater, advanced water treatment and drinking water treatment. WWT 2° = secondary wastewater treatment, WWT 3° tertiary wastewater treatment, ESB = engineered storage buffer, GW = groundwater, Duniform = discrete uniform, inv. gaussian = inverse Gaussian.

Of the studies which provided reasoning for using PDFs, three used point estimates for LRVs only when data was insufficient (Ander and Forss, 2011; Barker et al., 2013; Amoueyan et al., 2017, 2019a). Four studies (Page et al., 2010; Ayuso-Gabella et al., 2011; Bartak et al., 2015; Bergion et al., 2018) used triangular PDFs, citing multiple literature sources (Westrell, 2004; NRMMC–EPHC–AHMC, 2006; Smeets et al., 2006; NRMMC-EPHC-NHMR, 2008; Ødegaard et al., 2009). Smeets et al. (2006) was often cited as a source for using triangular distributions to describe removal during treatment, reasoning that the distribution is a good 'first-pass' representation of process variability and uncertainty when a Monte Carlo analysis is used to sum up pathogen removal over many treatments. Along with normal distributions, triangular distributions display a measure of central tendency to describe data more realistically than uniform distributions (Vose, 2008), but do not require that data is normally distributed. Therefore, it could be applied when enough point value LRVs exist to determine a minimum, maximum, and most likely/mean/median LRV value for a treatment, particularly for AWT unit treatments (see below).

AWT pathogen removal distributions were found to be site and assumption specific. Many treatment steps, including GAC, BAC, BAF, WWT 3°, O_3, and ESB were categorized only by point values or uniform distributions due to lack of empirical data. On the other hand, RSF, NF, and MBR were categorized only by PDFs and had no point value LRVs. Treatment steps where PDF ranges were greater included UV, RO, DWT, and Cl_2, while the opposite was true for UF, O_3, and MF (and Cl_2 for norovirus). However, most treatment steps utilized the same ranges of LRVs for PDFs and point values, leading to the suggestion that the discrete point values could be transformed to stochastic PDFs to supply more information about the uncertainty and variability embedded in the LRV of the treatment step.

Additionally, the relatively few studies describing DPR/IPR systems (in comparison to irrigation studies) investigating numerous treatment steps led to an overrepresentation of the same datasets from the same few authors, skewed towards point LRVs. This is especially noticeable for processes such as UF, UV and UV-AOP, RO, O_3, MF, and other DWT processes, which were mainly described by point values and uniform distributions in 6 studies by 2 authors (Amoueyan et al., 2017, 2019b, 2019a; Soller et al., 2017, 2018a, 2018b). Often the authors used the same dataset or changed the parameters only slightly, causing their results to be overrepresented in the overall results of this review. Since both of these authors conducted extensive literature reviews, the values they used are representative of removals found in research, framed in accordance to maximum attributable LRV guidelines. However, data from studies which describe large demonstration-scale facilities such as Pecson et al., (2017), or are based on extensive literature reviews such as Soller et al., (2017), as well as data available in other reports or publications which are not peer-reviewed like Salveson et al. (2018), could be anonymized and made available as open source, so that future screening level QMRAs would have access to empirical raw data to build their own PDFs, instead of relying on point value LRVs or reports of PDFs used in other studies.

Pecson et al. (2017) was the only study found which fit PDFs to empirical, albeit surrogate, data for the AWT investigated and explained how PDFs were selected. Although most studies adapted LRVs or sometimes PDFs from literature, care must be taken that operational parameters used to obtain the literature LRVs (i.e. ozone contact time, UV fluence) most closely reflect the desired treatment performance. Studies did not test multiple PDFs or discuss PDF effect on final risk, although the methodology of Pecson et al. (2017) is exemplary for studies wishing to do this. Due to the heterogeneous nature of literature reporting LRVs for AWT and DWT - i.e., whether LRVs were obtained from ambient concentrations or challenge tests or both (Chaudhry et al., 2017) – and until an open source database exists, risk assessors are encouraged to refer to the SI of this review and conduct their own literature reviews to collect LRVs which most accurately represent the particular treatment and operational conditions being investigated. If enough literature or empirical data exist, triangular

distributions as recommended in Smeets et al. (2006) could be considered, but readers are directed to statistical references to determine whether this is applicable for their data (Vose, 2008).

4.3.2.3 **Managed Aquifer Recharge**

Only 4 studies provided LRVs for MAR, bank filtration, or GW related treatment (Ayuso-Gabella et al., 2011; Bartak et al., 2015; Amoueyan et al., 2017; Bergion et al., 2018), the majority of which were point values. The lack of QMRA studies discussing removal in MAR is notable, and currently there is much debate around LRVs attributed to MAR systems. When there is information available, where the log reduction can be assessed either on a per meter (Bergion et al., 2018) or per day (Ayuso-Gabella et al., 2011) basis, this helps to determine the critical retention time required for the MAR system to reach a target LRV. In studies that used a PDF to describe removal or concentration, the PDF of choice was triangular: Verbyla et al., (2016) quantified pathogen concentrations in river samples and in riverbank filtrate, Bartak et al., (2015) characterized LRVs in bank filtrate, and Ayuso-Gabella et al., (2011) described residence time and pathogen decay rate, all using the triangular distribution.

The approach in Ayuso-Gabella et al., (2011) was particularly interesting, as it calculated MAR removal as the product of residence time and pathogen decay, both of which were mainly characterized by PDFs. Although removal was capped at 6 LRVs per regulatory guidelines (NRMMC-EPHC–NHMRC, 2009), this approach allowed the authors to examine LRVs achieved after certain travel times at higher resolution, and to determine which pathogens were most critical for their MAR systems (Ayuso-Gabella et al., 2011). Such an approach, where enough information is available or in combination with literature data, is recommended to allow a more quantitative assessment of efficacy on a site-specific basis (Page et al., 2010). Readers can consult recent die-off studies for more information on these parameters (Boehm et al., 2018), but assessors should consult their local guidelines to determine whether die-off is considered in the assignment of LRVs for MAR, and how regulatory LRVs can vary from observed LRVs. This can further optimize MAR removal, by narrowing the distribution describing the optimal residence time to determine optimal time for achieving proper reduction during subsurface treatment.

Likely due to the limited amount of empirical pathogen removal data available for the MAR systems investigated, no studies mentioned alternative PDFs, and therefore no evaluation of selected PDFs on final risk was possible. More publication of decay rates of pathogens in the subsurface is needed so that a better assessment of removal efficiency and health risk can be conducted (Toze et al., 2010; Gerba and Betancourt, 2019).

The importance of conducting a QMRA for a MAR system, due to increasing interest in non-membrane based reuse treatment trains, underlines the need for more empirical data collection as well as a discussion on how many LRVs MAR systems can and should be credited with. The usage of triangular distributions to characterize aspects of removal in MAR systems seems to be higher than in other treatment steps, and should continue to enable further optimization of systems.

4.3.2.4 **Failure and hazardous events**

Operational failure or other hazardous events can lead to increased final risk if not properly mitigated or planned for. Such extreme events, particularly in the short term, can result in the highest risk to consumers and underline the importance of selecting a PDF which correctly accounts for this region (Petterson et al., 2001; Smeets et al., 2006; Soller et al., 2018b; Amoueyan et al., 2019a). Failure was particularly relevant for IPR/DPR systems, noted by the distribution of studies discussing failure: one irrigation study (Agulló-Barceló et al., 2012) versus six potable reuse studies (Ander and Forss, 2011; Amoueyan et al., 2017, 2019a, 2019b; Pecson et al., 2017; Soller et al., 2018b), the majority of which also conducted a sensitivity analysis to determine how failure affected final risk, with the exception of

Soller et al. (2018b). Although not a focus of this review, both individual and compound failure in potable reuse systems (Amoueyan et al., 2017, 2019a), i.e. when one or more treatment steps fail, as well as frequency, magnitude and duration of failure should be carefully considered when discussing variability of treatment train efficacy and reliability, as well as redundancy (Pecson et al., 2017). For these systems, the comparison of acute failure events to an annual risk level, and whether acute risks should be emphasized more when setting future normative guidelines (Owens et al., 2020) is important. Again, providing open access to large datasets such as the ones referenced in (Pecson et al., 2017; Soller et al., 2017, 2018a) would immeasurably help future QMRA studies select PDFs.

4.3.3 Health effects assessment

The theory behind selecting the proper dose-response model for a pathogen depends on the approach taken: whether a blanket assumption will be made (exponential or beta Poisson) or whether a separate model for low-doses (linear) will be used (World Health Organization, 2016). Certain dose-response models adhere to the single-hit (also called independent-action) model theory, which says that every ingested pathogen acts independently and has an individual probability of causing infection (Haas, 1983; Teunis and Havelaar, 2000; Haas et al., 2014). Single hit models are usually exponential or Poisson distributions, where the upper limit of infection probability is the probability of exposure and is represented with a maximum risk curve, and a summary of models for 9 commonly studied pathogens is available (World Health Organization, 2016). High and low dose-response approximations are governed by different equations for *Campylobacter*, rotavirus, and *Cryptosporidium* in guidelines (World Health Organization, 2016). This has implications for risk calculated for the finished water, as the response of the general population, and especially susceptible individuals, to an ingested dose influences final risk.

4.3.3.1 **Dose-response**

Protozoa dose-response models were mainly exponential, whereas virus and bacteria dose-response models were mainly various Poisson distributions (Figure 4-5). Hypergeometric functions are used when the sample size in comparison to population size is small, while Poisson distributions (an approximation of the hypergeometric distribution) are used for large populations, random sampling, and if there is a constant chance for the event to occur (Vose, 2008).

In selecting appropriate dose-response models, certain elements should be carefully considered: which pathogen strain, exposure route, and population subset should be modeled; which model to choose if there is no universally accepted model (Teunis et al., 2008); how does model choice cover very low doses (Amoueyan et al., 2019a); how does aggregation affect pathogen concentration (Mok et al., 2014; Van Abel et al., 2017; Gerba et al., 2018); and whether units for characterizing concentrations are the same as those used in the selected dose-response model (i.e. gene copy number from PCR measurements vs. CFU from cultivation studies). While not an exhaustive list, these points were either mentioned in the studies or noted as having particular importance.

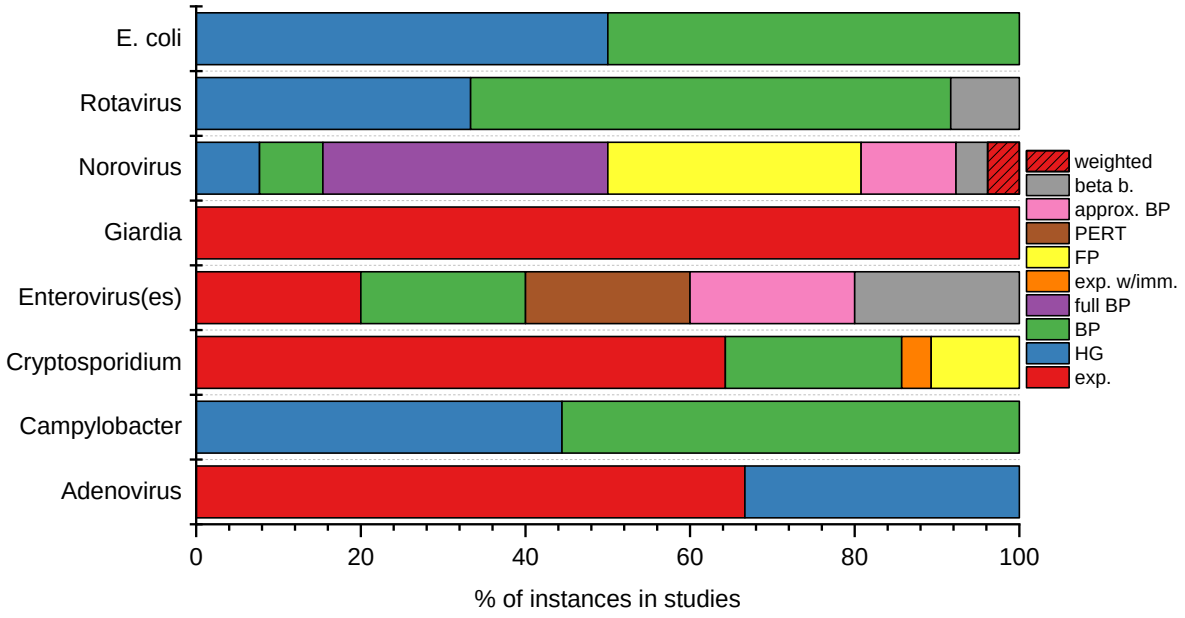

Figure 4-5: Dose-response models used in the studies. Beta b. = beta binomial, approx. BP = approximated beta poisson, FP = fractional poisson, exp. w/imm. = exponential with immunity, BP = beta poisson, HG = hypergeometric, exp. = exponential.

Ten studies explicitly tested different dose-response models (Agulló-Barceló et al., 2012; Barker et al., 2013; Verbyla et al., 2016; Chaudhry et al., 2017; Ito et al., 2017; Pecson et al., 2017; Soller et al., 2017, 2018a; Chandrasekaran and Jiang, 2018; Amoueyan et al., 2019a). Five additional studies mentioned testing alternative PDFs (Seidu et al., 2008; Barker-Reid et al., 2010; Ander and Forss, 2011; Symonds et al., 2014; Amoueyan et al., 2017), for a total of 15/43 (35% of papers).

Whether or not testing multiple dose-response models for all pathogens is a useful exercise is debated in the literature. One study mentioned that the testing of a fractional Poisson model in comparison to the baseline exponential model for *Cryptosporidium* increased the final risk nearly 8 times (Amoueyan et al., 2019a). Model selection and assumptions should be clearly explained in studies: exponential distributions are continuous, while beta Poisson distributions are discrete, and beta Poisson or fractional Poisson models are more suited to describe the higher risk at lower pathogen doses likely to be encountered in drinking water applications and therefore result in higher risk (Agulló-Barceló et al., 2012; Soller et al., 2017; Amoueyan et al., 2019a). On the other hand, Ito et al. (2017) tested a hypergeometric and a beta Poisson dose-response model for norovirus and determined that the selection actually had no effect on LRVs for norovirus in their irrigation scenarios (as both distributions are in the same family (Vose, 2008)). However, testing different models, even when dose-response models are widely accepted, can strengthen model certainty (Chandrasekaran and Jiang, 2018; Amoueyan et al., 2019a). Studies which did this highlighted the importance obtaining a wider estimate of the annual risk of infection by propagating variability through to final risk (Soller et al., 2017, 2018a). Required LRVs can differ by 3 orders of magnitude depending on which norovirus dose response model is used (Amoueyan et al., 2019a; Emelko et al., 2019), and Verbyla et al., (2016) showed that the correlation between dose-response model and disease burden was greater than between source water concentration and disease burden. Soller et al. (2018a) showed that changing the norovirus dose-response model increased the cumulative annual risks by 2 orders of magnitude. For norovirus, two studies from the same group found the lowest risk when using fractional Poisson models (Soller et al., 2017, 2018a), while another study found fractional beta Poisson to have highest risk (Chandrasekaran and Jiang, 2018). This, coupled with the increasing usage of norovirus in potable reuse QMRAs and recent evidence that norovirus concentrations in raw sewage are higher than previously assumed (Van Abel et al., 2017), shows that at least for norovirus, testing multiple dose-response models is a worthwhile exercise. A

critical consideration is the (dis)aggregation of norovirus, which is central to interpreting the magnitude of determined norovirus concentrations.

In order to determine whether testing multiple dose-response models is useful, assessors are encouraged to conduct a sensitivity analysis to determine how much the dose-response affects final risk, taking additional conservative estimates if/when necessary. If the treatment scenario warrants a higher certainty of treatment quality, or if the model choice greatly affects the final risk in a sensitivity analysis, testing multiple PDFs is recommended. If not, dose-response model selection should be informed by guidelines and databases (World Health Organization, 2016; CAMRA, 2020). Additional microbiological considerations include uncertainties about the infectious status of pathogens, and how they interact with other organisms within the water matrix, both of which were outside of the scope of this review.

4.3.3.2 **Health outcomes and disease burden**

Health outcome values are described by tolerable thresholds, either by the concept of DALYs per person per year, or by a likelihood of infection occurrence per subpopulation per year. DALYs can be adapted for different reference level of risks depending on the pathogen or disease being investigated.

However, these guidelines are not immune to debate: one study argued that 10^{-6} DALYs, which translates to a 10^{-3} disease risk pppy from consuming drinking water, should be reduced to a 10^{-2} infection risk pppy when dealing with water reuse in agriculture (Mara et al., 2007). The authors reasoned that a 10^{-2} tolerable infection risk pppy is already 1-2 orders of magnitude lower than the average instances of diarrheal disease, estimated to be between 10^{-2}-1 pppy (Mara et al., 2007). This proposed adjustment of tolerable disease risk to the community specific incidences of disease was then supported by a standalone publication (Mara, 2011), a publication discussing the reasoning behind the setting of threshold values (Sinclair et al., 2015) and subsequent QMRA studies, which tested lower thresholds of tolerable annual disease burden adapted to their socio-economic and local contexts (Barker et al., 2013; Pavione et al., 2013; Mok and Hamilton, 2014; Bartak et al., 2015; Beaudequin et al., 2016; Ito et al., 2017; Moazeni et al., 2017). The most recent WHO guidelines addressed this by stating that 10^{-6} DALYs may not be realistic in some locations and circumstances, especially where overall disease burden comes from multiple exposure routes, therefore setting a lower level of tolerable risk (10^{-4}-10^{-5} DALYs) would also provide safe water (World Health Organization, 2017b).

The studies evaluated in this review were almost evenly split between using 10^{-6} DALYs (27/43) and 10^{-4} risk of infections per year (23/43) (Table 11-3). Only point values or uniform distributions were used, with 30% of studies published after 2016 calculating both risk scenarios to better classify performance, which, although small, could be a trend. Interestingly, when more than one tolerable threshold is reported at the end of a QMRA, the model can have conflicting findings: the risk of infection may be under the appropriate threshold, while annual risk of infection or annual disease burden may not be (Beaudequin et al., 2017; Owusu-Ansah et al., 2017; Bergion et al., 2018; Amoueyan et al., 2019a). Such discrepancies can be addressed by using probabilities instead of point values, which would give better insight into how the system performs in relation to final risk. In this section, no alternative PDFs or values were tested and effect on final risk was not discussed.

4.3.4 Exposure

Exposure in potable reuse can occur by direct ingestion via drinking and in non-potable reuse via aerosols, incidental ingestion or crop consumption. High water intake via ingestion (drinking) was described using mainly lognormal but also normal, exponential and triangular distributions, in line with the WHO recommendation of using lognormal PDFs to describe daily consumption volumes (World Health Organization, 2016). Low unintentional water intake via aerosol and intentional consumption of

crops irrigated with reclaimed water was described by point values or a uniform PDF. It seems that high intake was modeled using skewed distributions (lognormal, exponential, triangular = more knowledge about predicted value), while low intake was modeled using uniform distributions or point values (less knowledge about predicted value), providing insight for future assessments. Considering all 3 distributions can be recommended. Studies neither tested alternative PDFs nor discussed effect on final risk.

As numerous guidelines controlling the quality of reclaimed water for agricultural reuse exist (World Health Organization, 2006; CDPH, 2014; EU Parliament, 2020), adhering to local guideline values is imperative. Studies undertaking a non-potable reuse assessment should additionally consider how far to model exposure – to farmers and field workers in industrialized vs. labor-intensive agricultural practices (Mara et al., 2007), to market workers selling irrigated vegetables, or to consumers eating lettuce-based salads (Owusu-Ansah et al., 2017) or other vegetables (Barker, 2013; Mok et al., 2014). Irrigation via restricted vs unrestricted scenarios also affects crop type the workers or consumers are exposed to (Mara et al., 2007). When enough data exists, a more comprehensive assessment depending on when harvest occurred in the life of the crop can be undertaken (Chandrasekaran and Jiang, 2018). Assessors should also consider how local consumption of crops could be different from WHO guideline values (Pavione et al., 2013; Verbyla et al., 2016).

4.3.5 Sensitivity analysis

Sensitivity analyses were conducted to determine the importance of a variable in most studies (32/43) (Figure 4-6). The importance is determined by the log of the ratio between the risk when one variable is excluded, and the risk when all variables are included. Studies use sensitivity analyses to estimate treatment barrier relevance and contribution (Page et al., 2010); to determine which variables contributed to the uncertainty (Chaudhry et al., 2017); to quantify the effect of pathogen concentrations in source water and dose-response models on final risk (Soller et al., 2017, 2018a); and to determine the impact of assumptions on daily per capita water consumption and different dose-response functions (Pecson et al., 2017). Out of these 32 studies, the majority (18/32) also evaluated alternative or mentioned alternative PDFs for treatment or dose-response (14/18).

Seven of the 32 studies further provided explicit factor sensitivity values, quantifying how much risk changed in the positive or negative direction in the absence of a specific variable. Another 13 of the 32 studies utilized the non-parametric Spearman rank order correlation, which defines a correlation between two variables to identify variables with the greatest influence on the uncertainty of the output, where high correlation indicates low uncertainty.

Relationships between variables in water reuse systems have also been described using various simulation and modeling approaches. Monte Carlo simulations are a class of computation algorithms for generating data from probability distributions, and a particularly useful way of assessing complicated risk scenarios with high inherent uncertainty. Latin Hypercube sampling and Markov Chain Monte Carlo methods are ways to sample the distributions generated in Monte Carlo methods if the PDF is parametrized (described by mean, standard deviation, etc.). Bayesian networks, which are directed acyclic graphs where variables, referred to as nodes and represented by PDFs, are causally connected to one another. Bayesian networks share some of the advantages of Monte Carlo simulations, such as the ability to express uncertainty using PDFs, but have additional benefits, as these networks can accommodate expert opinion/knowledge in addition to PDFs and are capable of immediately updating parameter values whenever new evidence is added into the network or a variable state is changed (Greiner et al. 2003; Jensen and Nielsen 2007). Drawbacks of Bayesian networks include absence of feedback loops and possibly large computational requirements as the inclusion of more variables causes networks to grow (Greiner et al., 2013).

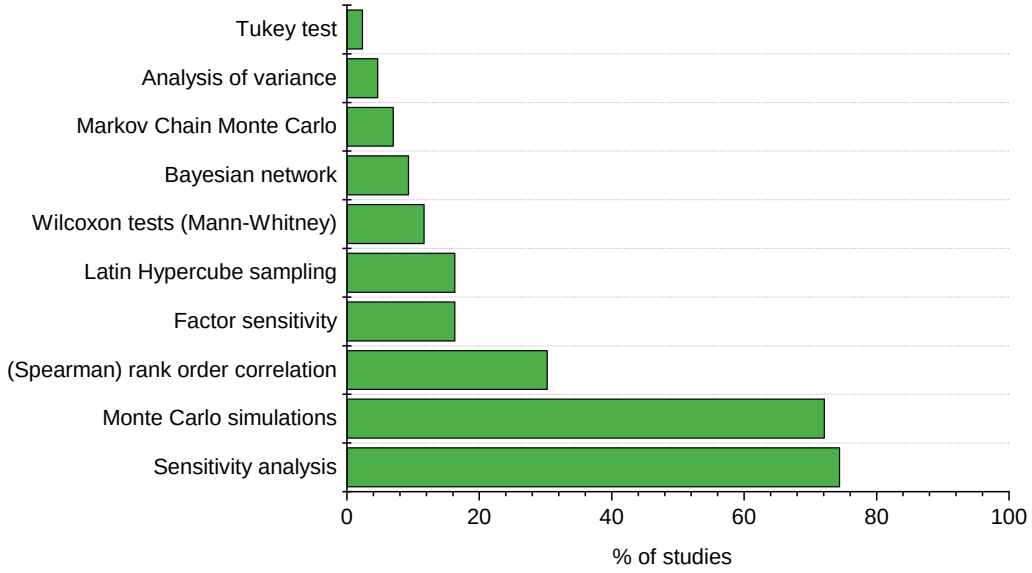

Figure 4-6: Approaches used by the studies for statistical modeling and sensitivity analysis. A 100% value on the x axis represents all 43 studies.

To determine whether results of different simulations were statistically significant, studies applied the Wilcoxon rank sum test, the Mann-Whitney-Wilcoxon non-parametric test, the analysis of variance, and Tukey's test (Barker et al., 2013; Verbyla et al., 2016; Soller et al., 2017). Further results are depicted in Table 11-4.

4.4 Conclusions

This review identified assumptions regarding whether distributions or point estimates were used in literature to characterize pathogen densities in raw wastewater, which distributions were used to describe pathogen removal of various wastewater and water reuse treatment steps, which distributions were used for dose-response models, and whether PDF choice affected final risk. The following key findings were revealed:

- The benefit of moving towards PDFs for describing concentration or LRV allows a more comprehensive assessment of final risk and a more nuanced inclusion of risks from failure events in potable and non-potable reuse scenarios.
- Pathogen concentrations in raw wastewater were described by lognormal PDFs and point values, in treated wastewater by point values, and in *de facto* source water by lognormal, uniform and gamma PDFs. Where a stochastic approach is desired for characterizing concentrations, uniform or triangular distributions can be fit to point value data, depending on the scale of the QMRA (site-specific vs. generalized risk) and whether a central tendency exists to employ the triangular distribution.
- Pathogen removal in wastewater treatment was most often described by point values and uniform distributions, and in advanced and drinking water treatment by point values and uniform and lognormal distributions. Treatment steps with the least LRV information were MAR, BAC, BAF, ESB, GAC, MBR, NF, and RSF. More data on pathogen removal is necessary for treatment trains which aim to include these steps. Most treatment steps were characterized by the same LRVs, regardless of whether PDFs or point estimates were used to describe removal. Assessors should therefore consider utilizing triangular distributions to better describe uncertainty and variability in the removal, in accordance with the discussion in the above bullet point.

- QMRA studies on MAR systems were few in number, highlighting the need for more assessments and a discussion on how many LRVs MAR systems should be credited with. Studies are already using triangular distributions for LRVs, and should continue to do so.
- While choice of dose-response model should be selected after consulting guidelines and databases (Haas et al., 2014; World Health Organization, 2016; CAMRA, 2020), testing multiple models can increase the resolution of final risk. Particularly for the high-risk end of the scale, as well as from a failure/hazardous event standpoint, testing different dose-response models should be done when the choice of PDF is insufficiently supported by literature, or when a sensitivity analysis reveals that PDF choice is a critical factor for final risk.
- Alternative PDFs for pathogen removal in treatment or different dose-response models were tested in 16/43 studies, with an additional 7 studies mentioning alternate PDFs. Of these 16, only 12 explicitly discussed the effect of PDF selection on final risk. Discussing this is recommended for all studies in the future as a detailed assessment of this will not only improve the reliability of the study, but also inform future studies conducted on similar treatment trains.
- Regardless of country of origin, calculating both risk levels (DALYs and annual risk of infection) is worthwhile to determine how the treatment train performs.
- Sensitivity analyses were used in 32/43 studies to determine which components in the treatment train exert the greatest influence on final risk, with most of the 32 studies also evaluating alternate PDFs or models. Identifying how assumptions affect final risk has been identified as incredibly important in guidelines (World Health Organization, 2016) and should become a standard part of future QMRA studies.
- An open source database for source water concentrations, and concentrations or LRVs for treatment steps (such as the information embedded in the Aquanes QMRA tool or QMRAspot (AquaNES, 2016a; RIVM, 2016)) would facilitate equal access to information for future QMRA studies. Facilities equipped with the ability to sample advanced treatment systems at high resolution (Smeets, 2008; Pecson et al., 2017) could upload their (anonymized) normal and event-monitoring data to allow new QMRA studies to access more comprehensive concentration information. The same anonymization and uploading of data could be done for MAR systems, which also likely have years' worth of logged data (Dillon et al., 2019; Donn et al., 2020). While this review focused on data presented in peer-reviewed articles, a notable amount of QMRA studies have not been published in journals, and data sits in institutional, project or agency reports, such as the notable amount of data in Salveson et al., (2018) not published in Soller et al. (2017, 2018a). Data used for such studies could also be anonymized and included in QMRA-source databases.

In addition to the aforementioned conclusions, future studies could also consider additional parameters, including how failure and hazardous events impact final risk and PDF selection; which surrogates are most informative for which pathogen(s) and treatment process combinations; conducting event monitoring sampling; and in what state pathogens are present in effluents (i.e., infectious vs dormant, independent or sorbed/embedded, etc.). This will improve the assessment of risk in water reuse systems as more treatment trains will come online in the coming years.

Competing Interests

The authors declare no competing interests.

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In conclusion, the frequency of PDFs and LRVs used for describing pathogen presence, removal and dose-response models informed the PDFs chosen for the QMRA conducted in chapter 5.

5. Quantitative microbial risk assessment of a non-membrane based indirect potable water reuse system using Bayesian networks

This chapter has been published with editorial changes as follows:

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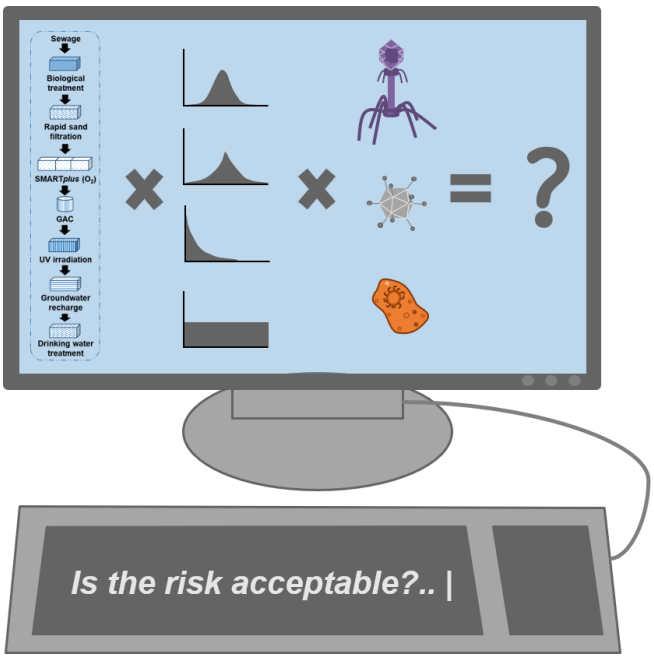
Abstract

Risk-based approaches are used to define performance standards for water and wastewater treatment to meet health-based targets and to ensure safe and reliable water quality for desired end use. In this study, a screening level QMRA for a non-membrane based indirect potable reuse (IPR) system utilizing the sequential managed aquifer recharge technology (SMART) concept was conducted. Ambient removals of norovirus, Campylobacter and Cryptosporidium in advanced water treatment (AWT) steps were combined in a probabilistic QMRA utilizing Bayesian networks constructed in Netica. Results revealed that all pathogens complied with disease burden at the 95th percentile, and according to the assumptions taken about pathogen removal, Cryptosporidium was the pathogen with the greatest risk. Through systematic sensitivity analysis, targeted scenario analysis, and backwards inferencing, critical control points for each pathogen were determined, demonstrating the usefulness of Bayesian networks as a diagnostic tool in quantifying risk of water reuse treatment scenarios.



Chapter 5: Quantitative microbial risk assessment of a non-membrane based indirect potable water reuse system using Bayesian networks

5.1 Introduction

Potable reuse has become a more viable option to combat water shortages as an increasing number of projects consistently produce appropriate water qualities (US EPA, 2017; World Health Organization, 2017a). These can be achieved through applying advanced treatment after conventional wastewater treatment by using combinations of oxidative, adsorptive, biological, or physical processes. Potable reuse can be either indirect or direct. In indirect potable reuse (IPR), advanced treated water is introduced into a groundwater aquifer or surface reservoir, where it undergoes further natural transformation processes before abstraction and use as raw water for drinking water treatment (DWT) plants. In direct potable reuse (DPR), advanced treated water is either directly fed into the raw water supply of a DWTP or into the distribution system, where it might be blended with other water sources (World Health Organization, 2017a). Potable reuse is now practiced on nearly every continent and many of these projects favor membrane-based treatment trains (Tang et al., 2018): Europe (Van Houtte and Verbauwhede, 2013), Africa (Ander and Forss, 2011; Khan, 2013; Lahnsteiner et al., 2018), Asia (Ghernaout et al., 2019), Australia (Radcliffe and Page, 2020), and North America (US EPA, 2017).

To reduce energy costs and brine disposal, in particular for inland applications, research groups have begun to explore alternative non-membrane-based treatment systems. Managed aquifer recharge (MAR) has been identified as a multi-objective treatment process, where a combination of different attenuation mechanisms (i.e., biodegradation, sorption, filtration, dilution, die-off) significantly improves the microbiological and chemical quality of the infiltrated water (Regnery et al., 2017a). MAR systems can be optimized by controlling key operational factors such as redox conditions and carbon concentrations in the subsurface, which determine the primarily biological removal efficiency of chemicals and pathogens (Hellauer et al., 2018; Regnery et al., 2017b, 2016; Zhang et al., 2019). Modified engineered biofiltration systems have shown that establishing controlled redox and carbon conditions can be achieved at a much smaller footprint than in conventional MAR systems (Müller et al., 2017). Another engineered solution, the sequential managed aquifer recharge technology (SMART), combines two infiltration systems with intermediate aeration (Hellauer et al., 2018, 2017; Regnery et al., 2016). This was further improved in the SMART*plus* concept, which utilizes high-rate trench infiltration technology and *in situ* oxygen injection through gas-permeable membranes to optimize flow, carbon concentrations and redox conditions for efficient removal of chemicals and pathogens during short travel times (Karakurt-Fischer et al., 2020b). Combining SMART*plus* with subsequent adsorptive or oxidative processes could potentially provide a reliable IPR treatment train at significantly lower energy demand than membrane based systems.

To consistently meeting stringent water quality requirements, preparing Water Safety Plans (WSP) can be used to identify health-based targets, ensure proper surveillance, and determine critical control points (CCP) (World Health Organization, 2017b). Proposed treatment trains can undergo a screening level risk analysis prior to construction, and validation and monitoring after commissioning. One tool used to determine whether health-based targets are met is quantitative microbial risk assessment (QMRA). QMRA is a probabilistic evaluation of the pathogens present at each treatment step, coupled with exposure scenarios and dose-response models, for an ultimate characterization of the risk from exposure to the treated water. This information can be used to analyze the efficacy of a treatment train, as well as to characterize how much the variability and uncertainty of individual treatment steps contribute to overall uncertainty in final water quality, and is particularly useful in the selection and design of multi-barrier reuse approaches. QMRA can be used as part of a WSP and considers local information when quantifying tolerable health burden in terms of disability adjusted life years (DALYs) (World Health Organization, 2016). Screening level QMRAs can evaluate whether a treatment train will be able to reach the health-based target before operation commences. However, a large amount of data is needed for QMRA, which can be difficult, time intensive, and cost-prohibitive to obtain. In these cases, different

statistical approaches, such as Bayesian networks (BNs), have been proposed to address the variability associated with environmental datasets and attempt to combat the lack of data.

BNs provide intuitive management of uncertainty and variability when assessing the risk of system and identifying management strategies (Beaudequin et al., 2016). They are probabilistic graphical models represented as directed acyclic graphs, where direct dependence relationships between variables (nodes) are represented by directed arcs connecting parent and child nodes (Scutari and Denis, 2015). Bayes theorem, the underlying equation behind BNs, allows the estimation of a likelihood of a certain outcome. BNs can be modeled in a probabilistic or a deterministic fashion, with nodes including two or more mutually exclusive states or values, and the reasoning or inference is conducted in the same or opposite direction to the causal arcs or links (depending on the type of inference) (Uusitalo, 2007). Nodes can be discretized using expert knowledge or numerical approaches to set meaningful thresholds relevant for removal verification. Three main types of inferences can be found in BNs, namely causal, diagnostic and intercausal reasoning. In causal reasoning, the information follows the direction of the arcs, whereas in diagnostic reasoning information flows against the direction of the arcs. Intercausal reasoning is also called the 'explaining away effect' and allows inference between competing hypotheses or causes of a common effect (Kjaerulff and Madsen, 2008). Such features are particularly useful when discussing risk scenarios and identifying CCPs. Likewise, since nodes are expressed as probability distributions, BNs are exceptionally suited to quantifying uncertainty, which is especially helpful when assessing risk in a water reuse system. However, BN usage in QMRAs has not been widely explored, with only individual applications in potable reuse practices (Beaudequin et al., 2017, 2016, 2015; Verbyla et al., 2016). More standard approaches for generating samples from probability distributions include Monte Carlo or Latin Hypercube simulations (Zhiteneva et al., 2020a). The lack of BNs in published QMRAs could stem either from the difficulty of integrating mathematical equations in a network which includes joint probability distributions of all nodes, or from resolution of the results, because of the exponential growth of the parameters required when many variable states are used. If a large network is constructed with many parameters, the size and processing time is large, a problem not experienced in Monte Carlo simulations. However, the benefits of using BNs in QMRAs warrant further exploration and utilization.

The aim of this study is to assess the operational feasibility of the newly developed SMARTplus concept as a key process of a non-membrane based IPR treatment train used for subsequent drinking water production. For this purpose, a screening level Bayesian network QMRA for key pathogens using a combination of literature and empirical data was conducted.

5.2 Methods

5.2.1 Treatment train of interest

The proposed IPR treatment train is comprised of advanced biological, chemical and physical processes providing a multi-barrier treatment approach for microbial and chemical contaminants (Figure 5-1). The starting point was pathogen concentrations in raw sewage, after which a biological wastewater treatment plant (WWTP) was modeled as a conventional activated sludge treatment plant with primary (mechanical) and secondary (biological) treatment for carbon, nitrogen and phosphorus removal. Further turbidity removal occurred during tertiary treatment comprised of rapid sand filtration (RSF). The SMART*plus* treatment step, a technical sand biofilter operated at a 0.58 m/h effective velocity and a hydraulic residence time of 12-13 h, provided 2.2-3.1 ambient log reduction of viruses and phages (Karakurt-Fischer et al., 2021). The SMART*plus* effluent was then fed to a granular activated carbon (GAC) filter contributing to chemical removal. However, as removal of viruses and protozoa in a GAC adsorber is rather low (Smeets et al., 2006), the GAC filter was omitted from the modeling. Subsequent ultraviolet (UV) irradiation at 180 mJ/cm^2 served as an additional pathogen inactivation barrier. Next, the advanced treated effluent was injected into a sandy aquifer with an assumed subsurface residence

time between 50 and 120 days. Finally, the abstracted water was subject to conventional drinking water treatment via aeration followed by dual media filtration (sand and anthracite) for iron and manganese removal. Given the long residence time in the subsurface, no additional post-treatment disinfection was considered.

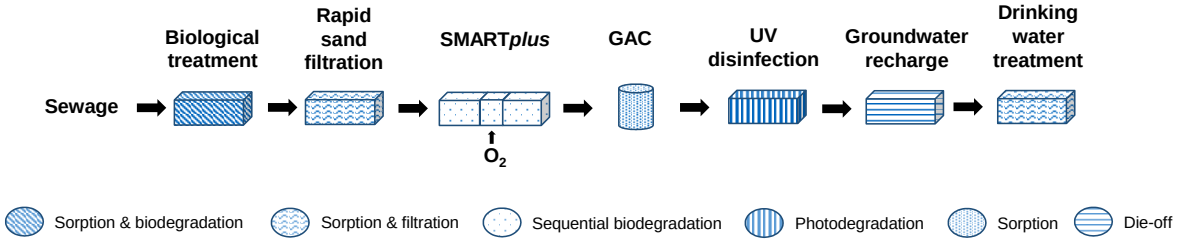


Figure 5-1: Investigated IPR treatment train employing sequential managed aquifer recharge technology followed by GAC filtration and UV disinfection prior to groundwater recharge.

5.2.2 Risk assessment

5.2.2.1 **Hazard identification**

Pathogens of interest in this study were norovirus (virus), *Cryptosporidum* spp. (protozoa) and *Campylobacter* (bacteria), which are recommended by the WHO when assessing potable reuse systems (World Health Organization, 2017a). All three pathogens cause gastroenteritis, warranting them relevant reference pathogens for assessing human risk (NRMMC–EPHC–AHMC, 2006). Although the WHO Guidelines for Drinking-water quality list rotavirus as the reference pathogen (World Health Organization, 2017b), the imminent development of a rotavirus vaccine, in addition to the fact that nearly 20% of acute diarrheal diseases worldwide are caused by norovirus, led the WHO to select norovirus as the reference virus in their potable reuse guidelines (World Health Organization, 2017a). Therefore, norovirus was evaluated in the present study.

5.2.2.2 **Determining source water concentrations and removal efficiencies**

As the proposed IPR treatment train was not yet operational at full scale, literature values for distributions and point values of each pathogen concentration in raw sewage, as well as ambient removal in each treatment step, were collected. Studies describing concentrations and removals were obtained by searching for the three aforementioned pathogens in water reuse studies in Scopus. Log reduction values (LRVs) and probability distribution functions (PDFs) from literature were compiled for similar operating conditions of the targeted individual processes to determine which distribution or point value best described performance. When numerous distributions were available, studies or guidelines whose operational parameters most closely matched the desired operational parameters of the current train were selected. Uniform distributions were applied to studies reporting minimum/maximum LRVs.

Only ambient pathogen concentrations studies were used in this analysis, as the focus was on observed removal, not treatment validation. This resulted in very conservative risk assessment, particularly in treatment steps where removal is biologically dominated.

5.2.2.3 **Health effects assessment**

Dose-response models were also obtained from literature. As noted in Zhiteneva et al., 2020a, dose-response model choice can noticeably affect the final risk, therefore two dose-response models were

assessed for each pathogen (Table 5-1). Reasoning for dose-response model selection can be found in the Supplementary Information (SI) (section 11.3).

Table 5-1: Dose-response models tested in this study.

	Model	Equation	Parameters	Source
Norovirus	Approximate beta Poisson (BP)	$P_{inf} = 1 - \left[1 + \left\{\frac{\text{dose}}{\beta}\right\}\right]^{-\alpha}$	α =0.104 β = 32.3	Van Abel et al. (2017)
	Fractional Poisson	$P_{inf} = P * (1 - e^{-\frac{d}{\mu}})$	P = 0.722 μ = 1106	Messner et al. (2014)
Cryptosporidium	Fractional Poisson	$P_{inf} = P(1 - e^{-D})$	P = 0.737	Messner and Berger (2016)
	Exponential	$P_{inf} = \mathrm{P}(1 - e^{-r*D})$	P = 0.737 r = 0.0022	
Campylobacter	Approximate BP	$P_{inf} = 1 - \left(1 + \frac{N}{\beta}\right)^{-\alpha}$	α = 0.145 β = 7.59	Medema et al. (1996), World Health Organization (2016)
	Exact BP		α = 0.024 β = 0.011	Teunis et al. (2005), World Health Organization (2016)

5.2.2.4 Exposure assessment

Exposure to pathogens in drinking water varies widely and often represents the greatest source of uncertainty in risk assessments (Haas et al., 2014). Intake via drinking is generally modeled using lognormal distributions (Åström et al., 2007; Barker et al., 2013; Sato et al., 2013; Chaudhry et al., 2017; Pecson et al., 2017). WHO guidelines recommend lognormal PDFs for describing daily high consumption (World Health Organization, 2016), which was the distribution taken for this study (μ = 0.65, σ = 0.53).

5.2.2.5 Risk characterization

The pathogen dose at the point of exposure D was calculated using Equation 5-1:

$$\mathrm{D} = \mathrm{C_{DWT}} * \mathrm{V} \qquad \textit{Equation 5-1}$$

where C_{DWT} is the pathogen concentration after the final drinking water treatment step and V is the volume in liters ingested by an individual. The daily risk of infection P_{inf} was estimated using the dose-response relationships identified for each pathogen.

The annual risk of infection $P_{\mathrm{inf}(ann)}$ was calculated using Equation 5-2 (World Health Organization, 2016), assuming that the consumers ingest only drinking water that has been augmented by reclaimed water and are thus exposed to the risk all year long.

$$\mathrm{P}_{inf(\mathrm{ann})} = 1 - (1 - \mathrm{P}_{\mathrm{inf}})^{365} \qquad \textit{Equation 5-2}$$

The annual risk of illness $P_{\mathrm{ill}(ann)}$ was modeled using Equation 5-3 (World Health Organization, 2016):

$$\mathrm{P}_{ill(\mathrm{ann})} = \mathrm{P}_{inf(\mathrm{ann})}\mathrm{R}_{\mathrm{ill|inf}} \qquad \textit{Equation 5-3}$$

where $R_{ill|inf}$ is the probability of illness given an infection. Finally, the annual disease burden of illness of each pathogen, DB_{ann}, expressed as DALYs per person and year, was modeled using Equation 5-4 (World Health Organization, 2016):

$$\mathrm{DB_{ann}} = \mathrm{DB_{case}}\ \mathrm{P_{ill(ann)}} \qquad \textit{Equation 5-4}$$

where DB_{case} is the pathogen specific disease burden per case of illness. In this study, the entire population was assumed to be susceptible.

5.2.3 Bayesian network construction and validation

The BN model (Figure 5-2) was constructed in Netica 6.07 (Norsys Software Corp, 2019), and comprised a number of variables including the type of pathogen to be analyzed, inlet and outlet concentrations of pathogens, treatment step LRVs, exposures, dose-response outcomes and risks. Netica allows higher resolution analytical and statistical evaluation of the network due to the much greater bin capacity than in Beaudequin et al. (2015b), which used GeNIe (BayesFusion) . Beaudequin et al. (2015b) employed a QMRA model in which 2-4 states were used, which did not display any numerical outputs and only provided information on the probabilities associated with each state. In contrast, Netica features a numerical output on its graphical interface, allowing the user to visualize statistics such as means, standard deviations, and 95th percentiles. Another advantage of Netica is the possibility of selecting a range of values as evidence instead of single states. In this paper, most child nodes were an algebraic transformation of one or more parent nodes: for example, outlet concentration for a particular treatment step was computed from the inlet concentration and the LRV of that step. Parentless nodes were defined using their individual distributions. A screenshot of the model is provided in Figure 11-5.

The model included an easy option to assess failure of each treatment step (i.e., 0 LRVs) by using selector nodes. Additionally, a second identical model with a common factor was built, which presented a rank correlation of 0.5 between the common factor and the LRV nodes. The idea behind this modification was to assess whether the performance dependency between the barriers would increase or reduce the final risk. The common factor allowed simulation of scenarios where the LRV nodes (WWTP, RSF, SMART*plus*, UV, MAR and DWT) were conditionally correlated, meaning the performance of one LRV node would be correlated by a factor of 0.5 to the other LRV nodes. Haas et al. (2014) indicated that correlations should be considered when modeling risks, and that the existence of correlations between variables will have an impact on the outcomes derived from such variables. Since the impact usually becomes more important at the extremes of the distribution, Haas et al. (2014) presented copulas as a useful methodology to simulate such conditions. The correlation factor was modeled via rank correlation, using normal copulas to define the dependence between the common factor and the correlated LRV nodes, and was incorporated into the model using Uninet (LightTwist Software, 2019). Uninet supports continuous, discrete and function nodes using non-parametric conditional correlations (i.e. conditional rank correlations) to capture dependencies between the variables. For the LRV nodes, data obtained from Uninet was also used when learning the parameters in Netica. Unlike the model without the common factor, in which the parameters were learned only from equations, the parameters were obtained both from equations and the Uninet data in the model with the common factor. A simplified illustration of how the common factor influences the Netica model is depicted in Figure 5-2.

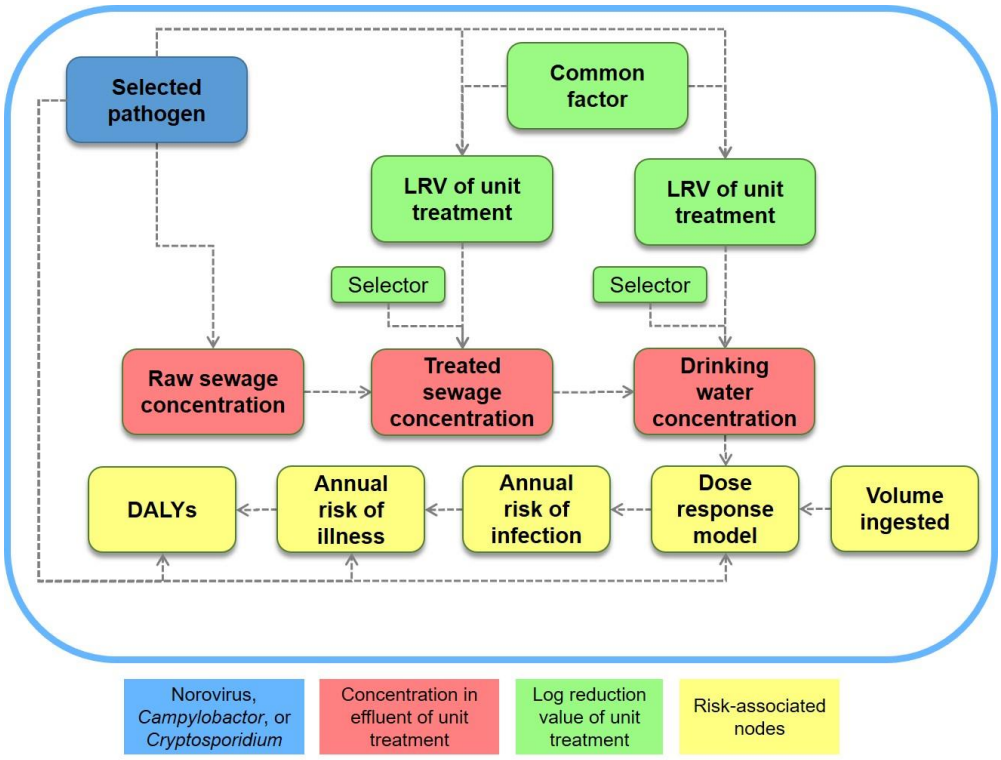


Figure 5-2: Simplified information flow within the common factor Netica model (not all LRV nodes shown).

Both models were built by evaluating the equations of the network 1,000 times for each combination of parent states without including uncertainty. To obtain numeric data from the nodes, the model was sampled 10,000 times, which allowed precise generation of the marginal distributions from one or more target nodes. Although Monte Carlo simulations are more suitable for forward prediction due to the continuous nature of distributions used, the benefits of a BN lie in the graphical representation, the large amount of data that can be represented, and the possibility of forward and backward inference, which is particularly useful for determining CCPs and evaluating how unit treatment processes react under particular risk scenarios. Although some model information is likely lost when discretizing continuous distributions, a BN is more suitable for diagnostic inference.

The models presented in this study were constructed following best QMRA modeling practices and their parameters were obtained from relevant published literature. Model validity was verified during the different steps of the model construction including model structure, model discretization, model parameterization and model behavior. Structure was based on the generic mathematical procedure to calculate microbial risks through a QMRA framework (World Health Organization, 2016). Because every node featured an equation, the inputs of such equations dictated the connections from parent nodes. Nodes were discretized using Netica's discretization tool for fixed and logarithmic divisions. Monte Carlo simulations (n = 10,000) of the same models were conducted in the mc2d package in R (R Core Team, 2019) to visually compare the BN results of the cumulative distribution function of the disease burden outcome (Figure 11-4). Model parameters were obtained from the equations defined in section 5.2.2 through the sampling procedure performed by Netica. Model behavior was tested through sensitivity analysis, which allowed all associations between variables to be evaluated for accuracy: for example, increasing the ingested volume of water should increase final risk.

5.2.4 Evaluation methods and scenario analysis

A sensitivity analysis was conducted to determine which nodes exerted the most influence on final risk and could be considered potential CCPs. The sensitivity analysis was performed by evaluating the change in the 95th percentile values of the DALYs node under minimum and maximum values of the tested node (i.e., raw sewage concentration, WWTP LRV, RSF LRV, SMART*plus* LRV, UV LRV, MAR LRV, DWT LRV, volume ingested, norovirus distribution and common factor nodes) and visualized in a tornado plot. Unless otherwise noted, all numerical results reported in this paper describe the 95th percentile value, which is a conservative value to assess when considering the uncertainty of using literature data for specific treatment trains (World Health Organization, 2016) . Finally, numerous scenarios were tested to evaluate the reaction of the model: 1) a high pathogen loading event; 2) SMART*plus* performance failure; 3) MAR failure; 4) experimental norovirus removal; and 5) the effect of the common factor. Additionally, a backwards inferencing exercise was conducted to determine where the likelihood of failure of the treatment scenario is located.

5.3 Results and Discussion

Numerous guidelines, peer-reviewed papers, and grey literature were consulted when deciding upon PDFs. Quite often the most reliable assumption came from guideline values (Table 5-2). Extended reasoning for PDF selection can be found in the SI (11.3.1).

Table 5-2: Distributions used for pathogen concentrations or presence in the evaluated treatment steps.

Pathogen	Treatment step (units of LRV, unless otherwise noted)	Distribution & parameters	Source
Campylobacter	Raw sewage (colony forming units (CFU)/L)	Triangular (min 10, mode 7,000, max 10^5)	Beaudequin et al. (2017), World Health Organization (2017b)
	Secondary treatment	Triangular (min 0.6, mode 2, max 3.5)	Ayuso-Gabella et al. (2011)
	Rapid sand filtration	Uniform (0.6, 2.8)	Mohammed and Seidu (2019)
	SMART*plus*	Uniform (2, 6)	World Health Organization (2017a)
	UV irradiation	Uniform (4, 6)	World Health Organization (2017a)
	Subsurface removal (log_{10} d^{-1})	Triangular (min 0.02, mode 0.08, max 1.5)	Ayuso-Gabella et al. (2011)
	Dual media filtration	Uniform (0, 1)	NRMMC-EPHC-NHMR (2008)
	Infection: illness ratio	0.3	NRMMC-EPHC-AHMC (2006), World Health Organization (2016, 2017a)
	Disease burden	4.6 x 10^{-3} DALYs per case	
Cryptosporidium	Raw sewage (oocysts/L)	Triangular (min 0, mode 2,700, max 10^6)	Beaudequin et al. (2017), World Health Organization (2017b)
	Secondary treatment	Triangular (min 0.5, mode 1, max 1.4)	Ayuso-Gabella et al. (2011)

	Rapid sand filtration	Triangular (min 0, mode 2, max 3.1)	Smeets et al. (2006)
	SMART*plus*	Uniform (0.3, 6)	World Health Organization (2017a)
	UV irradiation	Uniform (4, 6)	World Health Organization (2017a, 2017b)
	Subsurface removal (log_{10} d^{-1})	Uniform (0.025,0.082)	Toze et al. (2010)
	Dual media filtration	Uniform (1.5, 2.5)	NRMMC-EPHC-NHMR (2008)
	Infection: illness ratio	0.7	NRMMC-EPHC-AHMC (2006), World Health Organization (2016, 2017b)
	Disease burden	1.5 x 10^{-3} DALYs per case	
Norovirus	Raw sewage (units/L)	Triangular (min 0, mode 20,000, max 10^6)	Adapted from World Health Organization (2017b)
	Secondary treatment	Uniform (0.5, 2)	Karakurt-Fischer et. al. (2021)
	Rapid sand filtration	Uniform (0.06, 0.3)	
	SMART*plus*	Uniform (2.2, 3.0)	
	UV irradiation	Uniform (3.9, 4)	World Health Organization (2017a)
	Subsurface removal (log_{10} d^{-1})	Uniform (0.093, 0.174) (MS2 removal)	Regnery et al. (2017a)
	Dual media filtration	Uniform (0.5, 2)	NRMMC-EPHC-NHMR (2008)
	Infection: illness ratio	0.67	(Atmar et al., 2013)
	Disease burden	Uniform (3.71 x 10^{-4}, 6.23 x 10^{-3} DALYs)	Barker et al. (2013), Mok et al., (2014)
Volume ingested	Liters (natural log)	Lognormal (0.65, 0.53)	World Health Organization (2017b)
Residence time	Subsurface (d)	115-120	Expert opinion
Tolerable DALYs	$\leq 10^{-6}$	Threshold value	World Health Organization (2016)

5.3.1 Stochastic sampling of dose-response model scenarios

Two dose-response models per pathogen were tested to determine how model choice affected final risk, with the more conservative dose-response model predicting the closest risk to 10^{-6} DALYs (approximate beta Poisson for norovirus, fractional Poisson for *Cryptosporidium*, and exact beta Poisson for *Campylobacter*) chosen for further analysis. The cumulative distribution functions of the chosen models (with and without the common factor) are displayed in Figure 5-3, which shows that all pathogens comply with the DALYs threshold at the 95th percentile. The common factor was modeled to observe how the model would react if barriers were not independent, and although DALYs for all pathogens increased by 0.6-3.5 logs (1.5 log for *Cryptosporidium* and 3.5 for *Campylobacter*), they were still under the 10^{-6} threshold.

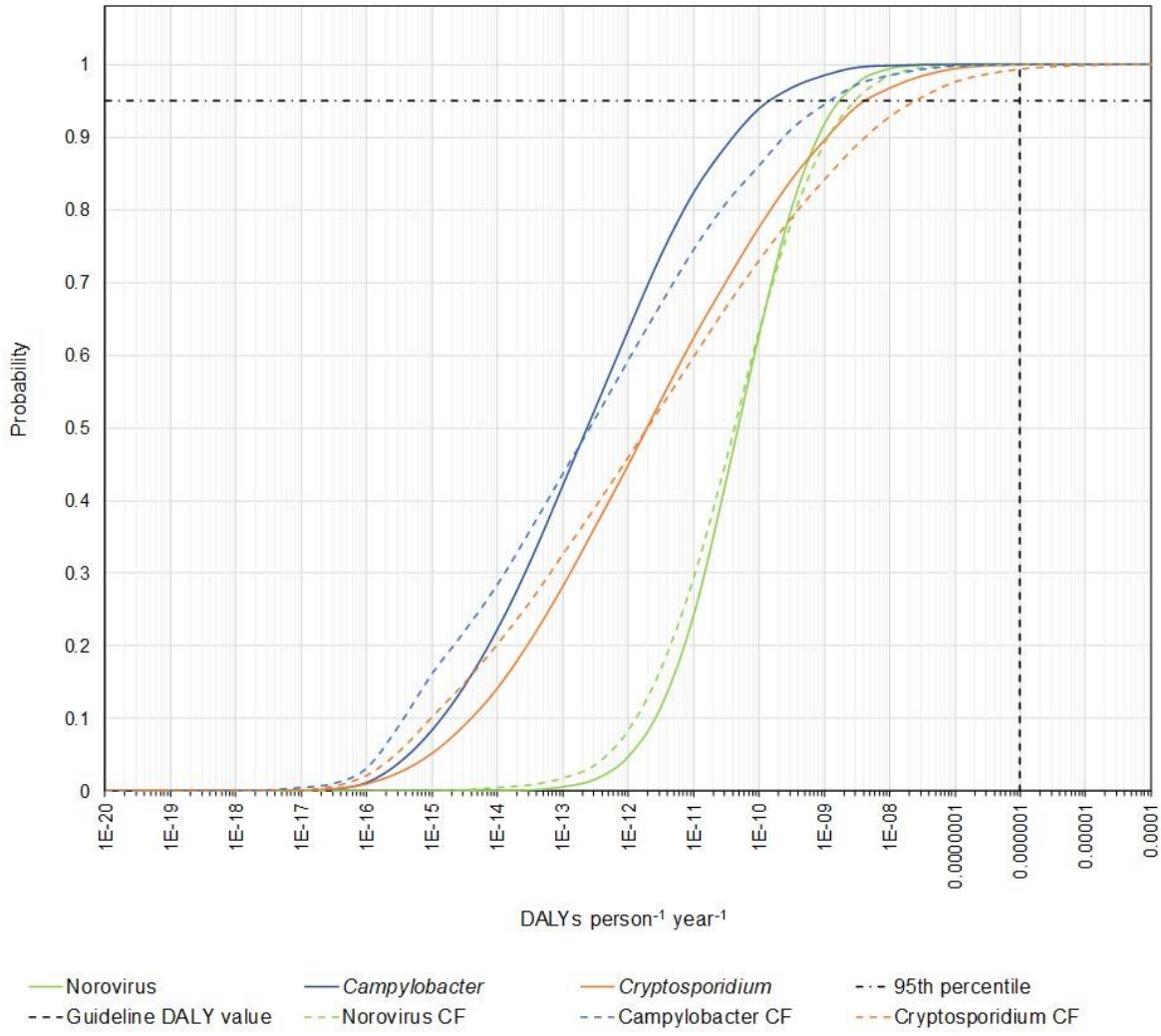


Figure 5-3: Cumulative distribution functions (CDFs) of DALYs achieved using the approximate beta Poisson for norovirus, the fractional Poisson for Cryptosporidium, and the exact beta Poisson for Campylobacter. Solid colored lines denote the results for the models without a common factor (CF), whereas dashed colored lines denote the results for the models with a CF.

However, maximum *Cryptosporidium* DALYs exceeded the 10^{-6} DALYs threshold, and in the model with the common factor node, maximum DALYs for all pathogens exceeded the threshold. This can be explained by the common factor affecting the associations between the unit treatment barriers by causing higher probabilities of exceedance at larger DALYs when compared to the model without a common factor.

Unlike previous studies assessing pathogenic risk in IPR systems , the pathogen of importance for this treatment train was deemed to be *Cryptosporidium* instead of viruses, which can be attributed to the broad LRV range for the SMART*plus* process (see Table 5-2 and SI). Prior QMRAs conducted on IPR systems without microfiltration or reverse osmosis also found that greatest disease burden or annual risk of infection (ARI) came from *Cryptosporidium* (Ayuso-Gabella et al., 2011; Soller et al., 2018a, 2017). The treatment trains investigated in Ayuso-Gabella et al. (2011) featured secondary treated effluent introduced via injection, recharge basin, or riverbank filtration into unconfined karstic or sandy aquifers, which was then either directly used for crop irrigation (Nardo, 20-25 days subsurface residence time), was treated with Cl_2 prior to crop irrigation (Shafdan, 270 days subsurface residence time), or underwent

UV and Cl_2 disinfection, rapid sand filtration and was then used for urban landscape and crop irrigation (Sabadell, ~7 days subsurface residence time). Despite describing *Cryptosporidium* removal using lower decay rates than in the current paper, protozoan risk was greater than viral risk for Sabadell and Shafdan, and though the median disease burden complied with the 10^{-6} DALYs, greater percentiles clearly above this threshold were not discussed (Ayuso-Gabella et al., 2011). This demonstrates a bias in selecting thresholds when reporting disease burden. Risk is perhaps more intuitively understood by using boxplots such as those in Figure 5-4 describing the cumulative LRVs of the treatment train.

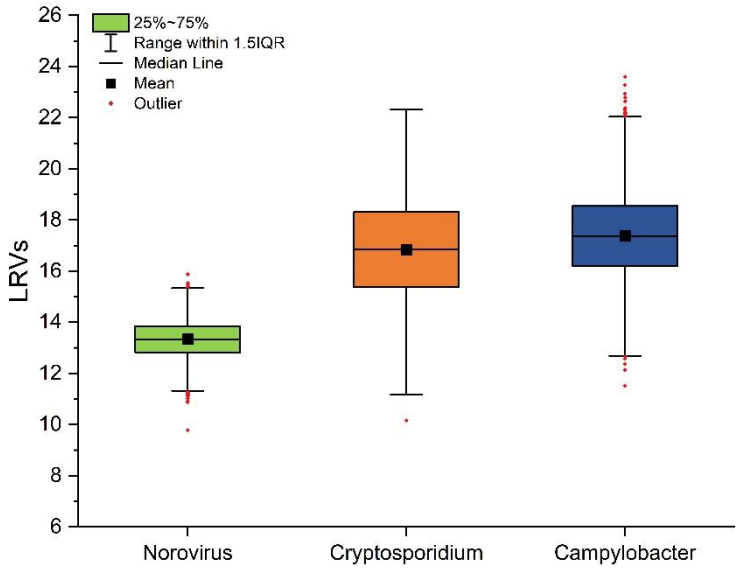


Figure 5-4: Box plots of LRVs for the proposed overall treatment train (n=10,000).

The treatment trains investigated in Soller et al. (2017, 2018a) included secondary effluent followed by ozonation, biologically active filtration, ultrafiltration, UV irradiation, an engineered storage buffer, and Cl_2 disinfection. The train was assessed with LRVs obtained from literature review as well as with regulatory LRVs obtained from Olivieri et al. (2016), demonstrating that predicted risk was substantially higher when using regulatory LRVs (Soller et al., 2018a). Furthermore, after updating the same treatment train investigated in Soller et al. (2017) with the latest dose-response models, raw wastewater pathogen densities, and treatment LRVs from literature, Soller et al. (2018a) observed that not only would the 12/10/10 LRVs required in California for viruses and protozoa no longer meet the 10^{-4} ARI threshold, but that depending on which final risk percentile was reported (i.e. 50^{th} vs 95^{th} vs maximum), the LRVs required to meet the 10^{-4} threshold varied. While differences between the health burden thresholds (10^{-4} ARI vs 10^{-6} DALYs) can be addressed by describing the uncertainty through the use of PDFs, a broader discussion within the water reuse and public health sector is needed to determine which percentile should comply: should the maximum value, i.e., the most conservative estimate, comply or is compliance of the 90^{th} or 95^{th} percentile sufficient?

Another important discussion relates to the LRVs credited to MAR by various guidelines. California regulations require that if 100% of water introduced into the subsurface is disinfected tertiary treated wastewater or advanced treated water and if the underground storage time is at least 6 months (180 days), then subsurface treatment can be credited with 10 LRVs for *Cryptosporidium* and *Giardia* (CDPH, 2014). The regulations also require at least three independent processes in the treatment train to each achieve at least 1 LRV (CDPH, 2014). The Australian guidelines credit a maximum of 6 LRVs to engineered treatment systems as a conservative approach to human health protection (NRMMC-

EPHC–NHMRC, 2009). In this study, MAR LRVs were capped at 4 logs due to the assumed subsurface residence time of no greater than 120 days (Regnery et al., 2017a). However, research has demonstrated that subsurface treatment is capable of more than 6 log removal of pathogens. Findings from field studies of bacteriophage or virus infiltration show that up to 8 LRVs have been achieved over a distance of 30 m in about 25 days, and 3-8 LRVs were obtained over distances between 2.4 and 100 m (National Research Council, 2012). Toze et al. (2010) showed a near linear decay for bacteria in MAR, resulting in complete removal within 10 days. The same study described a broken stick model for *Cryptosporidium* decay which resulted in faster protozoa removal than virus removal (Toze et al., 2010). Therefore, site-specificity of MAR removal can be underestimated when maximum removal is capped. If risk assessments should incorporate the most recent peer-reviewed research on raw wastewater pathogen densities and site-specific removals in QMRAs, the guidelines could also be updated and instead of limiting maximum LRVs, provide minimum LRVs along with detailed methods for determining removal on a site-specific basis (Rauch-Williams et al., 2021).

5.3.2 Sensitivity to findings

A sensitivity analysis, demonstrated for *Cryptosporidium* in Figure 5-5, was conducted to identify which parameters were most influential on final risk by observing the changes in the 95th percentile DALYs to the full range of the preceding nodes. The plot colors demonstrate the association between the assessed node and the target, i.e., whether the node change directly or inversely affected the DALYs. This revealed that norovirus was most sensitive to WWTP, SMART*plus* and DWT, *Cryptosporidium* was most sensitive to RSF, SMART*plus* and MAR (Figure 5-5), and *Campylobacter* was most sensitive to WWTP, SMART*plus* and MAR. The DALYs range calculated from the range of each unit treatment can be explained by the distributions used in the networks and listed in Table 5-2, but the order of nodes signifies the importance affected on the DALYs.

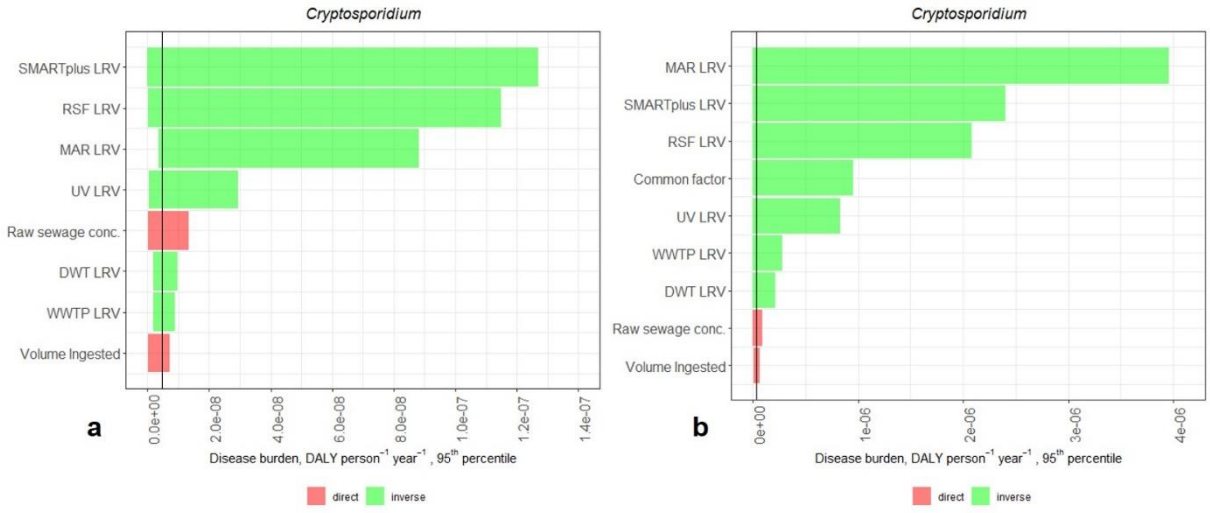


Figure 5-5: Tornado plots showing the range of Cryptosporidium DALYs achieved when minimum and maximum values of each node were used for the normal model (a) and the common factor model (b). Black vertical line denotes baseline 95th percentile DALYs.

Although the tornado plot mostly follows the range of LRVs attributed to each unit treatment for *Cryptosporidium* from Table 5-2 (only RSF and MAR order is switched), the change in the order of the top 3 and the greater influence of the common factor than of UV irradiation (whose range was 2 LRVs) in Figure 5-5 demonstrates that if/when failure is correlated within the model, the relative importance

of unit treatment processes in the treatment train changes. A similar trend was observed for *Campylobacter*, where the common factor was more influential than the 2.2 LRVs attributed to UV irradiation (Figure SI-2). However, for norovirus the findings were very different: SMART*plus* removal mattered more in the sensitivity analysis than could be attributed to its LRVs, and raw sewage concentration was also very influential. In the model with the common factor, SMART*plus* was the most influential and the common factor the second most influential, denoting SMART*plus* as a clear CCP for viruses despite the relatively narrow removal (0.8 LRVs). Nevertheless, the sensitivity analysis determined that SMART*plus* was a CCP for all pathogens, with MAR and WWTP also important for 2 of 3 pathogens, identifying the biological removal steps as most critical, in line with the conservative ranges for biological removal used in this paper. Correlations due to the common factor between the unit treatment barriers also produced larger 95th percentile DALY values, changing the order and magnitude of the estimations. Such results highlight the importance of considering correlated inputs in QMRA models when they exist.

5.3.3 Scenario evaluation

Scenarios to investigate CCP behavior and to determine how failures would affect the final risk were evaluated by comparing the scenario DALYs to baseline DALYs. However, it is worth noting that the scenario evaluations are specific to the thresholds used in the analysis (i.e., norovirus UV LRVs were very narrow). For simplicity this evaluation only included single events, but a combination of events could also be incorporated. Scenarios were evaluated only for the normal model without the common factor, and results of all scenarios are presented in Figure 5-6.

5.3.3.1 **Scenario 1: High pathogen loading**

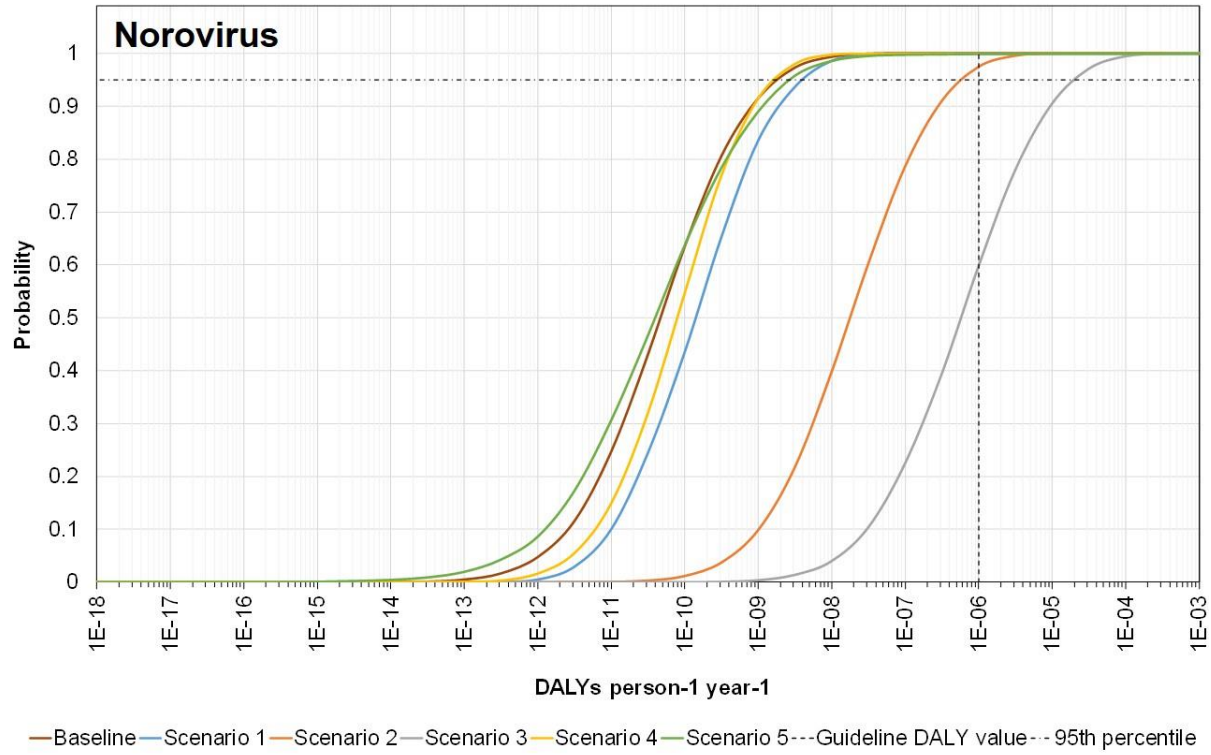
For this scenario, the effect of all concentrations greater than the 95th percentile of the raw sewage pathogen concentrations on final DALYs was tested. This corresponded to testing ~106 units/L of both norovirus and *Cryptosporidium*, and ~10^5 units/L of *Campylobacter*. For all pathogens, only a 0.3-0.5 log increase in final DALYs was observed. This demonstrates that the treatment train successfully buffers higher raw sewage concentrations without any notable effects on disease burden, even for norovirus and *Campylobacter*, which displayed high sensitivity to sewage concentrations.

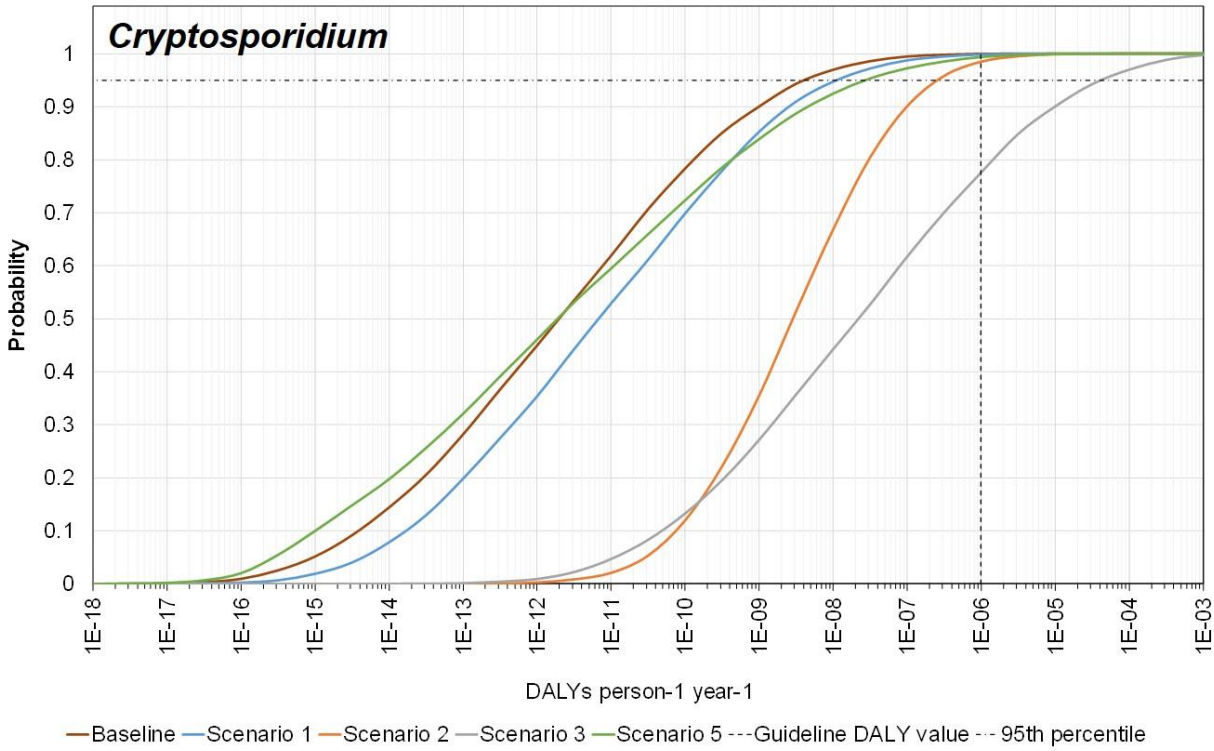
5.3.3.2 **Scenario 2: SMART*plus* performance failure**

SMART*plus* performance failure (0 LRVs) affected all pathogens differently. *Cryptosporidium* was least affected, with a DALY increase of 1.8 log, contrary to the sensitivity shown in section 5.3.2. This can likely be explained by the fact that the attributed LRV range was already close to zero (0.3, 6). Norovirus DALYs increased by 2.5 log and *Campylobacter* DALYs increased by 3.2 log. This 2-3 log change in DALYs for all pathogens solidifies the status of SMART*plus* as a CCP.

5.3.3.3 **Scenario 3: MAR failure**

MAR failure (0 LRVs) caused all pathogen DALYs to be 0.3-1.6 logs greater than the 10^{-6} threshold. This was the only scenario with failure of a biological removal step which resulted in DALYs above the acceptable threshold, and MAR was therefore thought to be a CCP after this scenario analysis, despite its lower rank in the norovirus sensitivity analysis (Figure 11-2). However, as microbial growth is difficult to monitor and correct at larger scale (Dewettinck et al., 2001), MAR is ultimately not considered a CCP.


Norovirus
Probability
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1E-18
1E-17
1E-16
1E-15
1E-14
1E-13
1E-12
1E-11
1E-10
1E-09
1E-08
1E-07
1E-06
1E-05
1E-04
1E-03
DALYs person-1 year-1
Baseline
Scenario 1
Scenario 2
Scenario 3
Scenario 4
Scenario 5
Guideline DALY value
95th percentile


Cryptosporidium
Probability
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1E-18
1E-17
1E-16
1E-15
1E-14
1E-13
1E-12
1E-11
1E-10
1E-09
1E-08
1E-07
1E-06
1E-05
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DALYs person-1 year-1
Baseline
Scenario 1
Scenario 2
Scenario 3
Scenario 5
Guideline DALY value
95th percentile

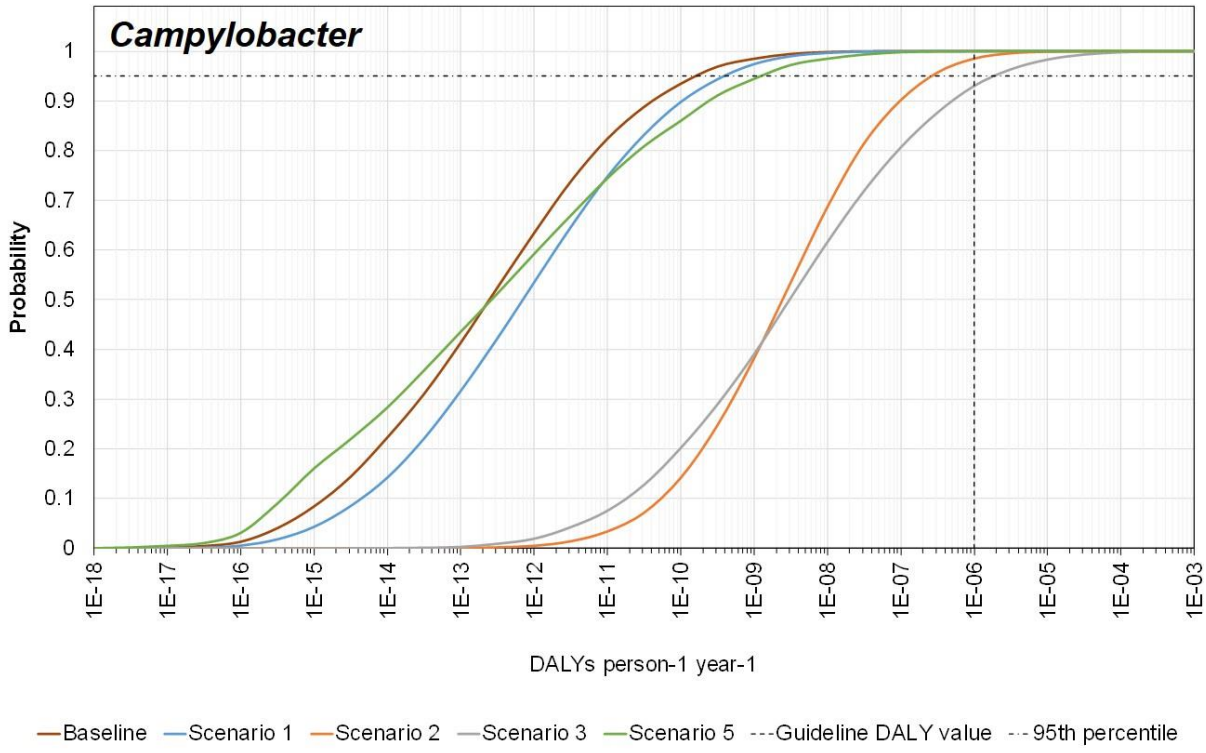

Figure 5-6: CDFs of DALYs resulting from scenarios 1, 2, 3, and 5 for all pathogens, with additional DALYs from scenario 4 (experimental data) shown only for norovirus. Results confirm that MAR (scenario 2) and SMARTplus (scenario 3) performance failure scenarios lead to the highest risk for all pathogens and supports their status as CCPs. Note that scenario 5 shows the same results as CF models in figure 5-3.

5.3.3.4 **Scenario 4: Experimental conditions**

This scenario was evaluated only for norovirus by using the ambient human norovirus removals calculated in Karakurt-Fischer et al. (2021). This meant that WWTP removal was set to 0.75-1 LRVs, RSF removal was set to 0.25-0.3 LRVs, and SMART*plus* removal was set to 2.5-2.75 LRVs. This resulted in DALYs nearly identical to the baseline ($2.1 * 10^{-9}$), which can be explained by the relatively narrow ranges taken for all 3 treatment steps from the phage and virus removals reported in Karakurt-Fischer et al. (2021). However, this demonstrates that the model provides a feasible outcome, as the evidence given was within the calibration range of the model and provided results similar to the baseline.

5.3.3.5 **Common factor effect**

The common factor was modeled to determine how the model would react if barriers were not assumed to be independent. For example, a common factor which could be considered is the influence of influent concentration on LRVs (Brown et al., 2019; Hirani et al., 2012). Although Pecson et al. (2017) mentioned that independence of barriers can be assumed, this has not yet been widely accepted, and therefore interdependence was modeled to determine how the model would respond. All DALYs increased by 0.6-3.5 logs but were still within the 10^{-6} threshold. Greatest increases were observed for *Campylobacter* (3.5 LRVs) and *Cryptosporidium* (1.5 LRVs).

5.3.1 Backwards inferencing

Backwards inferencing can be used to identify the most likely cause of an event and discriminate amongst competing hypotheses. To find the most likely cause, the ratio between the posterior and prior marginal probabilities can be evaluated for a state of a target node, with a larger ratio providing stronger evidence in favor of that particular node being the likely cause for the event. In this model, by switching the probabilities of the selector nodes from equal likelihood of working and not working to 99.9% working and 0.1% not working, a more likely outcome for the treatment train could be modeled. All DALY values $\geq 10^{-6}$ were selected to determine how the likelihood of the selector nodes working would change during such a high risk scenario. For all pathogens, as observed in Table 5-3, WWTP and RSF LRVs were the least likely to not work during a condition of $\geq 10^{-6}$ DALYs, but the unit treatment processes exhibiting the greatest change varied for each pathogen. For norovirus, MAR, UV irradiation, and SMART*plus* were most affected (in that order), for *Campylobacter* UV irradiation, MAR, and SMART*plus* were most affected, and for *Cryptosporidium*, UV irradiation, MAR, and DWT were most affected. Although UV failure was not explicitly investigated as a scenario due to the narrow range of norovirus removal during UV irradiation, and did not rank high during the sensitivity analysis for any pathogen, this backwards inferencing determined that it is also a CCP for all pathogens, along with SMART*plus*.

Table 5-3: Results of backwards inferencing on the selector nodes. Prior marginal probabilities for the "not working" state were all set to 0.1%, and the ratios between posterior and prior marginal probabilities for each selector node demonstrate the likelihood that the selector node is responsible for the $>10^{-6}$ DALYs.

Barrier selector	**Norovirus**		***Campylobacter***		***Cryptosporidium***	
	Posterior probability	Ratio	Posterior probability	Ratio	Posterior probability	Ratio
WWTP	0.26%	2.6	0.68%	6.8	0.48%	4.8
RSF	0.12%	1.2	0.45%	4.5	1.0%	10
SMARTplus	3.47%	34.7	7.50%	75	1.50%	15
UV irradiation	44.1%	441	64.1%	641	30%	300
MAR	52.8%	528	28.8%	288	17.7%	177
DWT	0.26%	2.6	0.16%	1.6	2.4%	24

5.3.2 Additional considerations

When evaluating statistical models, limitations should be made explicit. As only site-specific norovirus removal was available at the time of the study, validation of the model requires more site-specific data, particularly for pathogen removal processes in porous media, which is dependent upon further study of unit treatments where pathogen removal is biologically dominated. This screening level assessment can therefore only give an initial, generic estimate of predicted risk, which is especially useful when designing a new treatment train or system. The BN approach can be easily updated later as empirical data are obtained and additional considerations are identified.

Failure of treatment processes, especially short-term, drives risk (Amoueyan et al., 2019; Smeets et al., 2006; Soller et al., 2018b). This was noted as the DALYs increased the later in the treatment train the failure had occurred, as well as in the common factor model. This demonstrates how QMRA can assist

in identifying CCPs and ensuring proper measures are in place to mitigate such failures and prevent compromised water quality prior to commencing full-scale operation.

This QMRA did not account for dilution with native groundwater, which could impact concentrations at the point of abstraction for subsequent DWT. *Cryptosporidium* presence in groundwater is under studied but has been reported in the USA and Canada (Murphy et al., 2016; Rose, 1997; Stokdyk et al., 2020, 2019). A recent global review of *Cryptosporidium* concentrations in groundwater intended for human consumption suggested that it is present in 10-20% of domestic groundwater supplies (Chique et al., 2020). Hynds et al. (2014) found that nearly 90% of U.S. studies reported enteric viruses in groundwater, and they were detected more often than protozoa or bacteria (both 60%). Needless to say, better estimations of MAR LRVs and decay and retention rates at field scale are urgently required to improve risk assessments and models, and adapt removal observed at lab- to field-scale (Bradford and Harvey, 2017; Gerba et al., 2018).

Additionally, assuming that consumers would ingest up to 2 L of 100% reclaimed water is an extremely conservative exposure estimate. In IPR systems, advanced treated water is blended with native groundwater or surface water before it is abstracted by the DWT plant, which may also blend different source waters together and result in further dilution. Therefore, when considering such a treatment train for field-scale installation, it will be critical to update the assumptions presented in this paper to site-specific raw sewage concentrations, to more accurately quantify subsurface retention time, ideally via tracer tests and hydrogeological models, and to account for dilution in the DWT plant.

5.4 Conclusion

This study provides a probabilistic, screening level QMRA for a non-membrane based IPR treatment train. It quantified the disease burden for norovirus, *Cryptosporidium* and *Campylobacter* by encoding a number of probability distribution functions and general mathematical operations from QMRA within a BN. Conclusions of the study are:

- The IPR treatment train incorporating SMART*plus* can produce water meeting the tolerable health burden of 10^{-6} DALYs pppy for norovirus, *Cryptosporidium*, and *Campylobacter* at the 95^{th} percentile, even with the conservative LRVs adapted for unit treatment processes with biological removal. The greatest disease burden was posed by *Cryptosporidium*, similar to other non-reverse osmosis based IPR systems.
- Assessing multiple percentiles of disease burden confirms prior work that treatment train LRV requirements vary according to the percentile used for reporting final risk. Evaluation of multiple percentiles in conjunction with a scenario analysis would provide a more comprehensive illustration of risk, which is particularly useful for communicating with stakeholders as well as utilities seeking to make risk-based decisions.
- Assessing different dose-response models was critical to understanding how the choice of model affected calculated risk and whether additional removal would be needed.
- Simulating various plausible operational scenarios, in conjunction with a sensitivity analysis, can reveal which unit treatment processes are critical control points. Using this combination, unit treatment based on biological removal (SMART*plus*) were identified as CCPs in this treatment train. Further backwards inferencing revealed that UV was also a CCP for all pathogens.
- More studies should focus on quantifying removal, retention and/or decay rates of pathogens in field scale applications of subsurface treatment, at minimum for the pathogens investigated in this study, to better characterize subsurface removal for potable reuse systems.

- The benefit of a BN in providing backward and forward diagnosis cannot be underestimated, especially when updating the model with new empirical data and predicting how the model will respond to particular input conditions. The final models achieved their purpose of communicating a large amount of information in a structured and orderly manner, and simulated a number of scenarios which would be impossible to assess in a real setting. A relevant aspect to consider is the possibility of updating the parameters of the BN, employing the current model as starting point for a plant utilizing the proposed treatment train. Therefore, when more recent data become available, for example from challenge testing or ambient microbial analyses, the estimates obtained from literature can be updated using Bayes theorem.
- In comparison to prior BN work done for water reuse treatment trains (Beaudequin et al., 2016), this paper presents a more comprehensive (more variables, multiple dose-response models, failure analysis, more uncertainty) and sensitive (greater discretization) approach for quantifying risk with a more user-friendly interface. The benefit of Netica lies in the easy-to-interpret numerical changes in node probabilities when evidence into the network is given, and communicating the model's results via CDFs or box plots will enable political decision makers to adapt risk-informed policies to solve current and future water management concerns.

Competing Interests

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.

Acknowledgements

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In conclusion, **Hypothesis 1** – Risk to human health from pathogens present in a potable reuse train employing SMARTplus is below 10^{-6} DALYs – was accepted at the 95th percentile DALYs benchmark.

6. Quantitative chemical risk assessment of a non-membrane based potable reuse treatment train

6.1 Introduction

Recent advancements in chemical detection and effect-based toxicological monitoring (Brunner et al., 2020), international guidelines for potable reuse (World Health Organization, 2017a; ISO, 2018) and legislative proposals and regulations for governing chemicals in water reuse practices (US EPA, 2019; EU Parliament, 2020) have caused a boom in chemical risk or exposure assessments in literature as of late (Agerstrand et al., 2015; Semerjian et al., 2018; Ma et al., 2018; Compagni et al., 2019; Sharma et al., 2019; Song et al., 2019; Alygizakis et al., 2020; Imran et al., 2020). While municipal wastewater treatment plants (WWTPs) are designed to remove parameters specified by water quality legislation and thereby prevent their introduction into the environment, an increasing amount of chemicals detected in water bodies due to progress in analytical methods have been traced back to agricultural runoff or municipal wastewater discharges (Reemtsma et al., 2016; OECD, 2019; Tran et al., 2019). The health relevance of these trace organic chemicals (TOrCs), which include pharmaceuticals, personal care products and other chemicals of emerging concern, is not always known. As many regions already practice *de facto* reuse, which occurs when drinking water treatment plant (DWTP) source water is located downstream of a WWTP discharge, the inadequate removal of TOrCs could have public health consequences (Khan et al., 2018; Soller et al., 2019).

To reduce the concentrations of TOrCs discharged to the environment, advanced water treatment (AWT) can be employed, which includes oxidation, adsorption, membrane filtration, and biodegradation processes (Jekel et al., 2015; Fischer et al., 2019). Deliberate potable reuse, instead of unknown *de facto* reuse, can either be direct, when AWT effluent is supplied directly to the DWTP, or indirect, when AWT effluent is introduced into groundwater or surface water, which is subsequently used as source water for the DWTP. Introduction into the subsurface is referred to as managed aquifer recharge (MAR) which results in further attenuation of contaminants, such as pathogens and chemicals, via biodegradation or adsorption in the subsurface (Bekele et al., 2018). Several studies demonstrated that efficient TOrC removal in MAR systems can be improved by controlling redox conditions via aeration during sequential managed aquifer recharge treatment (SMART) (Hellauer et al., 2017, 2018a; Regnery et al., 2017c, 2017a). SMART was further optimized through controlled hydraulics and smaller physical footprints via sequential biofiltration (SBF) and SMART*plus*, which revealed an effective removal of chemicals (Müller et al., 2017; Karakurt-Fischer et al., 2020b) and viruses (Karakurt-Fischer et al., submitted) at shorter hydraulic retention times (HRT), and when coupled with subsequent adsorptive treatment, resulted in better final effluent quality (Müller et al., 2019a). The microbial risk from a SMART*plus*-based treatment train for indirect potable reuse has already been quantified (Zhiteneva et al., 2021).

While overall TOrC removal can be computed by simply summing the removal percentages of unit processes, this results in a deterministic assessment of removal at a single point in time. However, changes in operational parameters, influent water quality, and other site-specific considerations can notably affect removal over long-term operation. To more effectively include uncertainty, such as that associated with measuring trace concentrations (ng/L–µg/L) near the analytical detection limit, as well as variability due to seasonal, temporal, or weather related water quality changes, a probabilistic approach to chemical risk assessment, already established for microbial contaminants (Barker et al., 2014; Mok et al., 2014; Pecson et al., 2017), is beneficial. Utilization of probabilistic approaches is increasing in various studies (Khan, 2010; Compagni et al., 2019), and Bayesian networks are one such method for providing a more comprehensive assessment of risk (Beaudequin et al., 2017). Therefore, this study will conduct a probabilistic risk assessment to evaluate whether TOrCs present at the end of

an engineered indirect potable reuse train involving the SMART*plus* treatment concept comply with their monitoring trigger levels (MTLs).

6.2 Methods

6.2.1 Treatment train

While similar to our previous work on microbial risk assessment (Zhiteneva et al., 2021), the treatment train in this study was modified slightly to carry out the chemical risk assessment (Figure 6-1). Raw sewage undergoes primary and secondary treatment at the Garching WWTP, Germany (31,000 population equivalents). Secondary treated effluent received additional treatment through a rapid sand filter. Tertiary effluent is then introduced into the SMART*plus* biofilter, which is designed as a slow sand biofilter with a loading rate of 0.58 m/hr and an intermediate *in situ* aeration process (Karakurt-Fischer et al., 2020b, 2020a). Following this, a granular activated carbon (GAC) filter serves to adsorb remaining chemicals. Ultraviolet (UV) disinfection at 200 mJ/cm^2 is primarily aimed at removing remaining pathogenic risk and provides attenuation of some chemicals (Nihemaiti et al., 2018). The effluent of the last engineered unit treatment prior to introduction into the environment via groundwater injection, representing the TOrC concentrations after UV disinfection, was defined as the point of compliance (POC). After 120 days of subsurface travel time, the groundwater would be extracted as source water for conventional drinking water treatment, which includes aeration followed by dual media filtration (sand and anthracite) for iron and manganese removal. The long subsurface residence time rendered additional disinfection unnecessary.

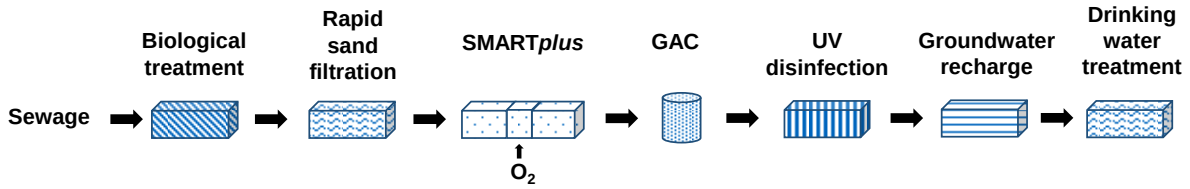

Figure 6-1: Schematic of the SMARTplus based indirect potable reuse treatment train under investigation.

6.2.2 Selection of chemicals

For a health-based risk analysis, MTLs for 16 of the 24 monitored TOrCs were specified in the risk assessment approach outlined in Drewes et al. (2018), with no values for citalopram, climbazole, erythromycin, sotalol, venlafaxine, 3-OH-carbamazepine or 4-formylaminoantipyrine provided. These TOrCs also do not have German health guidance values (GOW), which is a precautionary value for chemicals possibly present in drinking water and whose human toxicity is not well known (Umweltbundesamt, 2019). Caffeine was omitted from the risk assessment, as the MTL level was based on compound structure and mode of action instead of safe consumption levels, leading to the removal of caffeine as a performance-based indicator in the updated report (Drewes et al., 2018).

MTLs were established using Equation 6-1,

$$\mathrm{MTL} = \frac{\text{Screening Level ADI} * 60\ \text{kg} * \text{RSC}}{2\ \text{L per day}} \qquad \textit{Equation 6-1}$$

where screening level acceptable daily intake levels (ADI, μg^{-1} kg^{-1} d) for chemicals were identified from literature reviews (Drewes et al., 2013, 2018), and relative source contribution (RSC, unitless) were mostly 0.2.

After comparing the 90th percentile WWTP concentrations, which are referred to as measured effluent concentrations (MEC), to the MTLs of the 16 compounds, the MEC/MTL ratios of benzotriazole, diclofenac, gabapentin, and valsartan acid were found to be greater than 1. To ensure that all risk was considered, the maximum WWTP concentrations were also compared to MTL levels, which revealed that the MEC/MTL ratio was also greater than 1 for carbamazepine. Therefore, the five compounds in Table 6-1 were included in the risk assessment.

Table 6-1: Compounds whose maximum and 90th percentile MECs in WWTP effluent exceeded MTL levels. WWTP effluent concentrations for benzotriazole (n=74), carbamazepine (n=80), diclofenac (n=80), gabapentin (n=80), and valsartan acid (n=61) were monitored from March 2016 to June 2018.

ng/L	MTL	MEC 90th percentile	MEC maximum	MEC(90th)/MTL	MEC(max)/MTL
Benzotriazole	3,000	6,912	8,767	2.3	2.9
Carbamazepine	1,000	558	1,213	0.6	1.2
Diclofenac	1,800	2,113	5,181	1.2	2.9
Gabapentin	1,000	2,503	2,998	2.5	3.0
Valsartan acid	300	4,095	6,438	13.7	21.5

6.2.3 Experimental data

At the time of this study, the SMART*plus* sequential operation with *in situ* aeration dataset was too small to conduct a probabilistic analysis. Instead, the presence of 24 TOrCs monitored for over two years in the Garching WWTP secondary effluent and investigated within an SBF experiment conducted at the same institute with the same feed water (Müller et al., 2019a, 2019c, 2019d) provided a broad temporal dataset for the risk assessment. The SBF system was operated with intermediate aeration (SBF(O_2)) at a maximum hydraulic retention time (HRT) of less than 35 hours, whereas the HRT of SMART*plus* was 12-13 hours (Müller et al., 2017; Karakurt-Fischer et al., 2020b). Redox zonation in the SBF(O_2) ensured oxic conditions in the second stage sand filters, whereas SMART*plus* was operated as a slow sand filter with slightly elevated filtration rate prior to *in situ* aeration. As removal demonstrated by SBF(O_2) is likely more conservative than would be seen in SMART*plus* with aeration, empirical SBF(O_2) data were used to describe TOrC presence and removal in dual media filtration and the SMART*plus* bioreactor (Müller et al., 2017, 2019a). Probability distribution functions (PDFs) were fitted to SBF(O_2) effluent TOrC concentrations, with lognormal, normal, exponential, gamma, and Weibull distributions evaluated using the Kolmogorov-Smirnov or Anderson-Darling goodness of fit tests in Origin (OriginPro, version 2019). Based on goodness-of-fit, all 5 PDFs were rejected for benzotriazole, carbamazepine, diclofenac and valsartan acid: therefore, triangular PDFs were adapted to the minimum, mean, and maximum values for these chemicals. The final PDFs are displayed in Table 6-2.

GAC removal ranges obtained from experimentally treating the SBF(O_2) effluent through rapid small scale column tests (RSSCT) were adapted for each compound (Müller et al., 2019a). The removal range observed from 0-20,000 RSSCT BVT and corresponding to a GAC empty bed contact time of 24 minutes was used for this study (Müller et al., 2019a).

To remain consistent with assumptions taken for pathogen removal in our prior work (Zhiteneva et al., 2021), a fluence value of 200 mJ/cm^2 was assumed for UV disinfection, as this is approximately the fluence to target deactivation of adenovirus (U.S. Environmental Protection Agency, 2006; WaterReuse Research Foundation, 2015). Compound photo-susceptibility was determined from k_{uv} values provided in Nihemaiti et al. (2018) and Miklos et al. (2019).

Table 6-2: Distributions for presence in SMARTplus effluent, and reduction percentages used for subsequent treatment steps. All removal ranges were fitted to uniform distributions.

	SMART*plus* effluent[1]	**GAC[2]**	**UV disinfection[3]**	**GWT & DWT**
Benzotriazole	*Triangular (219, 780, 3,738)	90-100%	20-80%	No removal
Carbamazepine	*Triangular (338, 507, 1,193)	90-100%	0.1-5%	
Diclofenac	*Triangular (428, 1,335, 4,937)	80-100%	90-100%	
Gabapentin	Gamma (3.85, 55.2)	0.1-100%	0.1-15%	
Valsartan acid+	*Triangular (47, 757, 5,922)	50-100%	-- (0.1-15%)	

[1](Müller et al., 2017), [2](Müller et al., 2019a), [3](Nihemaiti et al., 2018) and unpublished data from (Miklos et al., 2019b). *denotes that all PDFs were rejected based on goodness-of-fit tests. +Valsartan acid removal during UV disinfection was adapted from gabapentin removal, as both compounds are poorly photo-degradable.

To determine whether the treatment train effluent quality met MTL levels at the point of compliance (POC, groundwater injection) rather than the point of exposure (POE, DWT effluent), no further removal during groundwater recharge or DWT was assumed. This is a rather conservative assumption, as the UV effluent would be injected into an open underground system, and if the impacts of landside groundwater, dilution, and dispersion on chemical removal were considered, would result in lower TOrC concentrations at the point of abstraction. However, as no notable removal is expected from aeration and filtration, which is common DWT practice in Germany, this study assessed risk at the POC to determine risk at the end of the engineered treatment train.

6.3 Environmental risk assessment

The principle of the risk assessment is to determine what risk the effluent water quality poses to human health, where risk is calculated as the product of impact and probability. The impact was calculated using a hazard quotient (HQ) approach, and the probability was determined using a Bayesian network approach, following Equation 6-2:

$$\text{Impact} = \text{HQ} * (\text{Probability of HQ} > 1) \qquad \textit{Equation 6-2}$$

The HQ was calculated as the ratio of concentration at POC divided by the MTL.

To conduct the risk assessment, the Bayesian network methodology described in Zhiteneva et al. (2021) was applied, but using GeNIe instead of Netica. Briefly, TOrC concentrations from the SMART*plus* effluent were fitted with the most appropriate PDF, removal percentage values from Table 6-2 were adapted to uniform distributions, and a network was created in GeNIe 2.3 (BayesFusion). Each treatment step was the product of the effluent concentration of the step before and the removal percentage of the

step itself (see Figure 6-2), except for SMART*plus*, which was characterized only by the PDF describing concentration. A final distribution of HQ at the POC was calculated by simulating the network 100,000 times. For TOrCs exhibiting HQ levels above 1, the data was further discretized into two bins using GeNIe's equal count discretization and the concentration thresholds were set to the appropriate MTL levels to determine the probability of HQ being above 1.

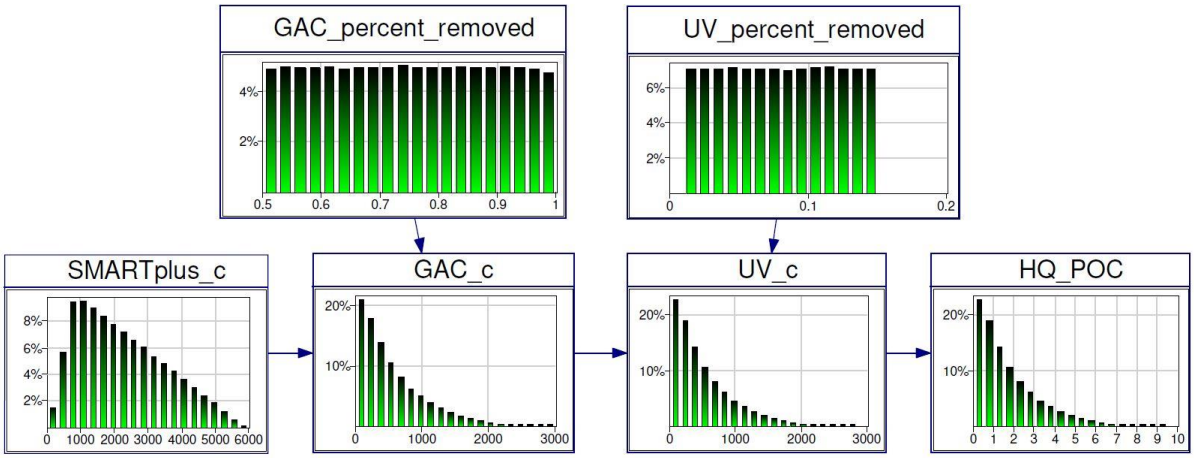

Figure 6-2: Demonstration of continuous distributions in the valsartan acid GeNIe network.

6.4 Results and Discussion

All compounds except valsartan acid displayed an HQ < 1. Gabapentin concentration in SMART*plus* effluent was already below its MTL. Benzotriazole and carbamazepine were both removed to below their MTL levels in GAC, whereas diclofenac needed the additional removal via UV disinfection to fall below its MTL. The maximum HQs were 0.05 for diclofenac, 0.09 for benzotriazole, 0.12 for carbamazepine, 0.92 for gabapentin, and 9.1 for valsartan acid.

The valsartan acid network was then discretized using the thresholds labeled in the discretized network provided in Figure 6-3 and in Table 6-2. The probability of valsartan acid HQ being greater than 1 was 58%.

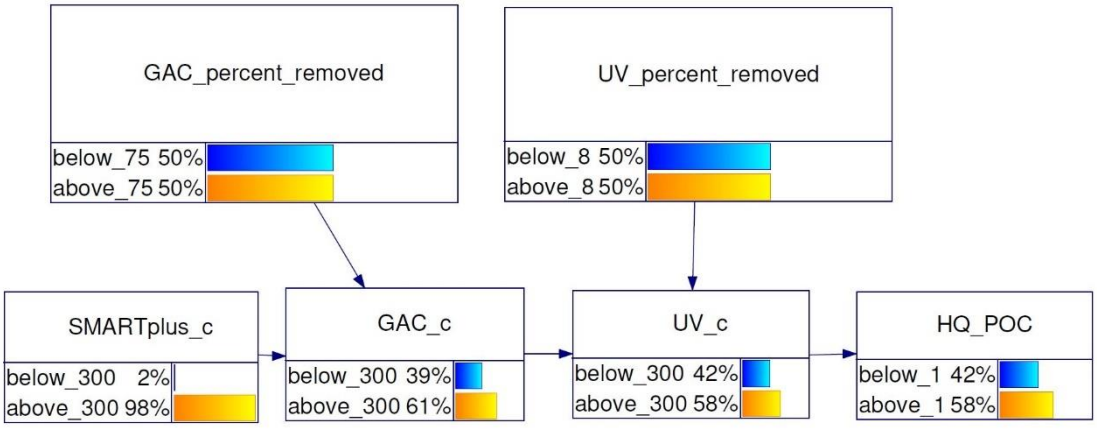

Figure 6-3: Discretized UV disinfection network for valsartan acid. Probability of a valsartan acid concentration greater than the 300 ng/L MTL is denoted as 'above_300.'

Evaluating multiple thresholds is worthwhile when calculating HQ to pinpoint where exactly the exceedance is occurring. Evaluating these thresholds revealed that the MTL was exceeded before the 50th percentile (Figure 6-4). Additionally, according to the impact calculation, which is the probability of exceedance multiplied by the HQ, the impact of valsartan acid is 5.3, which constitutes a high risk according to the labeling system of Zhou et al. (2019) (Table 6-3).

Table 6-3: Assessment of impact for TOrCs at the POC in UV effluent. BZT = benzotriazole, CBZ = carbamazepine, DCF = diclofenac, GBP = gabapentin, VSA = valsartan acid.

	DCF	BZT	CBZ	GBP	VSA
MEC 90th	29	90	64	205	1,188
MEC 95th	38	116	74	253	1,475
Max	93	274	116	922	2,724
HQ MEC 90th	0.02	0.03	0.06	0.21	4.0
HQ MEC 95th	0.02	0.04	0.07	0.25	4.9
HQ Max	0.05	0.09	0.12	0.92	9.1
Impact	0.00	0	0	0	5.3 (high)

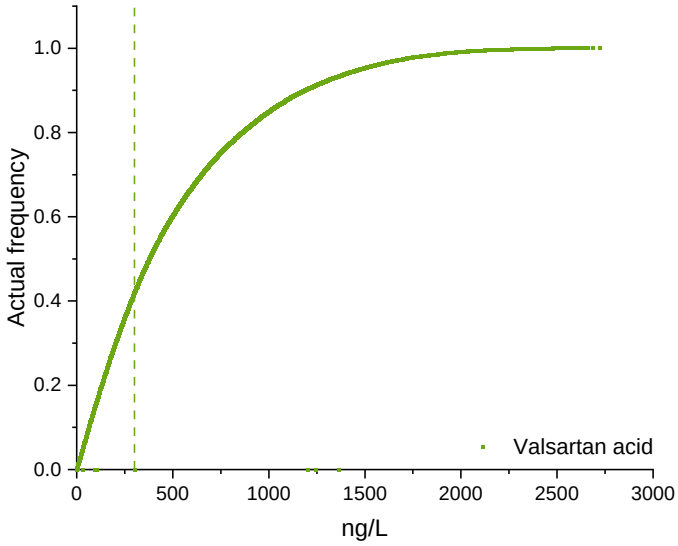

Figure 6-4: Cumulative distribution of valsartan acid in the UV effluent (n=100,000). Dashed green line denotes valsartan acid MTL.

Although valsartan acid is a biodegradable biotransformation product of sartan compounds (Yu et al., 2006; Letzel et al., 2015; Sperlich et al., 2017; Hermes et al., 2019) and persists during bank filtration, it can be adsorbed onto GAC (Nödler et al., 2013; Müller et al., 2019a). However, the throughtput of the adsorber can radically change the risk and impact: when using the 90-100% removal of valsartan acid due to adsorption described in Nödler et al. (2013) which was likely observed within <20,000 BVTs, the maximum HQ was 1.8, the probability of HQ > 1 was only 5%, and the impact was 0.1, which constitutes an endurable risk (Zhou et al., 2019). This demonstrates the magnitude of the impact that varied assumptions can have on the overall removal. Therefore, a more nuanced description of GAC operation and throughput is necessary for all compounds. Additionally, as very little empirical data was

found in the literature to describe valsartan acid removal during UV disinfection, removal assigned in this study may under or overestimate true removal.

In prior work on the same system which evaluated the sartan compounds (Hermes et al., 2019), valsartan was removed (100%), whereas candesartan, olmesartan and irbesartan were not (<10% removal). After initial valsartan removal in the anthracite filter, during which valsartan acid was produced, removal of valsartan acid was observed in the subsequent SBF sand columns (Hermes et al., 2019). A more comprehensive mass balance assessment could specify how much parent compound removal contributes to valsartan acid production.

Future recommendations for improving the methodology outlined in this study include a more nuanced take on adsorption removal during GAC filtration, including deciding on how much throughput to process before GAC media is regenerated (see 90-100% removal of valsartan acid due to adsorption in (Nödler et al., 2013)), and using a modeling strategy (i.e. pore surface diffusion model (PSDM)) to predict breakthrough curves to higher BVT, as done in Zhiteneva et al. (2020b). Likewise, conducting a scenario and failure analysis would be helpful: for example, observing how removal changes if adequate redox zones are not present for 5-10% of operational time, or if the GAC adsorber operates for 10,000 BVT after breakthrough of benzotriazole, diclofenac or carbamazepine. The inclusion of WWTP effluent concentrations and SBF removal percentage was not done in this study, but the product of these two nodes should validate the SBF effluent concentration seen. While SBF data was used for determining PDFs, validation of the model is also critical, which could be accomplished with removal data from SMART*plus* operated with *in situ* aeration.

6.5 Conclusion

This screening level chemical risk assessment produced a probabilistic estimate of water quality at the end of SMART*plus* based IPR treatment train. The treatment train involved biodegradation, adsorption and UV disinfection, and revealed that while benzotriazole, gabapentin, diclofenac, and carbamazepine were successfully reduced to below their MTL levels in the UV effluent, valsartan acid had a 58% probability of exceeding its MTL. A more comprehensive assessment of throughput is needed to determine optimal adsorber operational lifetime prior to GAC media regeneration to better characterize removals of all compounds. Additional work on failure and scenario analysis, as well as validation of the probabilistic models with empirical data from the SMART*plus* operation with *in situ* aeration would improve the forecasting.

This risk assessment approach presents a probabilistic methodology for determining which compounds in a treatment train are most critical for human health, but can also be used for environmental health assessments. As utilities and resource recovery/wastewater treatment/advanced water treatment plants look to improve their removal TOrC efficacy, this modeling strategy could help identify which treatment processes are needed on a site-specific basis to protect public health.

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In conclusion, the study demonstrated that valsartan acid was not reduced to below its MTL at the point of compliance of the SMART*plus* based indirect potable reuse treatment train, therefore **Hypothesis 2** – TOrC concentrations in the point of compliance of the potable reuse train employing SMART*plus* are above the corresponding MTL – **was accepted.**

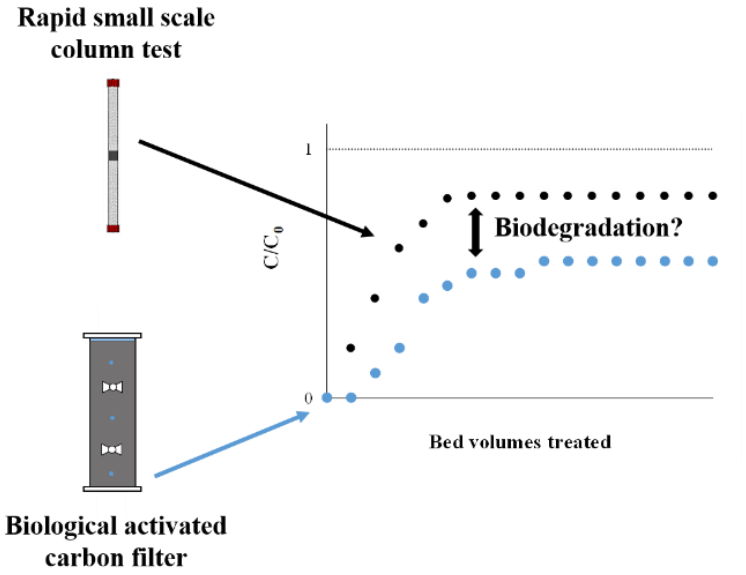
7. Differentiating between adsorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters

This chapter has been published with editorial changes as follows:

Zhiteneva, V., Ziemendorf, É., Sperlich, A., Drewes, J.E., Hübner, U. 2020. Differentiating between adsorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters. *Science of the Total Environment* 743, 140567. https://doi.org/10.1016/j.scitotenv.2020.140567.

Abstract

Efficient adsorption of certain trace organic chemicals (TOrCs) present in secondary treated municipal wastewater treatment plant (WWTP) effluents onto granular activated carbon (GAC) has already been demonstrated at lab- and full-scale. Due to high organic matter concentrations inWWTP effluents, GAC filters eventually develop a biofilm and turn into biological activated carbon filters (BAC), where removal of organic compounds is governed by biodegradation as well as by adsorption. However, determining TOrC breakthrough by conducting a long-term BAC column experiment to discern between the removal mechanisms is not possible due to competition for adsorption sites, fluctuating water quality, and other variables. Therefore, a rapid small scale column test (RSSCT) was conducted to determine the contribution of adsorption for select chemicals at 10,000 bed volumes treated (BVT). These results were then used in the pore surface diffusion model (PSDM) to model adsorption behavior at 40,000 BVTs. Pseudo-Freundlich K values obtained from the PSDM model were compared with K values obtained from an integral mass balance calculation. This comparison revealed that the modeling was most accurate for moderately to poorly adsorptive compounds. In comparing RSSCT results to long-term BAC columns, the modeling approach best predicted BAC removal of well adsorbing compounds, such as atenolol, trimethoprim, metoprolol, citalopram, and benzotriazole. However, differences in predicted vs observed BAC removal for the removals of venlafaxine, tramadol and carbamazepine revealed that BAC adsorption capacity was not yet exhausted for these compounds. Therefore, a comparison was not possible. The approach would be improved by operation at longer EBCT and improved calculation of compound fouling indices.



Chapter 7: Differentiating between adsorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters

7.1 Introduction

As conventional wastewater treatment plants are not designed for the removal of trace organic chemicals (TOrCs), certain chemicals persist at low concentrations (ng/L-µg/L) in treated secondary effluents and are subsequently discharged into receiving water bodies. These low concentrations can still have adverse impacts on downstream ecosystems (Reungoat et al., 2011; Jekel et al., 2013; Luo et al., 2014), requiring greater removal prior to discharge. Advanced treatment unit processes such as membrane treatment (Snyder et al., 2007), ozonation (Reungoat et al., 2011) or activated carbon adsorption (Benstoem et al., 2017) can successfully remove certain TOrCs, but might be associated with higher specific energy and maintenance costs (Nakada et al., 2007; Hollender et al., 2009; Wert et al., 2009; Kennedy et al., 2015; Zhang et al., 2017).

To minimize these costs, research into natural treatment systems, such as soil-aquifer treatment and biofiltration, where removal of chemicals and pathogens occurs without the addition of chemicals, has been increasing. Natural treatment systems are still considered 'black-box' technologies due to lack of knowledge about the underlying fate and transport mechanisms for TOrC attenuation. Removal has been shown to be very site-dependent and sometimes dynamic due to changing feed water matrices, subsurface soil characteristics and heterogeneity, and other factors contributing to the uncertainty and variability of the treatment efficiency (Greskowiak et al., 2017; Regnery et al., 2017). While it is generally accepted that TOrC removal in biological filtration systems is mainly attributed to adsorption and biodegradation processes, assigning relative removal contributions to either process with certainty is difficult, and synergies between both mechanisms are poorly understood (Vasiliadou et al., 2013; Bertelkamp et al., 2014, 2016; Banzhaf and Hebig, 2016). Research into activated carbon filtration has shown that when fed with secondary treated effluents, TOrC removal via adsorption is reduced in the presence of dissolved organic matter (DOM) (Zietzschmann et al., 2014), and varies depending on carbon type (Kårelid et al., 2017; Aschermann et al., 2018) and operational conditions (Benstoem et al., 2017). Once a granular activated carbon (GAC) filter has been in operation long enough, due to dissolved organic matter (DOM) concentration in the influent, a biofilm begins to grow on the surface of the GAC. Consequentially, microorganisms begin to break down the organic components including TOrCs in the water matrix, prompting the terminology switch from GAC to biological activated carbon (BAC). BAC filtration is a combination of natural/biological and technical removal technologies and mechanisms. DOM concentrations, which are higher in secondary treated effluents than in drinking waters (Zietzschmann et al., 2016b), influence the onset of biodegradation and the removal of TOrCs via cometabolic pathways (Tran et al., 2013; Alidina et al., 2014; Piai et al., 2020). Studies conducted on BAC filters most often used mature media from established biofilters (Reungoat et al., 2012; Zhang et al., 2017; Greenstein et al., 2018), used biological inhibitors (Paredes et al., 2016), used synthetic or simulated effluent (Liang et al., 2007; Paredes et al., 2016), were backwashed (Zhang et al., 2017; Greenstein et al., 2018; Ma et al., 2018), or received ozonated tertiary effluent (Reungoat et al., 2011). So far, no long-term experiment without backwash or inhibitors to continuously treat non-ozonated tertiary treated effluent, from virgin GAC to removal via biodegradation, has been conducted. This is particularly relevant for assessing methods which could improve the initial and long-term removal of TOrCs in engineered biodegradation-based unit operations, such as groundwater recharge though infiltration basins, soil retention filters, or more recently developed approaches like SMART*plus* and sequential biofiltration (Müller et al., 2017; Karakurt-Fischer et al., 2020b).

RSSCTs are an established way for achieving breakthrough of GAC adsorbers faster than by utilizing pilot-scale columns and thus minimize removal via biodegradation (Crittenden et al., 1986; Worch, 2012). RSSCT results can be proportionally scaled up to predict breakthrough of non-biodegradable compounds in the BAC filter by increasing the loading rate, decreasing the particle size, and keeping

certain dimensionless pore surface diffusion model (PSDM) parameters constant (see Supplementary Information (SI)).

The aim of this paper was to assess and predict the relative contribution of adsorption and biodegradation during initial breakthrough of TOrCs during BAC treatment using a two-pronged approach. Long-term effects of adsorption and biodegradation of TOrCs were assessed in BAC filter columns. The relative contribution of adsorption to TOrC removal was determined using an RSSCT to elucidate the adsorption behavior of TOrCs during initial breakthrough of the BAC filter. This can potentially help to determine additional removal through biodegradation for biodegradable TOrCs.

7.2 Methods

7.2.1 Biological activated carbon (BAC) columns

The experimental setup consisted of a 25 cm long (23 cm of media and 2 cm of liquid) BAC filter made of ISO 9002 certified acrylic glass ($\varnothing_{in}$ = 7.1 cm) filled with Chemviron CycleCarb 401 GAC (Chemviron, Belgium). Secondary treated wastewater from the WWTP in Garching, Germany (31,000 population equivalents) was additionally treated by UV disinfection and rapid sand filtration prior to entering the BAC filter. The rapid sand filter was backwashed twice a week and consisted of anthracite, sand and gravel, described in detail in Karakurt-Fischer et al. (2020b). The BAC filter was fed by a peristaltic pump (Cole-Parmer 7553–75 with a MasterFlex speed controller) at an initial rate of 225 mL/min, which corresponds to a filter loading rate of 3.4 m/h and an empty bed contact time (EBCT) of 4.4 min. The BAC filter was the first in a series of 5 BAC filters with an overall EBCT of 22 min, which was chosen so that steady-state removal via biodegradation in the BAC filter would occur within the project timeframe.

A stock solution of eighteen TOrCs was continuously spiked from a separate tank into the feed stream by a multi-channel pump (Ismatec IPC-04 V3.00). Sufficient mixing was assumed as the stock solution flow was 1% of the feed solution flow. The stock solution was refilled weekly. Sampling ports enabled collection of influent and effluent TOrC samples, where TOrCs were analyzed to calculate breakthrough (Figure 1). Measurements of influent (after the TOrC spiking tank) and effluent samples for TOrCs, dissolved oxygen (DO), dissolved organic carbon (DOC), and ultraviolet absorbance at 254 nm (UVA_{254}) were conducted weekly. DO was measured in flow-through cells using a PreSens Fibox 4 device further described in Karakurt-Fischer et al. (2020b). Polyurethane tubing with an inner/outer diameter of 4/6 mm (Festo, Germany) connected the filter to flow-through dissolved oxygen (DO) sensors (FTC-PSt3, PreSens, Germany).

The BAC filter was operated starting with virgin GAC for 40,000 BVTs. The filter was preloaded for 24 days (approximately 7,500 BVTs) with tertiary treated effluent prior to commencement of TOrC spiking. This preloading is reflected in the different total number of BVTs used for UVA_{254} and DOC compared to the BVTs used for TOrC. However, since this study focuses on the adsorption behavior of TOrCs and not DOC, the BVTs mentioned refer to the TOrC BVTs, unless otherwise stated. As the filter was not backwashed, clogging and particle deposition on the BAC surface, as well as biofilm build-up contributed to a change in initial operational conditions (Table 7-1). These effects are discussed later.

Table 7-1: Flow conditions of the BAC column experiment. Flow rate and EBCT are given as average ± standard deviation (coefficient of variance).

Flow condition	Flow rate (mL/min)	Loading rate (m/h)	EBCT (minutes)	Duration of conditions (TOrC BVTs)
1	220.6 ± 6.6 (0.03)	3.3 ± 0.1 (0.03)	4.5 ± 0.1 (0.03)	-7,500 – 27,741 (n=17)
2	124.3 ± 29.3 (0.24)	1.9 ± 0.4 (0.24)	8.3 ± 1.8 (0.22)	27,741 – 38,348 (n=7)
Overall	192.5 ± 47.5 (0.25)	2.9 ± 0.7 (0.25)	5.6 ± 2.0 (0.36)	-7,500 – 38,348 (n=24)

7.2.2 GAC characterization

To correctly prepare an RSSCT experiment, information on the intraparticle porosity, apparent particle density, porosity, and particle size of the GAC is required. The apparent particle density was calculated using the bed density (450 kg/m^3, provided by the manufacturer) and the bed porosity, which was obtained through a conservative tracer test. 5 mL of a 120 g/L potassium bromide solution was injected into the BAC filter during operation and effluent conductivity was monitored to verify the movement of the tracer through the filter. Conductivity was then converted to mass concentrations and analyzed using CXTFIT 2.0 (Toride et al., 1999), and bed porosity was found to be 0.64. Intraparticle porosity was determined twice by following the procedures outlined in Worch (2012): a known dry GAC mass (m_A) was saturated with Milli-Q water and boiled for 30 min, after which the suspension was drained through a sieve, the particles were rolled on a paper towel until the outer surface was dry, and the GAC was weighed again to obtain the wet mass weight (m_{wet}). The average porosity was found to be 0.81 (n=2, ε_p= 0.79-0.82) using equations S2.1-2.2 (SI). Apparent particle density was found to be 1,250 kg/m^3 according to equation S2.4 (SI).

The particle size of the GAC was determined using a novel static imaging technique to determine the geometric mean diameter (GMD), important for determining a representative particle size for the RSSCT and facilitating comparison of results. Further details of this method are documented in the SI.

7.2.3 RSSCT columns

A constant diffusivity RSSCT (CD-RSSCT) design was used in the experiment, which assumes intraparticle diffusion is not related to particle size. A glass column ($\varnothing_{in}$ = 10 mm) was filled with 1.0 mm glass beads, glass wool, and the same GAC as in the BAC filter (Figure 7-1). The GAC was crushed using a mortar and pestle and the fraction between 180 and 125 µm sieves was collected for the RSSCT, corresponding to a mean particle size of 150 µm. By using a scaling factor of 8, keeping the Reynolds number and other dimensionless parameters constant, and assuming that GAC characteristics such as particle and bed porosity remain the same after crushing the particles, results can be scaled up and directly compared to filter columns (Worch, 2012). Bed porosity was not re-measured after crushing, as CD-RSSCTs assume both particle and bed porosity remain the same after crushing (Crittenden et al., 1991). Dimensionless numbers and calculations are reported in the SI.

The RSSCT setup was fed continuously for 42 h from one batch of tertiary effluent. The same Festo tubing type which was used for the BAC setup also connected the RSSCT column to a membrane pump (ProMinent GmbH, Germany) drawing from an influent storage tank. An airstone (Koiland Kehr, Germany) in the storage tank was used in reverse mode as a particle filter to prevent any suspended solids in the feed water from clogging the RSSCT. The RSSCT was run until 40,000 BVTs.

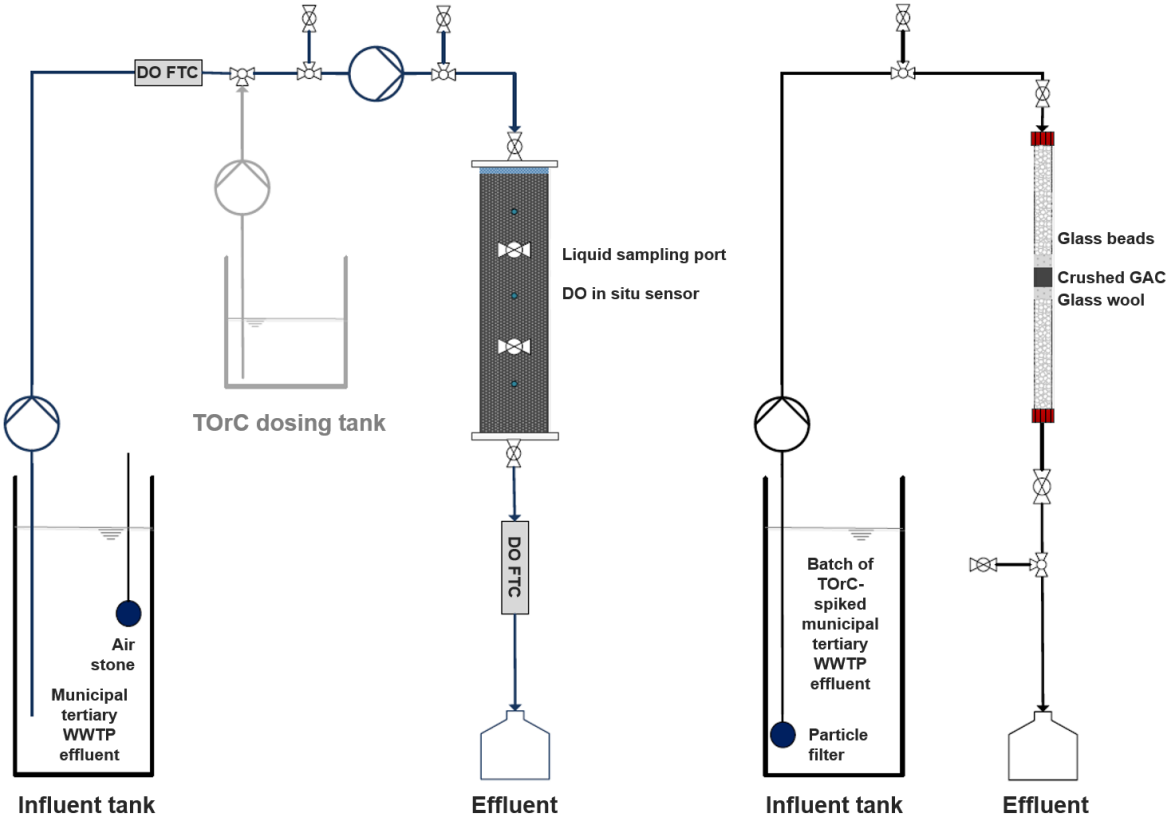


Figure 7-1: Schematic of the BAC filter (left) and RSSCT column (right) experimental setups (not to scale).

7.2.4 Analytical procedures

For DOC and UVA_{254} analysis, samples were first filtered through 0.45 µm micropure cellulose acetate filters (Altmann Analytik, Germany). Then, samples were acidified to a pH of 2 with 3 drops of 32% HCl solution, and subsequently analyzed for DOC on a vario TOC cube analyzer (elementar, Germany). For UVA_{254}, filtered samples were analyzed using a DR 6000 UV/vis spectrophotometer (HACH, Germany) in a 1 cm quartz glass cuvette.

TOrC samples were frozen immediately after sampling at -20°C. For TOrC analysis, 1900 µL of sample were mixed with 100 µL of an isotope solution, filtered through 0.22 µm polyvinylidene difluoride (PVDF) membrane filters, and then analyzed using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Further information on TOrC sample preparation and analysis can be found in Müller et al. (2017). TOrC spiking concentrations were selected considering concentrations present in secondary treated effluent, to ensure that 99% removal could be quantified in regards to the method dependent LOQ of each compound using LC-MS/MS. All compounds spiked were analyzed in ESI positive mode and specific spiking concentrations can be found in the SI. Caffeine and erythromycin, though spiked, were not evaluated in this study due to inconsistent analytical results. Carbamazepine and benzotriazole were not explicitly spiked due to sufficiently high background concentrations, but were analyzed due to their environmental relevance.

7.2.5 Modeling TOrC breakthrough from RSSCTs

7.2.5.1 **Fouling index correction**

As larger GAC particles, in comparison to smaller GAC particles, have more surface area blocked behind their blocked macropores, this reduces adsorption kinetics and, when experimental run time is short, adsorption capacity (Corwin and Summers, 2010). This phenomenon results in the smaller particle RSSCT overestimating the adsorption capacity of larger particle BAC filters, which can be corrected using the fouling index.

The fouling index can be determined from the ratio of the particle sizes $d_{p,BAC}$ of the BAC filter and $d_{p,RSSCT}$ of the RSSCT column (mm), the dimensionless scaling factor SF (which was found to be 8), and the dimensionless fouling factor Y, according to Equation 7-1 (Corwin and Summers, 2010):

$$FI = SF^Y = (\frac{d_{p,BAC}}{d_{p,RSSCT}})^Y \qquad \textit{Equation 7-1}$$

The scaling factor is raised to a fouling factor to account for variability in scaling which accounts for the reduction in adsorption capacity attributed to fouling (Corwin and Summers, 2010). Ideally Y is calculated from multiple CD-RSSCTs with different particle sizes operating simultaneously, but this was not possible within the framework of this study. In this study, the fouling factor was calculated based on previously published linear free energy relationships (LFER) between compound Abraham descriptors and fouling factors (Reinert, 2013; Kennedy et al., 2015). The Abraham descriptors included McGowan molecular volume (V), hydrogen bonding acidity (A), hydrogen bonding basicity (B), dipolarity/polarizability (S) and excess molar fraction (E). This LFER was developed from breakthrough curves of TOrCs which were not investigated in this study, possibly influencing the accuracy of the fouling factor if the TOrCs investigated herein have different correlations to the Abraham descriptors. The approach and equations used as well as individual fouling indices and factors are outlined in the SI. The fouling index can then be used to adjust the timescale of the RSSCT breakthrough curves to include the particle-size dependent DOM fouling, using Equation 7-2, modified from Kennedy et al. (2017):

$$BVT_{BAC} = BVT_{RSSCT,normalized} = \frac{BVT_{RSSCT,experimental}}{FI} \qquad \textit{Equation 7-2}$$

This will make the normalized RSSCT breakthrough curve steeper than the experimental breakthrough curve if FI > 1. As the fouling factor is unique to each TOrC, this adjustment reduces the total RSSCT BVT from 40,000 to a different BVT for each TOrC.

7.2.5.2 **RSSCT modelling in AdDesignS**

Modeling RSSCT results back up to 40,000 BVTs was accomplished using the pore and surface diffusion model (PSDM) in AdDesignS (AdDesignS 1.0, Michigan Technological University, USA), which is a finite element model utilizing the Freundlich isotherm to describe TOrC adsorption equilibrium in combination with the ideal adsorbed solution theory (Hockanson et al., 1999; Sotelo et al., 2014). The PSDM was manually calibrated with the following variables for each TOrC: molar volume at normal boiling point, initial averaged RSSCT influent concentration, and experimental RSSCT effluent breakthrough percentage with the corresponding normalized breakthrough time in days.

The Freundlich isotherm was used to describe the adsorption of organic compounds in aqueous solution onto activated carbon (Worch, 2012) and is described by Equation 7-3 ,

$$q = K * C^{\frac{1}{n}} \quad \textit{Equation 7-3}$$

where q is the mass of TOrC per mass GAC (ng/kg), K is the Freundlich adsorption coefficient (L/kg), C is the concentration of TOrC in the liquid phase (ng/L), and $\frac{1}{n}$ the dimensionless Freundlich exponent determining the shape of the isotherm curve. The exponent was set to 1 due to low TOrC concentrations in the presence of DOM in the system (Knappe et al., 1998; Graham et al., 2000; Corwin and Summers, 2011), which turned the isotherm linear.

The program also includes kinetic parameters. The surface to pore diffusion flux ratio (SPDFR) was set to near zero as surface diffusion was assumed to be negligible in adsorption systems containing DOM (Carter and Weber, 1994; Jarvie et al., 2005; Corwin and Summers, 2011; Chowdhury et al., 2013; Kennedy et al., 2017). Correlations coded into the program were used to determine kinetic parameters for each TOrC: the pore diffusion coefficient D_p was calculated using the Hayduk and Laudie correlation, the surface diffusion coefficient D_s was calculated using the Sontheimer correlation, and the film mass transfer coefficient k_f was calculated using the Gnielinksi correlation, used for spherical particles under laminar flow conditions (Hayduk and Laudie, 1974; Gnielinksi, 1978; Sontheimer et al., 1988). The value of both the D_s (~10^{-40} cm^2/s) and SPDFR (~10^{-30}, unitless) terms was negligible. The complete input parameters and associated equations are outlined in the SI.

7.2.5.3 **Model fit**

A local Freundlich adsorption coefficient K_{RSSCT} (for $BVT_{RSSCT,normalized}$) was first visually estimated from the PSDM fit. This K_{RSSCT} value was iteratively refined using Matlab until the K_{RSSCT} with the minimal root mean square error (RMSE) between the PSDM predicted breakthrough and the normalized RSSCT breakthrough was found. The RMSE calculation and explanation are outlined in the SI. The same K_{RSSCT} value was then used to fit the PSDM model to the BAC results.

7.2.5.4 **Mass balance verification of PSDM-modeled K_{RSSCT} with experimental results**

In order to determine how much DOC or TOrC mass was sorbed onto the carbon at the end of experimental run, an integral mass balance was performed according to equation S2.14 (Table 11-6), similar to the approach described in Corwin and Summers, (2011). However, the equation was solved for the maximum BT for each TOrC, as certain compounds did not reach 50% BT during the RSSCT experiment. When calculating the DOC concentration in the solid phase, the RSSCT BVTs were not normalized by the FI value. For mass balance calculation with TOrC concentration in the solid phase, the normalized BVTs were used to facilitate comparison with the PSDM-modeled K values. In addition, the mass balance from RSSCT data without BVT correction was calculated to compare with previously reported breakthrough in RSSCT experiments (Müller et al., 2019a). After plotting effluent concentration against throughput, the resulting breakthrough curve was integrated in Origin (OriginPro, version 2019) according to equation S2.14.

7.3 Results and discussion

7.3.1 Feed water quality and redox conditions

The use of tertiary WWTP effluent to continuously feed the BAC filter and RSSCT column proved challenging. DOC fluctuations in the BAC influent made a direct comparison between the constantly fed BAC filter and the batch-fed RSSCT difficult. The BAC filter was operated at oxic conditions (DO >1 mg/L) (influent = 5.8 ± 1.8 mg/L, effluent = 4.4 ± 1.9, n=46). Breakthrough of DOC and UVA_{254} (C/C_0 = 80%) in the BAC filter was reached within 5,000 BVTs, but was prone to fluctuations due to influent variability as mentioned (Figure 7-2). Breakthrough of DOC and UVA_{254} in the RSSCT was

reached within 5600 BVTs. Using a two sample t-test, the difference in influent DOC concentrations of the two systems was not statistically significant (BAC DOC = 8.0 ± 3.1, n=10, vs RSSCT DOC = 6.77 ± 0.2, n=3, $p < 0.05$), but the difference in UVA_{254} was (BAC UVA_{254} =17.9 ± 7.1, n=10 vs RSSCT UVA_{254} = 12.4 ± 0.1, n=3, $p < 0.0358$). As DOC and UV_{254} represent the sum of the organic matter competing for adsorption sites, their breakthrough is important to discuss in the context of TOrC removal. The two breakthrough curves of DOC from the BAC filter and the RSSCT column follow a similar trend until ~7,000 BVT (albeit BAC DOC breakthrough is ~10-20% lower than RSSCT breakthrough), after which RSSCT DOC breakthrough is consistently over 90% due to the batch feeding mode, whereas BAC DOC breakthrough notably oscillates due to changing influent DOC concentrations. When comparing the UV_{254} breakthrough, the entire breakthrough trend is similar, and no oscillation in the BAC filter (with the exception of ~21,000 BVT) is observed. As UV_{254} is a surrogate for mainly aromatic compounds, this more consistent breakthrough demonstrates the relatively quick saturation of adsorption sites by organic matter, regardless of fluctuating influent DOC concentrations. Coupled with the difference in DOC breakthrough, these graphs indicate that DOC removal initially due to adsorption is followed by removal via combined adsorption and biodegradation in the BAC filter.

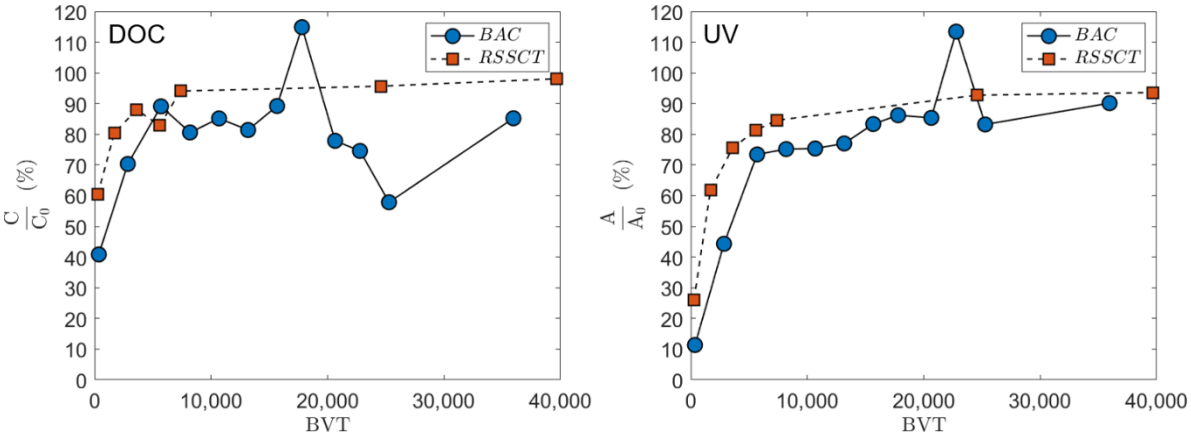


Figure 7-2: DOC and UV_{254} breakthrough comparison between the BAC filter and RSSCT column. RSSCT raw data (not normalized) is shown. For the integration approach, averaged DOC concentrations for the influents of BAC (5.0 mg/L) and RSSCT (6.77 mg/L) were used.

To verify this, the mass balance integration approach outlined in section 7.2.5.4 was used. In comparing the mass of DOC removed per mass GAC used for the RSSCT column (41,724 mg/kg) and BAC filter (79,699 mg/kg) normalized to the throughput, the DOC loading on the BAC filter was determined to be twice that of the RSSCT column. This is in line with the aforementioned lack of biological removal in the RSSCT, and further supports the claim that both adsorption and biological processes are removing the DOC in the BAC filter.

7.3.2 Adsorption prediction based on RSSCT results

As the fouling index adjustment reduced the RSSCT predictions to varying bed volumes, the compounds were initially classified based on the greatest common amount treated after adjustment, which was 10,000 BVTs. The PSDM modeling approach for scale-up to 40,000 BVT was then tested on the moderately sorbed and non-biodegradable compound primidone (Figure 7-3). After verification, it was applied to other compounds. Determined K_{RSSCT} values from the model were finally validated with results from mass balance calculations.

7.3.2.1 Adsorption classification

The adsorption results for the compounds of interested were separated into 3 groups. Compounds were classified as well (breakthrough<50%: citalopram, trimethoprim, atenolol, metoprolol, benzotriazole) (Figure 7-4) moderately (50%<breakthrough<75%: climbazole, phenytoin, tramadol, venlafaxine, primidone, diclofenac, carbamazepine) (Figure 7-5), or poorly (breakthrough > 75%: antipyrine, iopromide, sulfamethoxazole, gabapentin) adsorbed (Figure 7-6) at 10,000 adjusted RSSCT BVTs (Table 7-2).

When comparing adsorption classification from Table 7-2 with literature studies conducted with a variety of influent water qualities, varying DOC, and a range of EBCTs, all compounds which were well to moderately sorbed in this study displayed similar removal tendencies in literature. Among poorly sorbed compounds in this study, antipyrine was better removed according to literature data and sulfamethoxazole showed a range of removal efficiencies in literature. Iopromide and gabapentin were also classified as poorly adsorbing in most literature studies. Summarized results for all compounds are presented in Table 11-11.

Table 7-2: Summary of experimental and modeling parameters obtained for the RSSCT. Compounds ordered based on increasing RMSE.

TOrCs	**RSSCT adsorption classification at 10,000 normalized BVT**	**PSDM model on normalized RSSCT data**		**Mass balance comparison**		
		K_{RSSCT} (L/g)	RMSE (-)	This study $K_{MB,\ normalized}$	This study $K_{MB,\ experimental}$	Müller et al., 2019 K_{MB}
Venlafaxine	Moderate	40	0.017	18	44	--
Tramadol	Poor	44	0.018	19	46	35
Carbamazepine	Moderate	34	0.024	15	48	37
Antipyrine	Poor	14	0.025	10	35	--
Primidone	Moderate-Poor	20	0.028	16	31	29
Climbazole	Moderate	55	0.032	22	58	--
Sulfamethoxazole	Poor	12	0.033	12	20	26
Atenolol	Well	130	0.033	29	57	39
Trimethoprim	Well	141	0.037	44	52	40
Metoprolol	Well	136	0.037	23	60	40
Citalopram	Well	227	0.039	33	63	41
Diclofenac	Moderate-Poor	20	0.043	16	28	31
Gabapentin	Moderate	0.85	0.044	2	8	9
Phenytoin	Moderate	37	0.061	20	42	33
Iopromide	Poor	30	0.061	33	13	5
Benzotriazole	Well	129.5	0.143	28	66	42

7.3.2.2 PSDM modeling and mass balance verification of modeled pseudo-Freundlich K values

Adsorption coefficients determined from the PSDM modeling of normalized RSSCT data are provided in Table 7-2. A graphical comparison of experimental, normalized, and modeled breakthrough is shown in Figure 7-3 for the moderately-poorly sorbed and non-biodegradable primidone and the moderately-poorly sorbed diclofenac, showing that the model fitting is accurate for non-well adsorbed compounds. Although classified as moderately-poorly sorbed, the breakthrough of primidone at 10,000 BVT was close enough to 75% that it was deemed suitable for comparison purposes. It should be noted that while the PSDM-modeled coefficients and coefficients obtained through integral mass balance are not directly comparable as they are determined via different principles (PSDM model fit to breakthrough data vs. integral mass balance after complete breakthrough), both are calculated from a multi-solute matrix and are therefore pseudo-Freundlich K values. Using RMSE as a basis for judgement, the PSDM seemed to predict breakthrough best for compounds which exhibited poor to moderate adsorption.

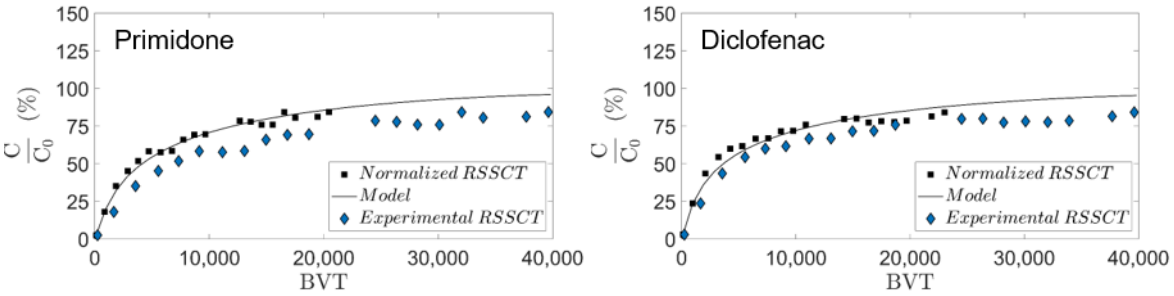


Figure 7-3: Fitting of the PSDM model to the experimental RSSCT, and comparison to the normalized RSSCT data for primidone and diclofenac.

To determine how reliable the PSDM-modeled K_{RSSCT} was, the mass balance integration described in section 7.2.5.4 was conducted for RSSCT breakthrough data. After calculating the mass in the solid phase, the adsorption coefficient K_{MB} was solved for using the Freundlich isotherm (Equation 7-3) and compared to the PSDM-modeled K_{RSSCT}. The mass balance was initially performed on FI-normalized RSSCT BVTs, to compare to the PSDM prediction. However, in order to compare with previous RSSCT results, this approach was also applied to non-normalized data from this study and from experiments by Müller et al. (2019a) conducted with effluent from the same WWTP as feed water. All results are shown in Table 7-2.

The PSDM-modeled K_{RSSCT} was greater than the mass balance K_{MB} for all compounds except iopromide, which can be explained by its low FI value (0.40, Table 11-8). Although carbamazepine displays moderate adsorption, the very short EBCT in this study likely negatively affected the adsorption potential, and could have caused the PSDM to underestimate the true K value. In this study, the greatest percent difference between K values predicted from PSDM and mass balance approaches was observed for the well adsorbed compounds atenolol, trimethoprim, metoprolol, citalopram, and benzotriazole, with a 66% difference on average. The moderately adsorbed compounds diclofenac, venlafaxine, carbamazepine, primidone, climbazole, phenytoin, and tramadol exhibited a 45% difference on average, and the poorly sorbed compounds sulfamethoxazole and antipyrine exhibited a 14% difference on average. The ratio between the experimental and normalized mass balance K values is equal to the compound FI. As gabapentin exhibited almost immediate breakthrough and the iopromide FI was the

lowest of any compound, they were omitted when calculating the average percent differences mentioned above. Conclusions in regards to adsorption modeling for these two compounds should be made with caution.

Possibly due to higher effluent concentrations of these chemicals due to lower removal, or because breakthrough of these compounds is less influenced by the estimated mass transfer or kinetic parameters, the difference is more likely attributed to the mass balance integration approach. Not all well adsorbing TOrCs reached 50% breakthrough at the end of the RSSCT: benzotriazole, metoprolol, citalopram, and atenolol BT was ≤51% and trimethoprim BT was 61%. Compounds which reached ≥80% BT (gabapentin, iopromide, antipyrine and sulfamethoxazole) showed a notably lower difference (14% on average). Since the integration was performed to the maximum BT achieved for each compound, rather than the 50% BT mentioned in Corwin and Summers (2011), this possibly underestimated the GAC adsorption capacity and the removal of the better adsorbing compounds. This is evident in the 66% difference on average between K_{RSSCT} and K_{MB} for benzotriazole, metoprolol, citalopram, atenolol and trimethoprim.

Notable differences in RSSCT experiment design between this study and in Müller et al. (2019a) include bed volume (Müller et al. (2019a): 6 cm^3, this study: 2.26 cm^3), EBCT (22 seconds vs 3.8 seconds), and percent breakthrough at the end of the experiment for each chemical, among other factors. Despite these design differences, the mass balance results show K values in similar ranges for both experiments. In comparison to Müller et al. (2019a), K_{MB} values obtained from experimental values in this study were greater for all chemicals except gabapentin, diclofenac, and sulfamethoxazole. Similar to the comparison with PSDM-modeled results, differences were also greatest for well adsorbed compounds, with a 39% difference on average, while moderately and poorly adsorbed compounds exhibited 14% and 4% difference on average. This leads to the overall conclusion that while both the PSDM modeling and mass balance approaches to calculating pseudo-Freundlich K values showed similar results, both approaches agreed more for moderately to poorly adsorbing compounds. These implications are discussed later.

The calculation of the solid phase concentration showed that the mass balance approach is useful for comparing results of different studies. Further comparison of the modeled and calculated pseudo-Freundlich K values with other studies reporting K values for WWTP effluents would be ideal. However, studies investigating K values either derived them from drinking water, surface water, or pure water matrices (Nam et al., 2014; Zietzschmann et al., 2016; Aschermann et al., 2018) did not report an exponent or K value (Sotelo et al., 2014; Altmann et al., 2015, 2016; Jeirani et al., 2017; Aschermann et al., 2018), or reported K values far from the results of this study (Sotelo et al., 2012; Delgado et al., 2019; Varga et al., 2019), as K values obtained from pure water matrices are 1-2 orders of magnitude greater than in WWTP effluent (Guillossou et al., 2020). Ideally, complete breakthrough of compounds is required for calculating Freundlich K values, which may be difficult to obtain from literature. To enable comparison across experiments, future studies of adsorption in real WWTP effluent are encouraged to report values for both variables of the Freundlich equation.

7.3.3 BAC modeling for biodegradation estimation

After calculating the K_{RSSCT}, the PSDM was used to predict breakthrough in the BAC filter, to estimate how much removal would have been seen in the BAC filter only due to adsorption. To accomplish this, most parameter values from the RSSCT modeling prediction were carried over to the BAC modeling. However, run time, flowrate, initial concentration, tortuosity, and effluent concentrations were adjusted to BAC values (see Table 11-9). Run time was adjusted to 155 days and flowrate and influent concentration were averaged over the longer time period, resulting in one flowrate value and one influent concentration for each chemical. Using the correlation coded into AdDesignS, tortuosity was set to 1 when run time is ≤70 days, then calculated using equation 5 in Table 11-10 to be 1.81 for the BAC run

time of 155 days. Experimental effluent breakthrough values for each individual BVT were loaded into AdDesignS. Afterwards, the PSDM was run and produced a predicted breakthrough curve for the BAC column. Measured results at 544 BAC BVTs were determined to be an outlier and excluded from the modeling, as the concentrations were outside the third quartile when using the interquartile range rule for 12 of the 16 investigated compounds. All modeling parameters are provided in the SI.

While the K values determined from the model are specific to assumptions taken in the experiment and the PSDM model, results in Figures 7-4-7-6 confirm that the PSDM predicted BAC breakthrough (denoted by a black line in Figures 7-4-7-6) fits well to the experimental RSSCTs data. To determine which compounds are likely being removed by biodegradation, the observed BAC breakthrough (adsorption and biodegradation, denoted by blue diamonds in Figures 7-4-7-6) was subtracted from the PSDM predicted BAC breakthrough (only adsorption) for 10,900 – 38,348 BAC BVTs (n=8-9). As the PSDM model outputs a text file of point values instead of an equation, the closest PSDM BVT for each individual BAC BVT was identified for the calculation. The difference was evaluated using a student's two sample t-test. This led to identifying 3 groups: 1) compounds for which biodegradation was not observed, 2) compounds for which the difference potentially caused by biodegradation was insignificant, and 3) compounds for which the difference was significant.

Compounds for which biodegradation was not observed include metoprolol, sulfamethoxazole, phenytoin, primidone, iopromide, atenolol, and trimethoprim. This also includes compounds where observed breakthrough was even higher than PSDM predicted adsorption-only breakthrough. Apart from metoprolol, all other compounds showed BT > 100% in at least 3 of the 8-9 sampling points evaluated (no statistical outliers). Phenytoin and primidone breakthrough fit well to the PSDM model, as both are resistant to biological treatment (Heberer, 2002; Müller et al., 2017; Hermes et al., 2019). In a biofilter study, atenolol exhibited high removal (90%), trimethoprim and iopromide exhibited moderate removal (50 ± 30% and 60 ± 20%), and metoprolol and sulfamethoxazole exhibited low removal (20 ± 10%) (Hermes et al., 2019), albeit at a notably higher operational EBCT of 90 minutes.

Compounds which showed an insignificant difference between BAC filter breakthrough in comparison to PSDM predicted adsorption breakthrough include antipyrine, benzotriazole, citalopram, and climbazole. Although other studies have found a good adsorption tendency and a poor biodegradation tendency for antipyrine (Sun et al., 2018; Karakurt-Fischer et al., 2020b), the results observed here seem to indicate that biodegradation contributes to removal (Figure 7-6). Benzotriazole showed moderate removal (30 ± 10%), while citalopram showed poor removal (10%) in 90 min EBCT (Müller et al., 2017; Hermes et al., 2019). Based on these results, a significant contribution of biodegradation would not be expected for the current setup, which tested a much lower EBCT of 4-10 min. The current study found similar or slightly higher removal for benzotriazole and higher removal for citalopram (Figure 7-4) than prior work (Müller et al., 2017; Hermes et al., 2019). This is likely attributed to the high removal by adsorption during the initial operation of the BAC filter, since both benzotriazole and citalopram were classified as well adsorbed in Table 7-2.

Compounds for which the difference was significant were gabapentin, diclofenac, venlafaxine, tramadol, and carbamazepine. Gabapentin is moderately to well biodegraded (Hellauer et al., 2017, 2019; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) and very redox sensitive, with greatest degradation occurring under oxic conditions (Hellauer et al., 2017; Müller et al., 2019d, 2019c). Diclofenac is well biodegraded in certain systems (Wiese et al., 2011; Regnery et al., 2016; Hellauer et al., 2017) but not in others (Müller et al., 2017; Karakurt-Fischer et al., 2020b), and the current approach suggests that biodegradation is likely contributing to removal in this system (Figure 7-5). Both compounds were moderately to poorly adsorbed in this study, in line with literature results (see Table 11-11). The complete RSSCT breakthrough of gabapentin, along with its susceptibility for

biodegradation under oxic conditions, supports the conclusion that biodegradation was likely occurring in the BAC filter. It should be noted that during the June–December operation of the BAC filter, a seasonal influent water temperature decrease and influent DO concentration increase was observed. During the latter stages of operation, increased clogging and consequentially EBCT led to lower DO concentrations in the BAC column effluent during the time between the last two BVTs, possibly impacting the removal of redox-sensitive compounds.

Based on literature data, the results for venlafaxine, tramadol, and carbamazepine were unexpected. Both venlafaxine and tramadol were poorly removed in biofilter studies with HRTs between 1.5-13 hours (Müller et al., 2017; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) but well biodegraded in systems with HRTs of several days (Hellauer et al., 2017, 2018b, 2019). Venlafaxine breakthrough in this study seems to suggest removal via biodegradation after 10,000 BAC BVTs, reaching PSDM predicted breakthrough by ~32,000 BAC BVTs. Tramadol removal in this study is also greater than in the mentioned literature. Although carbamazepine has been characterized as a highly sorptive (Snyder et al., 2007; Reungoat et al., 2011; Sperlich et al., 2017; Sbardella et al., 2018; Sun et al., 2018; Müller et al., 2019a; Guillossou et al., 2020) but not biodegradable compound, the visual difference between BAC and PSDM suggests that carbamazepine is also removed via biodegradation. However, it is far more likely that all 3 compounds are still adsorbing to an even greater extent than predicted by the RSSCT experiment. Therefore, estimated contributions of biodegradation to the removal of other compounds (diclofenac, gabapentin) should be carefully evaluated and validated with other methods, such as detecting biodegradation transformation products.

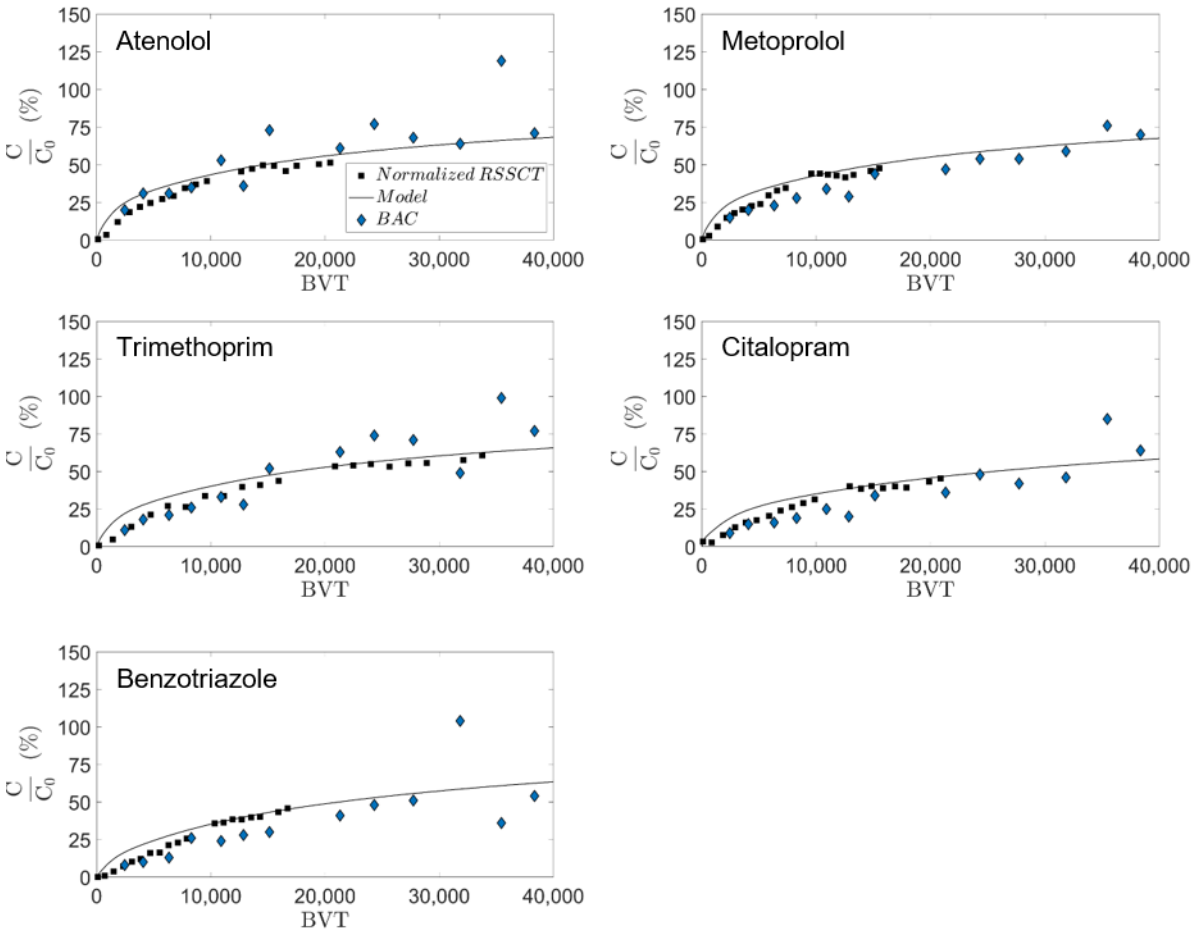


Figure 7-4: TOrCs well adsorbed at 10,000 RSSCT BVTs (breakthrough <50%): metoprolol, atenolol, trimethoprim, citalopram, and benzotriazole. Blue diamonds denote experimental BAC breakthrough, black squares denote normalized RSSCT breakthrough, and black line denotes the PSDM predicted BAC breakthrough.

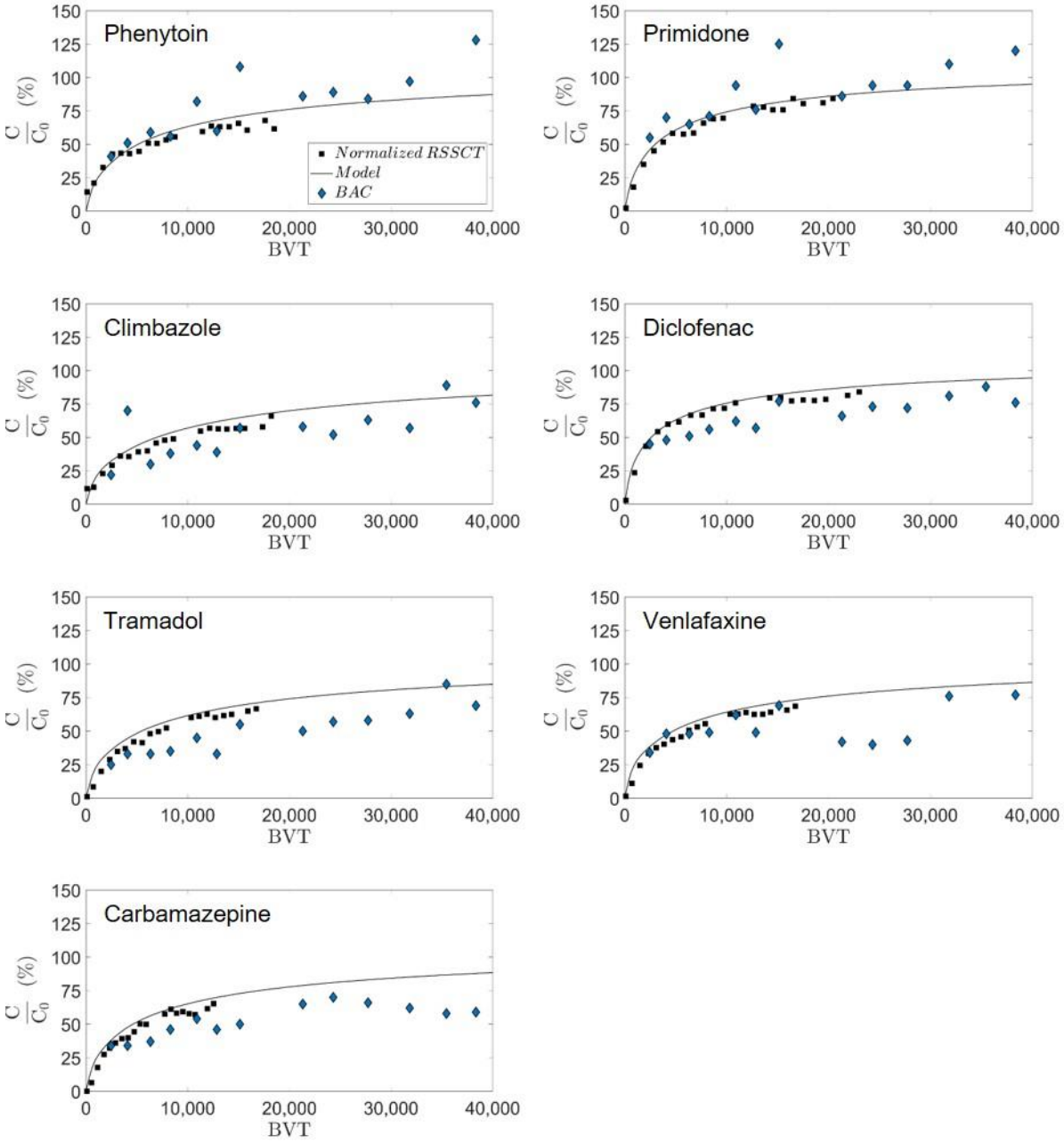


Figure 7-5: TOrCs moderately adsorbed onto RSSCT at 10,000 BVT (50%<BT<75%): phenytoin, primidone, climbazole, diclofenac, tramadol, venlafaxine, and carbamazepine. Blue diamonds denote experimental BAC breakthrough, black squares denote normalized RSSCT breakthrough.

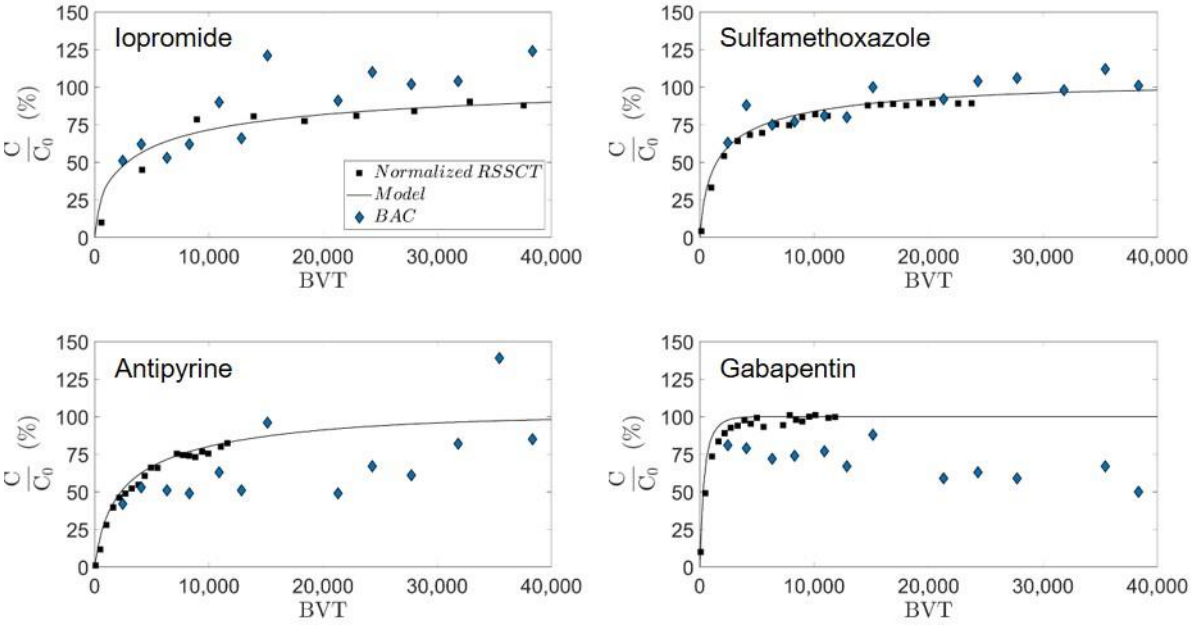


Figure 7-6: TOrCs poorly adsorbed onto RSSCT at 10,000 BVT (BT>75%): iopromide, sulfamethoxazole, antipyrine, and gabapentin. Blue diamonds denote experimental BAC breakthrough, black squares denote normalized RSSCT breakthrough, and black line denotes the PSDM predicted BAC breakthrough.

7.3.4 Implications for future research

Applying RSSCT column experiments and PSDM modeling to predict adsorption in BAC filters at extended BVTs has some potential limitations.

If bed porosity changed after crushing, this would be reflected in the ratio of the dimensionless Stanton and Biot numbers, which is the basis of RSSCT scaling. Depending on the absolute value of these dimensionless numbers, the impact on the model output would vary. As the PSDM model results were fit to the RSSCT data (see section 7.3.2.2), the possibly small variations in porosity likely would not significantly affect the result of the model output. A detailed study on the influence of broad ranges of Biot and Stanton numbers on a similar fixed-bed adsorber model (HSDM) was published by Sperlich et al. (2008). Setting the Freundlich exponent to 1 for all TOrCs and making the adsorption isotherm linear, while justified when DOC concentrations are greater than TOrC concentrations, affected the results. Fixing the exponent has been attributed to discrepancies between experimental and modeled data, as the fixed slope of the breakthrough curve generated by the model is not reflective of the experimental data (Zietzschmann et al., 2014).

High fluctuations in breakthrough behavior for phenytoin, venlafaxine, and atenolol can be explained by feed water quality variability during long-term BAC filter operation. The PSDM model requires influent and effluent concentrations to be loaded into the program, and as all BAC filter influent concentrations were averaged to one value, this could have led to inaccuracies in the model prediction and therefore the comparison.

Since K_{RSSCT} was solved for in AdDesignS, a more precise approach would be to determine K for each compound by conducting single-solute isotherm tests, since the accuracy of film diffusion coefficients is critical, especially when predicting high removal (Yu et al., 2009). The likely disproportionately large effect of the kinetic parameter values on the modeling results due to the extremely short EBCT could be determined by conducting a scenario analysis and changing the values of D_s, k_F, K, and n and seeing how the PSDM prediction changes, which was outside the scope of this study. After modeling the

RSSCT breakthrough data using the PSDM, results suggested that the modeling was most accurate for moderately to poorly adsorbed compounds. This assumption is supported by the small RMSE values between the PSDM model and normalized RSSCT breakthrough curves for these compounds. Finding experiment-specific film diffusion coefficients and surface diffusion coefficients, instead of relying on correlations, could also improve the model fit to the experimental data (Ye et al., 2018).

Despite potential limitation of pseudo-Freundlich K values and high fluctuations for some compounds, the PSDM model agreed very well with experimental data from (normalized) RSSCT experiments. The poor alignment of the PSDM model with the BAC results for some compounds is due to compound-specific breakthrough difference between BAC and normalized RSSCT. Estimating fouling indices from compound-specific fouling factors could have contributed to this error, as the fouling factors were calculated using a LFER based on TOrCs which were not investigated in this study. While this approach showed good visual fit between PSDM model (for RSSCT data) and BAC for compounds such as sulfamethoxazole, metoprolol and primidone, it did not provide an accurate prediction for other non-biodegradable compounds. Prior studies calculating fouling factors utilized a more narrow range and larger values (Y = 0.6-0.8 (Kennedy et al., 2017)) than the range of fouling factors calculated in this study (Y = -0.44-0.59 (Table 11-8)).

While compound characteristics have not been extensively discussed in this study, it is clear that log D, charge and pKa, among other chemical characteristics (Hermes et al., 2019), experimental parameters such as pH and temperature (Piai et al., 2020), and GAC characteristics (Worch, 2012; Hu et al., 2016; Guillossou et al., 2020) affect compound adsorption. Taking GAC aging into consideration through the use of a time-variable empirical function (Ye et al., 2018), which has not yet been applied for WWTP effluent matrices, could also be useful when comparing RSSCT results to BAC filters.

A potential solution to increase accuracy of compound-specific fouling index determination and avoid the multiple modeling steps could be to conduct a proportional diffusivity (PD) RSSCT instead of the CD-RSSCT used in this study. As PD-RSSCTs assume intraparticle diffusion decreases linearly with particle size, it could better account for DOM breakthrough when removal via biodegradation is not considered (Crittenden et al., 1991; Kennedy et al., 2017). This would involve setting the Reynolds number to 1 to ensure that intraparticle diffusion would be rate limiting and that external mass transfer and dispersion would not be greater in the RSSCT than in the large column (Worch, 2012), which would affect bed height and filter velocity. As PD-RSSCTs have shown better DOM and transformation product removal prediction, building upon the work of Kennedy et al. (2017) by conducting parallel PD-RSSCTs to more accurately calculate the fouling index of each TOrC could improve the model prediction.

7.4 Conclusion

A RSSCT was conducted to predict removal of numerous trace organic chemicals via adsorption to GAC. The RSSCT results were compared to results from a BAC filter operated in parallel to determine the relative contribution of biodegradation to TOrC removal. After correcting RSSCT results for adsorption overprediction, a PSDM model was constructed to predict adsorption through 40,000 BVTs. The modeled results were then compared to experimental BAC breakthrough.

Results revealed that the PSDM fit using AdDesignS predicted the breakthrough for poorly to moderately adsorbing compounds, such as venlafaxine, tramadol, and carbamazepine, the best. However, the comparison of PSDM results to BAC breakthrough indicated biodegradation of persistent carbamazepine, venlafaxine, and tramadol, which is very unlikely to occur for these compounds. Therefore, determining removal via adsorption by comparing RSSCT and BAC breakthrough was not possible. Recommendations for optimizing the predictability of the outlined approach are to

experimentally obtain more accurate individual fouling indices as well as to operate the BAC filter at longer EBCT.

CRediT authorship contribution statement

Veronika Zhiteneva: Conceptualization, Methodology, Software, Investigation, Formal analysis, Writing - original draft, Writing – review & editing, Visualization, Project administration. **Éric Ziemendorf**: Methodology, Software, Investigation, Formal analysis, Writing - review & editing. **Alexander Sperlich**: Methodology, Visualization, Writing - review & editing. **Jörg E. Drewes**: Writing - review & editing, Funding acquisition. **Uwe Hübner**: Conceptualization, Methodology, Resources, Visualization, Writing - review & editing, Funding acquisition.

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Notes

The authors declare no competing interests.

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In conclusion, **Hypothesis 3.1 –** Rapid small scale column tests (RSSCTs) can accurately differentiate between TOrC removal attributed specifically to biodegradation and to adsorption – **could not be fully tested**, as the RSSCT approach for determining the contribution of adsorption to removal in a BAC filter requires optimization to better compare the RSSCT and BAC filter.

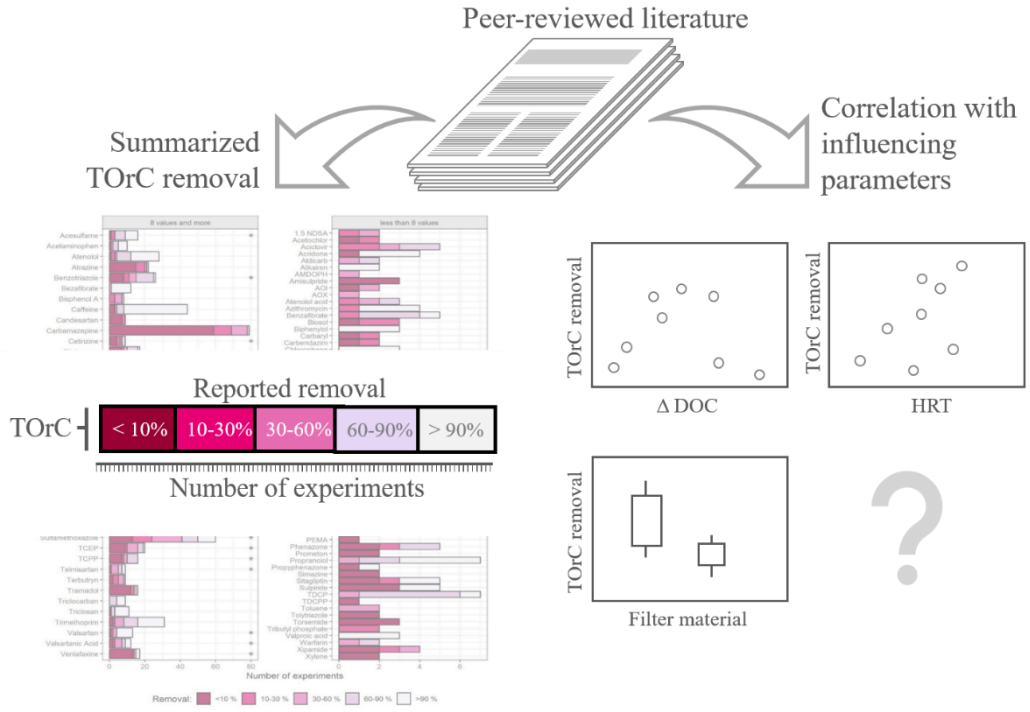
8. Varying attenuation of trace organic chemicals in natural treatment - A review of key influential factors

This paper has been published with editorial changes as follows:

Filter, J.+, Zhiteneva, V.+, Vick, C., Ruhl, A.S., Jekel, M., Hübner, U., Drewes, J.E. 2021. Varying attenuation of trace organic chemicals in natural treatment - A review of key influential factors. *Chemosphere*, 274, 129774. https://doi.org/10.1016/j.chemosphere.2021.129774

Abstract

The removal of trace organic chemicals (TOrCs) from treated wastewater and impacted surface water through managed aquifer recharge (MAR) has been extensively studied under a variety of water quality and operating conditions and at various experimental scales. The primary mechanism thought to dictate removal over the long term is biodegradation by microorganisms present in the system. This review of removal percentages observed in biologically active filtration systems reported in the peer-reviewed literature may serve as the basis to identify future indicators for persistence, as well as variable and efficient removal in MAR systems. After conducting a review of removal percentages observed in biologically active filter systems reported in the peer-reviewed literature for 901 lab-scale and 351 field-scale experiments, a noticeable variation in reported removal percentages (standard deviation above 30%) was observed for 24 of the 49 most commonly studied TOrCs. Such variations suggest a rather inconsistent capacity of biologically active filter systems to remove these TOrCs. Therefore, operational parameters such as the change in dissolved organic carbon (ΔDOC) during treatment, hydraulic retention time (HRT), filter material, and redox conditions were correlated to the associated TOrC removal percentages to determine whether a data-based relationship could be elucidated. Interestingly, 11 out of the 24 compounds demonstrated increased removal with increasing ΔDOC concentrations. Furthermore, 10 compounds exhibited a positive correlation with HRT. Based on the evaluated data, a minimum HRT of 0.5-1 day is recommended for removal of most compounds.



Chapter 8: Varying attenuation of trace organic chemicals in natural treatment
- A review of key influential factors

8.1 Introduction

With increasing population growth as well as reduced natural discharge of rivers and increased evapotranspiration due to climate chance impacts, the relative contributions of wastewater treatment plant (WWTP) effluents discharged into surface water bodies can become significant, most notably in years with extended dry periods (Karakurt et al., 2019). As a consequence, more trace organic chemicals (TOrCs) have been detected in watersheds globally (Tran et al., 2019). TOrCs include numerous classes of chemicals, such as pharmaceuticals and personal care products, and their removal in wastewater treatment has been the focus of many studies and research groups in the last decades. Treatment barriers critical for reducing their presence in the environment include wastewater treatment plants (Alvarino et al., 2018; Tran et al., 2018) and advanced water treatment processes, such as activated carbon (Benstoem et al., 2017; Guillossou et al., 2019), membrane processes (Snyder et al., 2007), ozonation and advanced oxidation processes (Lee and von Gunten, 2016; Miklos et al., 2019), biological activated carbon or sand filtration, and moving bed biofilm reactors (Falas et al., 2012; Gerrity et al., 2011). Natural treatment systems, such as managed aquifer recharge (MAR) including soil-aquifer treatment, aquifer recharge and recovery or induced bank filtration, where water is infiltrating through a vadose zone into a saturated aquifer can also achieve further TOrC removal via adsorption and biodegradation (Rauch-Williams et al., 2010). In contrast to engineered systems, where operational parameters can be optimized to select for maximum removal (Karakurt-Fischer et al., 2020b; Regnery et al., 2016), TOrC fate and transport in natural treatment systems is more difficult to control. Understanding how individual factors influence compound removal can help improve removal and reduce TOrC concentrations in the environment.

Numerous studies have identified relevant parameters for TOrC removal in these natural treatment systems, including but not limited to the concentration and composition of biodegradable dissolved organic carbon (BDOC), redox conditions, subsurface material composition, and hydraulic retention times (HRT). Although individual studies usually provide clear trends, a direct comparison of studies often leads to inconclusive or contradictory results. For example, some studies demonstrated that removal efficiency of target substances is independent of pre-adaptation (Alidina et al., 2014a) while others observed significant adaptation to target compounds (Baumgarten et al., 2011). Hoppe-Jones et al. (2012) showed efficient removal at both high and low BDOC concentrations.

This literature study aims to identify TOrCs exhibiting strongly varying removal tendencies and correlate their removal with relevant parameters affecting the biodegradation of TOrCs in MAR treatment systems. Although removal might also be influenced by numerous other variables, this study focused on the effects of BDOC, predominant redox conditions, media material and HRT, as these potential influencing factors were reported in most studies.

8.2 Methods

8.2.1 Literature review

A comprehensive review of the peer-reviewed literature regarding the biological degradation of TOrCs in MAR systems was conducted. Google Scholar and OPACplus were used to search for studies using lab-, pilot-, or field-scale experiments with technical or natural filter material. Combinations of strings using the terms ‘biological removal’, ‘biological degradation’, ‘trace organic chemicals’, and ‘TOrCs’ were used to collect peer-reviewed literature published between 2010-2018. For inclusion into this review, the study must have focused on TOrC biodegradation and provided sufficient information about the observed removal percentage, the change in DOC concentration (ΔDOC), redox conditions, and HRT. After screening abstracts and then full-length documents for the aforementioned parameters, as well as inclusion of 16 studies published before 2010 or in 2019 as grey literature, a Microsoft Excel™ database comprised of 1,476 entries from 39 studies covering lab-scale column (901 entries), field-scale

(351 entries), and batch (139 entries) experiments was compiled. The full list of chemicals and parameters is provided in the SI (section 11.5).

8.2.2 Data processing and analysis

The reported removal percentages of TOrCs in these studies were compared to the corresponding filter material, redox condition, HRT, and ΔDOC concentrations to determine whether a significant relationship between compound removal and influencing factor could be derived. When only a removal range was given, the mean value was calculated and used for further analysis. Many studies use the term 'BDOC' to describe the biodegradable dissolved organic carbon by subtracting effluent DOC from influent DOC, despite the existence of a defined protocol for accurate determination of BDOC (Servais et al., 1989). Therefore, this study will denote the reported removed DOC (i.e., $DOC_{influent}$-$DOC_{effluent}$) as ΔDOC, even if cited literature used the term 'BDOC'. Filter materials were classified as natural material taken from environmental samples (native soil, riverbed sediments or aquifer samples), or fresh technical filter material including sand, anthracite, or a mixture of anthracite and sand, which usually was exposed to feed water for a specific time prior to conducting the experiments. For correlation analysis, studies were classified simply as either natural or technical filter material to have more independent data points. As many studies reported the results of multiple experiments in a single paper, the number of experiments was chosen to denote the actual quantity of individual experiments performed per chemical. For 117 entries in the database (8% of total entries), information on HRT was only reported as empty bed contact time (EBCT), which was converted from minutes to days and multiplied by 0.45, assuming a bed porosity of 45% to obtain a conservative estimate (DVGW, 2015).

To identify the most inconsistent compounds for further investigation, two statistical parameters were used. Compounds for which the number of experiments (N_{exp}) was ≥ 8, and for which the standard deviation of removal percentage (sd) was greater than 30%, were classified as 'inconsistent' for correlation analyses. This definition ensured that enough data was available and that notable variation in the compound removal behavior was observed.

Multiple statistical tests and parameters were calculated for each inconsistent compound. To check if filter material influenced the removal, the removal percentage was compared to both materials and tested for differences in the mean values. To check if HRT or ΔDOC concentration influenced removal, a correlation analysis was conducted. The removal percentage data for every inconsistent compound was first tested for normality. When grouped by filter material, 20.8% of cases of removal percentage data were normally distributed. For correlation analysis, a bivariate normal distribution was indirectly tested by checking the univariate normal distribution of both variables. ΔDOC concentration and removal percentage (but only for technical material, see next paragraph) and HRT and removal percentage were normally distributed in 20% and 0% of all cases. Since normality was not present in most compound data sets, only non-parametric tests for all substances and groupings were employed to ensure better comparability. All graphs, data and results of normality tests are presented in the SI.

The Spearman's correlation coefficient (r_s) was calculated between the ΔDOC concentration and the removal percentage for technical filter material. Natural filter material was omitted from the correlation analysis, since desorption and biodegradation of particulate organic matter content could lead to interference with TOrC removal (see section 8.3.2). A Spearman's rank correlation coefficient was also calculated between the HRT and the removal percentage. No non-linear model between HRT and decay (i.e. 1st order kinetics or similar) was assumed or constructed due to a lack of similarity between experiments and a lack of data on individual time series.

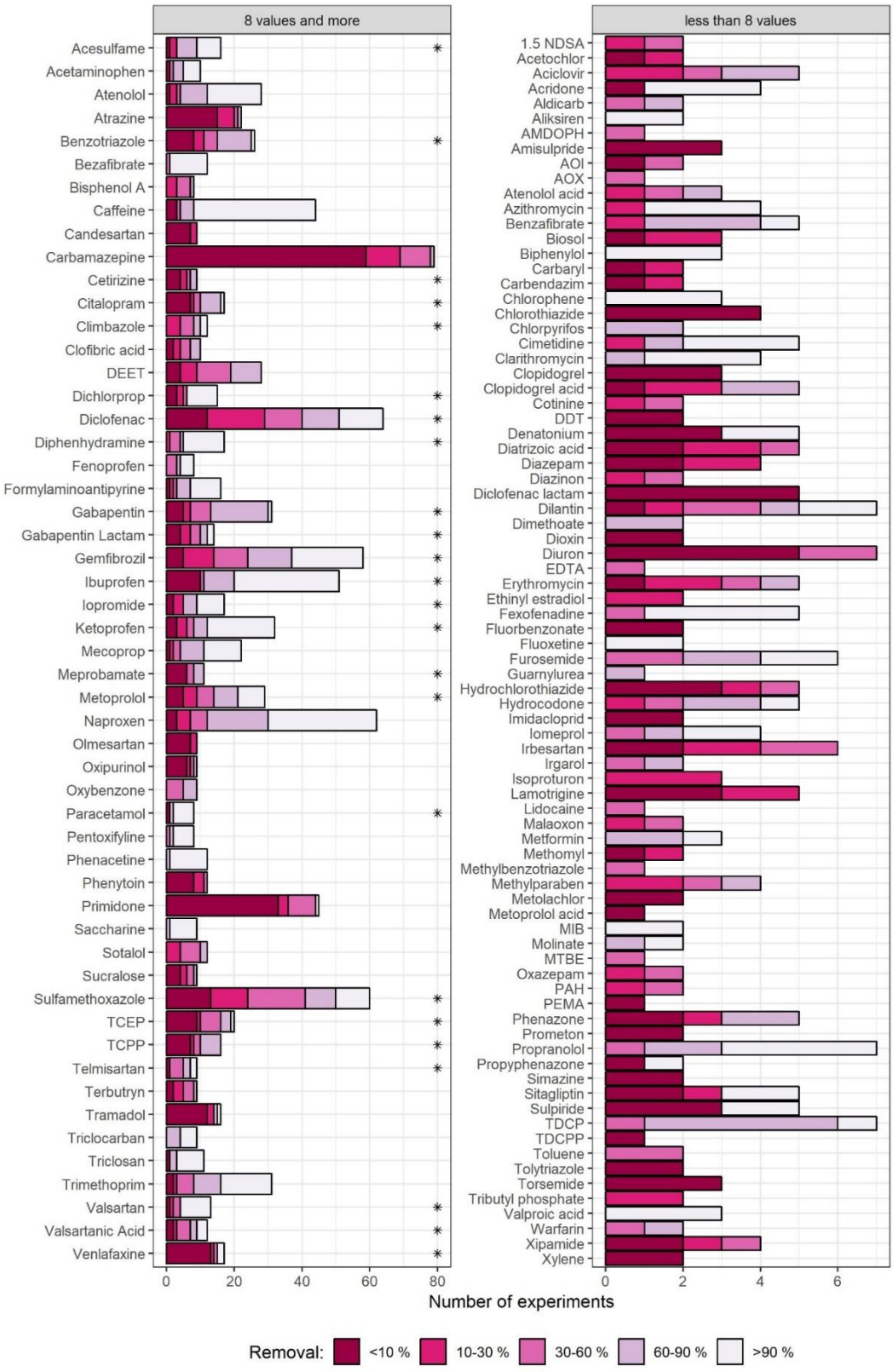


Figure 8-1: Removal results for compounds from the catalogued studies, with more commonly studied compounds depicted in the left column (N_{exp} > 8) and less commonly studied compounds in the right column. The star (*) denotes compounds for which the standard deviation in removals was above 30%.

Table 8-1: Correlation coefficients of inconsistent TOrCs. Bolded values denote significant correlation between the parameter and the TOrC.

Substance	ΔDOC Spearman r_s >0.5	HRT Spearman r_s >0.5	Filter material Wilcoxon test: p<0.05; natural (N) vs. technical (T)
Acesulfame	0.09	-0.18	**0.02 (T)**
Benzotriazole	**0.66**	-0.36	**0.00 (T)**
Cetirizine	**0.89**	**0.92**	0.05
Citalopram	**0.67**	**0.88**	0.06
Climbazole	**0.76**	**0.94**	-
Dichlorprop	-	0.24	-
Diclofenac	0.49	**0.55**	**0.00 (N)**
Diphenhydramine	-0.22	**0.79**	0.11
Gabapentin	**0.88**	0.03	0.29
Gabapentin Lactam	**0.82**	0.41	**0.03 (N)**
Gemfibrozil	-0.06	0.43	**0.00 (N)**
Ibuprofen	-0.10	0.33	0.17
Iopromide	**0.92**	**0.83**	0.05
Ketoprofen	0.25	0.1	0.51
Meprobamate	-	0.15	0.05
Metoprolol	**0.79**	**0.78**	**0.02 (N)**
Paracetamol	-0.47	-0.29	-
Sulfamethoxazole	**0.75**	0.36	0.23
TCEP	-	**0.52**	0.10
TCPP	-	0.27	0.30
Telmisartan	0.7	**0.78**	0.06
Valsartan	**0.87**	0.49	0.20
Valsartan acid	-0.87	0.04	0.74
Venlafaxine	0.47	**0.79**	0.10

Furthermore, to check if filter material had an influence on removal percentages, two-sided Wilcoxon rank-sum tests (i.e. Mann-Whitney tests) were conducted. The following null hypothesis (H_0) was used for the Wilcoxon test between material and removal percentage: there is no difference in the medians of removal percentages between experiments using natural or technical column material (equal medians). The alternative hypothesis (H_A) was that there is a difference in the medians of removal percentages, greater or smaller, when different column material was used (two-sided alternative). The null hypothesis was rejected when the H_0 p-value was less than $\alpha = 0.05$.

Data gathering and organization was done in Microsoft Excel™. All analysis and visual representation was performed in R (version 3.6.0, R Core Team, 2019).

8.3 Results and Discussion

8.3.1 TOrC classification

The removal percentages and the number of experiments per compound were plotted to determine how frequently compounds were studied (Figure 8-1). This analysis revealed that an impressive number of chemicals has been studied and that many of them exhibit varying degrees of removal. Well studied compounds included carbamazepine, diclofenac, naproxen, sulfamethoxazole, gemfibrozil, and caffeine, which were covered in more than 40 experiments in the 39 studies evaluated. Well-studied compounds showing consistent removal efficiency in most studies (standard deviation <30%) are recommended as future indicators for persistent behaviour (e.g. atrazine, carbamazepine, primidone, sucralose or tramadol) and efficient removal (e.g. atenolol, naproxen, trimethoprim) in MAR systems. As literature results show large discrepancies in removal behavior of several compounds, the inconsistent chemicals showing standard deviation of >30% are denoted with an asterisk in Figure 8-1. Inconsistent TOrCs include acesulfame, benzotriazole, cetirizine, citalopram, climbazole, dichlorprop, diclofenac, diphenhydramine, gabapentin, gabapentin lactam, gemfibrozil, ibuprofen, iopromide, ketoprofen, meprobamate, metoprolol, paracetamol, sulfamethoxazole, TCEP, TCPP, telmisartan, valsartan, valsartanic acid, and venlafaxine (24 of 160 substances). These compounds were chosen for further analyses to determine whether a relationship between the reported removal and one of the influencing factors could be established. All correlations are listed in Table 8-1.

8.3.2 Influence of redox conditions on removal

Redox conditions are often considered a crucial parameter in the biological transformation of TOrCs. The presence and concentration of DO in water dictates the degradation rate of chemicals by aerobic microorganisms. Sufficient levels of DO allow TOrC transformation under oxic conditions (Baumgarten et al., 2011; Massmann and Du, 2008; Regnery et al., 2015). Improved removals of numerous compounds under low DOC concentrations and oxic conditions have been shown at lab- as well as field-scale (Hellauer et al., 2019, 2018, 2017; Müller et al., 2017; Regnery et al., 2016). A comparison of dissipation time (DT_{50}) further supports the faster transformation of TOrCs under oxic conditions compared to anoxic conditions (Regnery et al., 2017a). Likewise, 1-2 orders of magnitude differences in biodegradation rate constants under oxic conditions for compounds such as naproxen, sulfamethoxazole, and triclosan often differ between batch, column, and field-scale experiments (Greskowiak et al., 2017). Oxygen consumption depends on other parameters such as ΔDOC or particulate organic carbon (POC), HRT, and temperature, which strongly affect the extent of oxic zones within the system. Even if low oxygen concentration is present in the influent, a small oxic zone might still be sufficient for catalyzing biotransformation of TOrCs.

In the present study, correlating the reported redox conditions with TOrC removals was not possible. The experimental redox regimes were often ambiguously reported in literature: sometimes only influent DO concentrations were reported and sometimes the regime was labeled simply as oxic or anoxic without specifying DO concentrations. Given the importance of redox conditions for TOrC biotransformation, proper characterization and distinction of redox zones, especially between oxic and anoxic zones in experiments is strongly recommended for future studies, which could be accomplished through higher resolution sampling along the flow path of the system but should at least include reporting of influent and effluent DO concentrations. In addition, anoxic conditions should be monitored by analysis of nitrate and nitrite concentrations in the samples. Although more recent studies have begun to provide more detailed redox zonation information (Burke et al., 2014; Hellauer et al., 2017; Müller et al., 2019), this amount of data could not be compared with the studies providing only influent

concentrations. Due to this limitation, a classification of different redox conditions as a basis for correlation analysis was not possible with available data.

8.3.3 Influence of ΔDOC on removal

Organic compound removal in MAR systems has been attributed to adsorption and biodegradation (Drewes et al., 2003; Regnery et al., 2017b). Microorganisms degrade organic matter present in the water by using organic compounds as their primary substrate and producing enzymes to metabolize them (Tran et al., 2013). Under oxic conditions, high concentrations of easily biodegradable primary substrate have been shown to result in more biomass, while the presence of poorly-biodegradable or refractory dissolved organic carbon can increase the structural and functional diversity of microorganisms (Alidina et al., 2014b; Li et al., 2014, 2013, 2012). Diversity of microorganisms has been shown to improve removal of certain TOrCs (Alidina et al., 2014b).

Hoppe-Jones et al. (2012) showed that while higher ΔDOC concentrations (>1.6 mg/L) were needed for initial microbial adaptation during groundwater recharge using reclaimed water, after acclimatization, efficient removal was also attained under lower ΔDOC concentrations (<1.0 mg/L) representing starving conditions. While some studies confirm this lag phase adaptation time, particularly for chemicals like sulfamethoxazole (Baumgarten et al., 2011) or acesulfame (Castronovo et al., 2017), other studies have shown that microbial pre-exposure to TOrCs does not increase their biotransformation, and microbial communities in MAR systems are robust regarding their removal capabilities to changes in influent water quality (Alidina et al., 2014a). Low carbon and oxic conditions have been confirmed to facilitate better removal of TOrCs at lab-, pilot-, and field-scales (Rauch-Williams et al., 2010; Regnery et al., 2016). However, a certain minimum biological activity might be required to initiate TOrC transformation.

Based on the hypothesis of co-metabolic degradation, studies have also attempted to distinguish how composition of DOC influences biodegradation of TOrCs (Alidina et al., 2014a; Rauch-Williams et al., 2010). According to this, primary metabolic degradation occurs when microorganisms use fractions of DOC or dissolved organic material (DOM) as their main carbon and energy source. Co-metabolism occurs when enzymes expressed during the degradation of the primary carbon leads to the transformation of TOrCs without an energetic or growth benefit for the bacteria (Alidina et al., 2014a). Alidina et al. (2014b) showed that changing the organic carbon composition by decreasing easy degradable peptone yeast and increasing refractory humic acids can enhance TOrC attenuation efficiency for select TOrCs. The assumption of co-metabolic degradation with increasing humic acid concentration, however, was not confirmed in subsequent research (Hellauer et al., 2019). Other studies indicated increased removal efficiencies of some TOrCs with higher biological activity indicated by ΔDOC and ΔDO measurements (Müller et al., 2019).

The ΔDOC in the investigated studies ranged from 0 to 9.2 mg/L. If not explicitly stated as 'BDOC' in the respective study, the ΔDOC was calculated from the reported $DOC_{influent}$-$DOC_{effluent}$ difference observed during the experiments. In this way, it only represents an approximate amount and does not necessarily equal the total amount of biodegradable DOC, since longer retention times or different redox conditions might lead to increased DOC decomposition. However, as the ΔDOC can affect TOrC removal, possible correlations for the inconsistent TOrCs were analyzed considering only the data from experiments with technical material. Experiments with natural material were omitted from the correlation analysis, as natural sediments might provide additional POC which can contribute to ΔDOC as a co-substrate or sorbent and thus distort the possible effects of ΔDOC on TOrC removal.

The oxic biodegradation of ΔDOC is associated with the consumption of oxygen, which influences the redox conditions in sediments. According to the molar mass ratio of molecular oxygen and carbon with

an assumed zero valence, 2.7 mg of oxygen are consumed during the oxidation of 1 mg C to CO_2. Using this estimated ratio, 4 mg/L ΔDOC in a saturated influent water (10 mg/L DO) would already result in anoxic conditions. If not all the oxygen in the influent water is consumed for ΔDOC degradation, the remaining oxygen could be used for the biological oxidization of possibly present POC. Therefore, decreasing influent DOC concentrations can extend the penetration of oxic conditions to deeper zones.

Although no generalization about the primary substrate concentration on TOrC removal could be made in this study, 11 of 24 inconsistent compounds showed a positive correlation (Spearman $r_s > 0.5$) between their removal and the reported ΔDOC. A possible change of redox conditions caused by high concentrations of biodegradable DOC might distort the correlations, especially at ΔDOC concentrations exceeding 4 mg/L. However, positive correlations were found for eleven compounds including climbazole, gabapentin, iopromide, metoprolol, sulfamethoxazole, and benzotriazole, among others (Figure 8-2). Illustrations of correlations for the remaining compounds can be found in the SI. The data indicates better removal of TOrCs with higher influent biodegradable DOC concentration, which is likely associated with increased organo-heterotrophic biomass and biological activity. This correlation was also observed by Schaper et al. (2019) for the biotransformation of many TOrCs in river sediments.

Iopromide displayed the greatest r_s, which was confirmed by a detailed study on its biodegradation dependence on ΔDOC and redox conditions by Müller et al. (2019b), demonstrating that a correlation between removal in technical filter material and ΔDOC concentration seems to exist across multiple studies. Gabapentin and benzotriazole exhibited similar enhanced transformation in the presence of higher DO consumption and ΔDOC, whereas metoprolol transformation efficiency was stable under varying substrate conditions (Müller et al., 2019). In contrast to this individual study, the correlation of metoprolol removal across multiple studies indicates that its removal improved with increasing microbial activity indicated by ΔDOC.

Furthermore, substrate characteristics and composition can play an important role for compound biodegradation. Alidina et al. (2014b) found that increasing the share of refractory carbon (e.g. humic substances) increased the removal of TOrCs such as atenolol, gemfibrozil and diclofenac. Onesios and Bouwer (2012) observed adverse effects of acetate spiking with increased removal of TOrCs like gemfibrozil under low (~50 µg/L acetate) compared to high (1,000 µg/L acetate) primary substrate concentrations. These results demonstrate the complex interaction of TOrC and DOC biodegradation in MAR systems and indicate that effects are highly compound and system specific. This conclusion is supported by the fact that removal of >50% of investigated compounds (including diclofenac and ketoprofen in Figure 8-2) did not show significant correlation with ΔDOC.

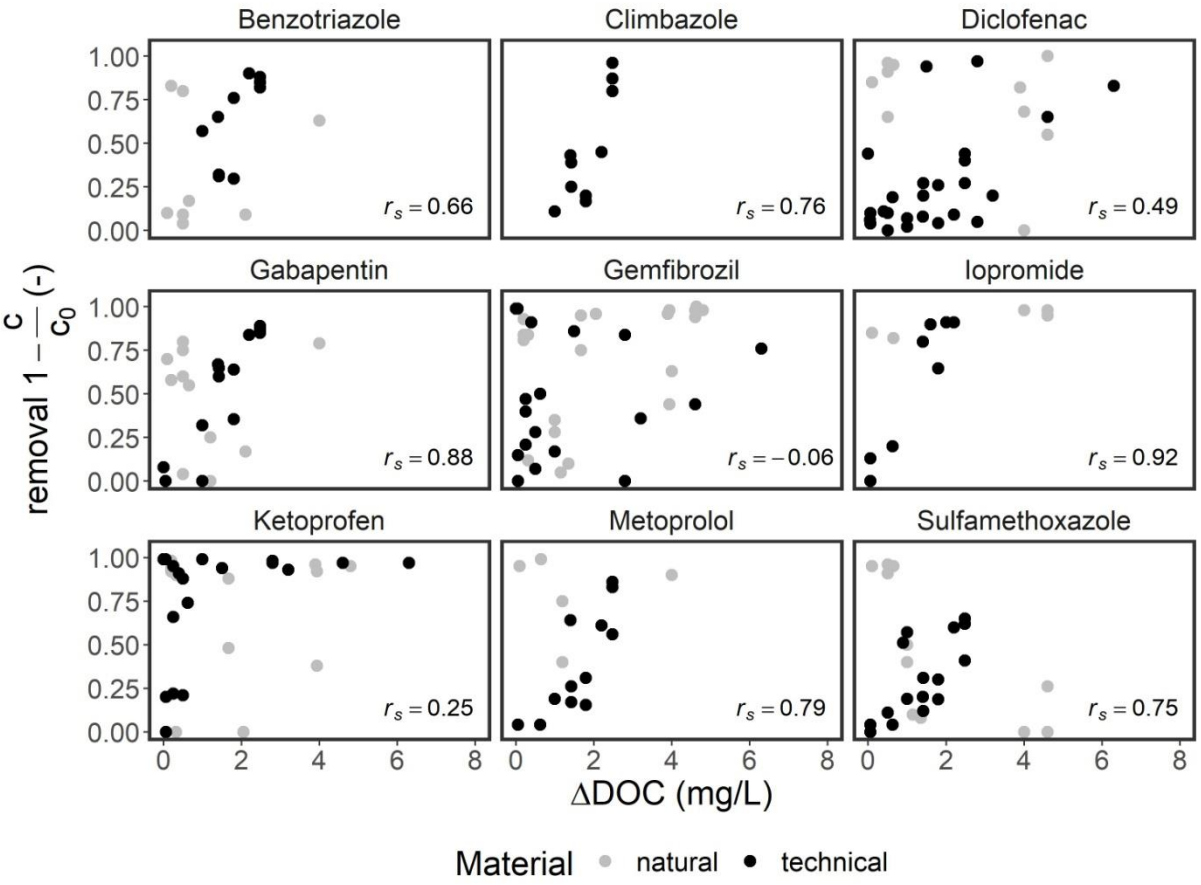


Figure 8-2: Scatterplot of feed water ΔDOC versus removal percentage. Statistical analysis was only performed on technical column material (denoted by black dots). Compounds were selected to demonstrate the range of correlations found.

Furthermore, substrate characteristics and composition can play an important role for compound biodegradation. Alidina et al. (2014b) found that increasing the share of refractory carbon (e.g. humic substances) increased the removal of TOrCs such as atenolol, gemfibrozil and diclofenac. Onesios and Bouwer (2012) observed adverse effects of acetate spiking with increased removal of TOrCs like gemfibrozil under low (~50 µg/L acetate) compared to high (1,000 µg/L acetate) primary substrate concentrations. These results demonstrate the complex interaction of TOrC and DOC biodegradation in MAR systems and indicate that effects are highly compound and system specific. This conclusion is supported by the fact that removal of >50% of investigated compounds (including diclofenac and ketoprofen in Figure 8-2) did not show significant correlation with ΔDOC.

8.3.4 Influence of hydraulic retention time (HRT) on removal

The time spent in the subsurface also affects the removal of chemicals, in conjunction with sorptive and biodegradative processes. Insufficient TOrC removal due to short HRT (several hours) might occur especially in technical systems as described by Karakurt-Fischer et al. (2020b) and Müller et al. (2017). Technical systems aim to treat large water volumes within a limited reactor space by decreasing the HRT, whereas soil-aquifer treatment systems and other MAR systems often operate with HRTs on the order of weeks and months (Zucker et al., 2015). A recent review of groundwater degradation rates at various experimental scales concluded that high uncertainty is associated with any type of rate constant prediction due to variability of several influencing factors (Greskowiak et al., 2017).

The HRT reported in literature ranged from several minutes to more than 100 days. In this review, the median reported HRT in field studies was 3 days, which was notably higher than the median HRT of

0.6 days in lab-scale column tests. This difference in resolution might contribute to the wide range of biodegradation rates for TOrC removal as reported by Greskowiak et al. (2017). To provide sufficient resolution of reported removals at low HRT, the data for the inconsistent compounds is shown using a logarithmic x-axis (Figure 8-3). Again, 10 out of 24 inconsistent compounds showed a positive correlation (Spearman $r_s > 0.5$) with HRT, revealing a higher removal with increasing HRT. The removal of several compounds including citalopram, climbazole, and metoprolol (Figure 8-3) is strongly correlated with HRT for HRT below 2 days (Spearman $r_s > 0.78$).

However, increased residence times often led to decreased oxygen availability, shifting redox conditions from oxic towards anoxic and influencing compound removal. This might be a reason for the weak correlations between removal and HRT for some compounds. Despite weak correlations, HRT could also be limiting for TOrCs like sulfamethoxazole and diclofenac, since less than 50% removal was observed in all studies with HRT below 0.1 day (2.4 hours). More efficient removal in several studies with longer HRT indicates that these compounds can be biodegraded if adequate redox and substrate conditions are applied. Removal of those compounds might be challenging for technical systems with limited HRT and their removal dependency on HRT has been suggested by Müller et al. (2017).

Benzotriazole, gabapentin, or gemfibrozil were not correlated with HRT albeit showing efficient removal in several studies at HRTs below 1 day. This indicates that other parameters are more relevant for their removal at short HRT. While redox sensitive degradation of gabapentin is well-documented ((Müller et al., 2019; Sperlich et al., 2017)), removal of benzotriazole was inconsistent in different systems with similar oxic and carbon-limited conditions (Hellauer et al., 2019). For some compounds, such as TCEP, available data was not sufficient to draw substantial conclusions (or hypotheses) on dependency of removal on HRT.

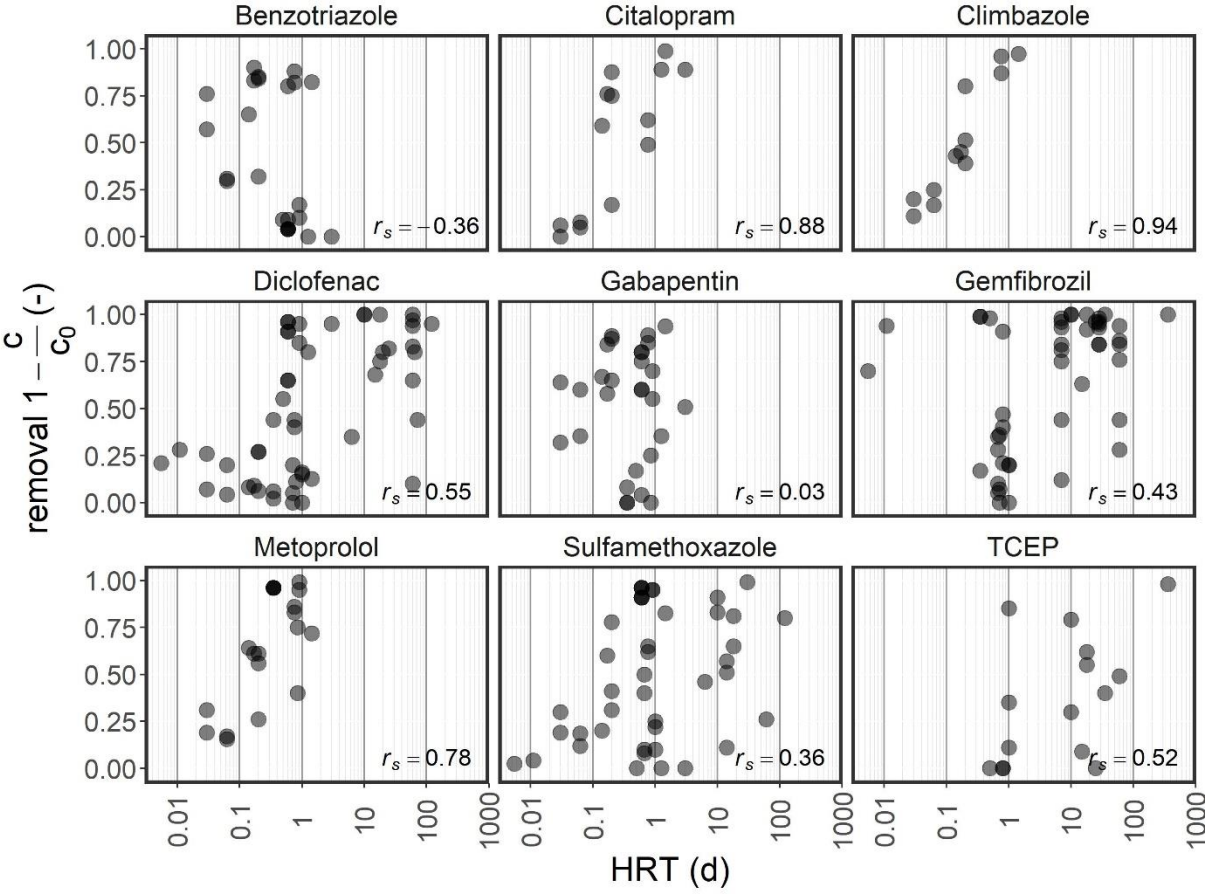


Figure 8-3: Reported TOrC removals on the linear y-axis plotted against corresponding HRT on the logarithmic x-axis. Points are displayed with 50% transparency to show overlapping data, with darker points signifying more than 1 study with similar results.

8.3.5 Influence of filter material on removal

The materials used in the analyzed studies can be classified into technical (379 entries) and natural material (621 entries). Natural materials were taken from the environment and include riverbed sediments, soils or sand from MAR sites, which could contain POC and are expected to generally display a more diverse microbiome, whereas technical material refers to technically cleaned and sieved sand or anthracite for commercial use as filter material. Although not explicitly considered in the meta-analysis of this study, adaptation and growth of the biofilm is an important factor which influences how quickly steady-state removal can be observed. However, this study did not factor in pre-adaptation or media age at the time of sampling.

Comparing TOrC removal in the different filter materials, only 6 out of 24 compounds demonstrated a significant difference in removal between natural and technical material (all results in Table 8-1). A potential reason for better removal in natural material could be increased biodiversity from long-term exposure to environmental conditions (Alidina et al., 2014a). Although the dominant removal mechanism in natural treatment systems is considered to be biodegradation, simultaneous removal by adsorption onto sediments or biofilm should not be neglected. Removal via adsorption is relevant for systems with natural sediments or sand with particulate organic matter. Adsorption is governed by polarity (described by logD which is pH dependent), solute charge, cation exchange capacity, pH, and chemical and media charge (Biel-Maeso et al., 2019). Retardation factors (Rf) (Alidina et al., 2015; Schaper et al., 2019) and distribution coefficients (Kd) (Alidina et al., 2014b) can assist in determining whether a compound is predisposed to adsorption. As adsorption is governed by the equilibrium between adsorption capacity of the material and the concentration of the chemical in the liquid phase, the contact time and the concentration of potential co-adsorbents are important.

However the differentiation between biological and adsorptive TOrC removal is challenging. The influence of adsorption can be estimated by breakthrough curves, batch tests with the respective filter material or quantifying the removal of non-biodegradable compounds with low polarity such as carbamazepine, as done in prior studies (Bertelkamp et al., 2014; Müller et al., 2017). The removal of diclofenac, gemfibrozil, benzotriazole, acesulfame, gabapentin lactam and metoprolol (Figure 8-4 and in SI 11.5) in natural and technical media is significantly different, and material preference can be visually deduced from the median line of the box plot for each compound. For the majority of compounds the filter material was not considered to be a major influencing factor for biological removal. However, especially when assessing removal in technical material, the amount of independent experiments must be critically considered. Therefore, colored graphics in the SI display the study origin of each data point. Additionally, it should be noted that a lack of significant difference does not necessarily mean there is no difference in removal between the media type. The dataset provided could be too small to adequately differentiate between media types.

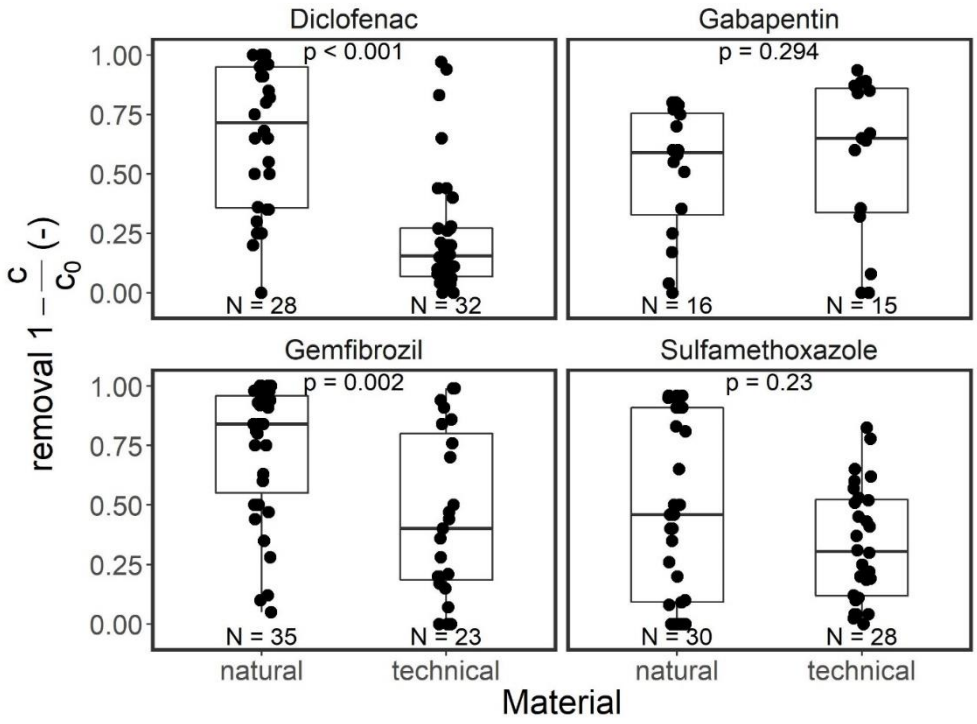


Figure 8-4: Impact of filter material on relative removal of diclofenac, gabapentin, gemfibrozil and sulfamethoxazole, with the N value denoting the number of data points available for each media.

8.4 Conclusion

The reported removals of TOrCs in biological systems can show strong discrepancies. In this study, 24 TOrCs were identified which might be challenging for biologically active filter systems due to their variable removals reported in the literature. Detailed analyses of influencing factors ΔDOC concentration, HRT, filter material and redox conditions revealed potential options for improving the removal of the 24 TOrCs.

In general, results from literature showed highly system- and compound-specific behavior. ΔDOC concentration seems to be a crucial parameter for TOrC removal, since nearly half of the 24 inconsistent TOrCs showed a better removal with increasing ΔDOC concentration (i.e. increasing biomass or activity). A minimum HRT of 0.5-1 day can be recommended for most compounds. Furthermore, an increased HRT can improve TOrC removal especially for compounds like diclofenac or sulfamethoxazole if favorable conditions for their removal are applied. Preferences for filter material could not be determined from the Wilcoxon rank-sum tests. The findings in this study were inferred based on 1,252 lab- and field-scale experiments and the evidence was weighed accordingly. Upscaling is a problem for many technical systems and the transferability of the findings to other treatment sites could be part of future studies.

The list of well-studied compounds identified in this study could be used to update the list of suitable performance indicator chemicals for MAR previously published by Jekel et al. (2015). The number of inconsistent TOrCs which are removed in MAR systems may also be valuable for assessing MAR performance. Additionally, as correctly classifying the prevailing redox conditions of the studies was difficult in this evaluation, future MAR studies investigating TOrC removal are called on to better characterize the DO concentrations and redox regimes with higher resolution sampling.

Competing Interests

The authors declare no competing interests.

Acknowledgements

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In conclusion, the correlations determined in the study provide more insight on optimal conditions for removal of TOrCs showing inconsistent removal behavior, suggest compounds which could be used as indicators for MAR systems, and recommend higher resolution redox zone characterization in future biofiltration studies.

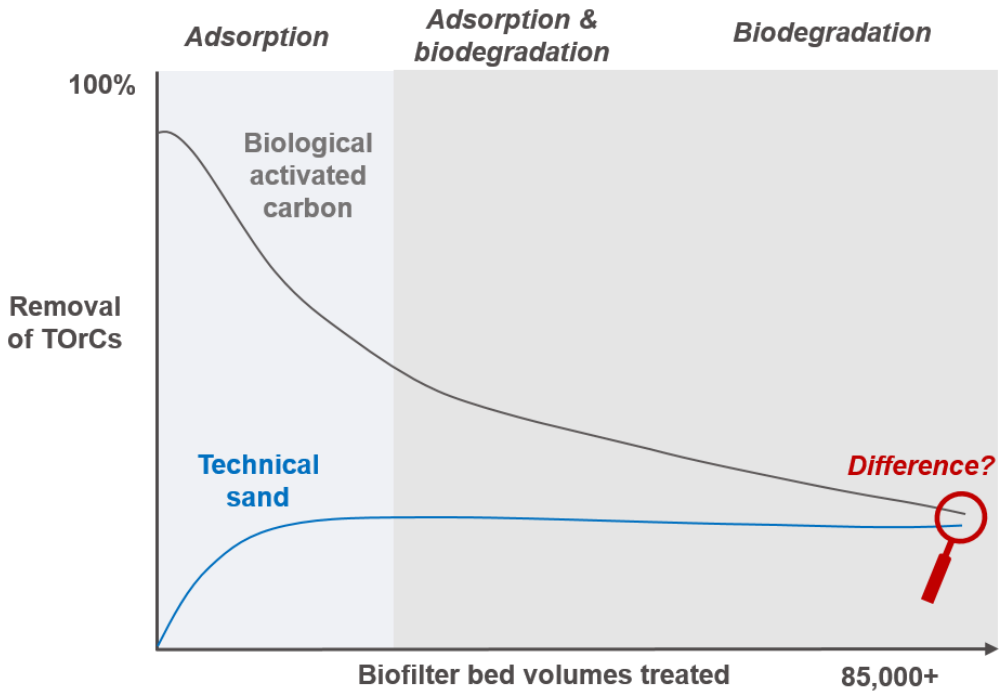
9. Removal of trace organic chemicals during long-term biofilter operation

This chapter has been published with editorial changes as follows:

Reproduced with permission from Zhiteneva, V., Drewes, J.E., Hübner, U. Removal of trace organic chemicals during long-term biofilter operation. 2020. *ACS ES&T Water* 1 (2), 300-308. https://doi.org/10.1021/acsestwater.0c00072.

Abstract

Removal of environmentally relevant trace organic chemicals (TOrCs) was investigated in technical sand and biological activated carbon (BAC) biofilters processing nearly 90,000 bed volumes. This long time period allowed assessment of potential synergies from the interplay of adsorption, desorption, and biodegradation after full breakthrough. Long-term operation of the biofilters continuously fed with real wastewater effluent mimicked field conditions and consequentially encountered numerous mechanical and chemical issues. However, results of high resolution sampling during which the system was fed from a single batch of tertiary effluent revealed compound-specific removal patterns. Comparison of persistent compounds like carbamazepine, primidone and tramadol suggested that removal by adsorption onto activated carbon was still occurring after almost 90,000 bed volumes treated. No notable difference in biodegradation could be observed between sand and BAC. Results from a subsequent batch biodegradation test mostly confirmed conclusions about removal from high resolution sampling. Overall, this study could not provide evidence that usage of activated carbon as a biofilter medium is beneficial for long-term removal after full breakthrough of individual TOrC adsorption capacity.



9.1 Introduction

Since complete removal of trace organic chemicals (TOrCs) is not achieved in conventional wastewater treatment plants (WWTP), advanced water treatment, which includes oxidative (ozonation or advanced oxidation processes), biological, and/or physical processes (powdered or granular activated carbon or membrane filtration)(Yang et al., 2017; Fischer et al., 2019) is employed for greater removal. In certain indirect potable reuse systems, advanced treated effluent is then introduced into the subsurface during managed aquifer recharge (MAR), where TOrCs are further removed through biodegradation. Improved removal of recalcitrant compounds has been observed under oxic and oligotrophic conditions using the sequential managed aquifer recharge technology (SMART) concept.(Regnery et al., 2016; Hellauer et al., 2018a) SMART was further optimized to shorter hydraulic retention times (HRT), smaller physical footprints, and with technical sand filter media in the sequential biofiltration and SMART*plus* biofilters.(Müller et al., 2017; Karakurt-Fischer et al., 2020b) However, certain compounds such as carbamazepine are resistant to biodegradation and must therefore be removed through other mechanisms.(Jekel et al., 2015) This can be accomplished by using an adsorptive porous media in biofiltration, such as granular activated carbon (GAC).(Müller et al., 2019a)

Biological activated carbon (BAC) biofilters, composed of GAC, are often proposed to reduce the time needed for the onset of biodegradation and to enhance TOrC removal efficiency. TOrCs are initially removed via adsorption to the carbon surface as a function of hydrophobicity, pK_a value, and charge.(Hermes et al., 2019) With increasing bed volumes treated (BVT), microorganisms present in the feed water establish a biofilm on the carbon surface, thought to actively transform the TOrCs and eventually both adsorption and biodegradation provide removal.(Alidina et al., 2014a) Once adsorption sites are exhausted, microorganisms in the biofilm degrade TOrCs in solution.(Simpson, 2008; Rattier et al., 2012b) In technical sand biofilters, little to no adsorption to the sand particles is expected, and so the removal of TOrCs is attributed to biodegradation only.(Zearley and Summers, 2012)

Studies have looked at the long-term BAC removal performance after treating 35,000-60,000 bed volumes (BVT).(Rattier et al., 2012a; Sundaram et al., 2020) However, TOrC removal in different media should be compared in parallel to elucidate how removal differs and develops over time. Prior studies evaluating both BAC and sand biofilters have been conducted with synthetic wastewater and ozonated WWTP effluent.(Gerrity et al., 2011; Reungoat et al., 2011; Reaume et al., 2015; Paredes et al., 2016; Bourgin et al., 2018) Less removal of numerous TOrCs, including atenolol, diclofenac, and sulfamethoxazole, was observed in sand biofilters as compared to BAC biofilters, which had been pre-exposed to TOrCs prior to the experiment.(Gerrity et al., 2011; Reungoat et al., 2011)

However, the onset of biodegradation is affected by many variables, including but not limited to media type, effective filter velocity, organic content in water, and redox conditions, and can therefore vary. Additionally, since SMART*plus* is intended for long-term operation without media exchange or backwash, observing the long-term TOrC removal during steady-state biofiltration using either sand or activated carbon as media is of high interest.

Little is known about the long-term (>20,000 BVT) TOrC removal behavior of sand versus BAC filters continuously fed with tertiary treated wastewater effluents. Therefore, this study investigated the long-term removal of 19 environmentally relevant TOrCs in two parallel biofilters to determine whether removal after adsorption sites have been exhausted and without carbon regeneration in the BAC filter is greater than in the technical sand filter.

9.2 Methods

9.2.1 Experimental setup

Two identical lab-scale column systems were set-up with technical sand (0.71-1.25 mm, Quartzwerke Group, Germany) and GAC (Chemviron CycleCarb 401, Chemviron, Belgium) and operated for a period of 28 months from June 2017 to October 2019 to process roughly 89,000 BVT under various operational procedures. Filter columns were 25 cm long (23 cm of media and 2 cm of liquid) and made of ISO 9002 acrylic glass with $\varnothing_{in}$ =7.1 cm. To ensure that TOrC breakthrough results were comparable, both column systems continuously received the same secondary treated wastewater from the WWTP in Garching, Germany (31,000 population equivalents) which was undergoing UV disinfection during the summer months (April through October) and year round rapid sand filtration (RSF) and later Dynasand filtration (Dynasand, Nordic Water GmbH).(Karakurt-Fischer et al., 2020b) Both media were virgin at the beginning of the experiment, in order to pre-load media adsorption sites, both columns were fed with non-spiked tertiary effluent for ~7,500 BVT before TOrC spiking commenced. The same TOrC spiking solution described in our previous work was also used in this experiment, with the addition of sotalol: 19 TOrCs were spiked at concentrations between 500-2,000 ng/L.(Zhiteneva et al., 2020b) A summary of the spiked chemicals and their initial concentrations is presented in the supplementary information (Table 11-12).

The calculated BVT in technical sand and BAC were slightly different due to different media porosities, therefore the BVT discussed herein are always the average values of both systems. An air stone was installed in the feed tank at 29,000 BVT to ensure that dissolved oxygen (DO) concentrations in the feed water were always above 1 mg/L. Samples for dissolved organic carbon (DOC), DO, ultraviolet absorbance at 254 nm (UVA_{254}), and TOrC concentrations were taken from the influents and effluents of both columns over the entire experimental duration.

Due to clogging at high loading rates, the column setup had to be adjusted several times during long-term operation. The initial GAC column setup operated from 0-59,000 BVT with decreasing flow rates and is described in our previous work.(Zhiteneva et al., 2020b) The installation of a pre-filter storage column filled with glass beads at ~57,000 BVT did not verifiably mitigate increasing back pressure. Therefore, the initial column composition was reconstructed in such a way that 10 cm of the original media was sandwiched between 2 cm of glass beads above and 13 cm of glass beads below, to minimize back pressure build up while continuing to observe TOrC breakthrough, although the previous mass transfer zone was not preserved. The final set-up is presented in Figure 9-1.

Around 63,000 BVT, the influent water quality composition began to change due to operational problems at the WWTP, resulting in high NH_4^+-N concentrations which subsequently altered the redox conditions in the columns. Despite in-line H_2O_2 dosing into the RSF in attempts to mitigate NH_4^+-N concentrations to <1 mg/L, oxic conditions in the columns could not always be maintained.(Karakurt-Fischer et al., 2020a) Additionally, high turbidity in the RSF/Dynasand effluent was mitigated by dosing a coagulant ($FeCl_3$) prior to RSF/Dynasand between 76–80,000 BVT, and the precipitation of iron hydroxide species also affected the back pressure of the filters. All operational issues encountered due to chemical and mechanical disruptions are summarized in Table 11-13.

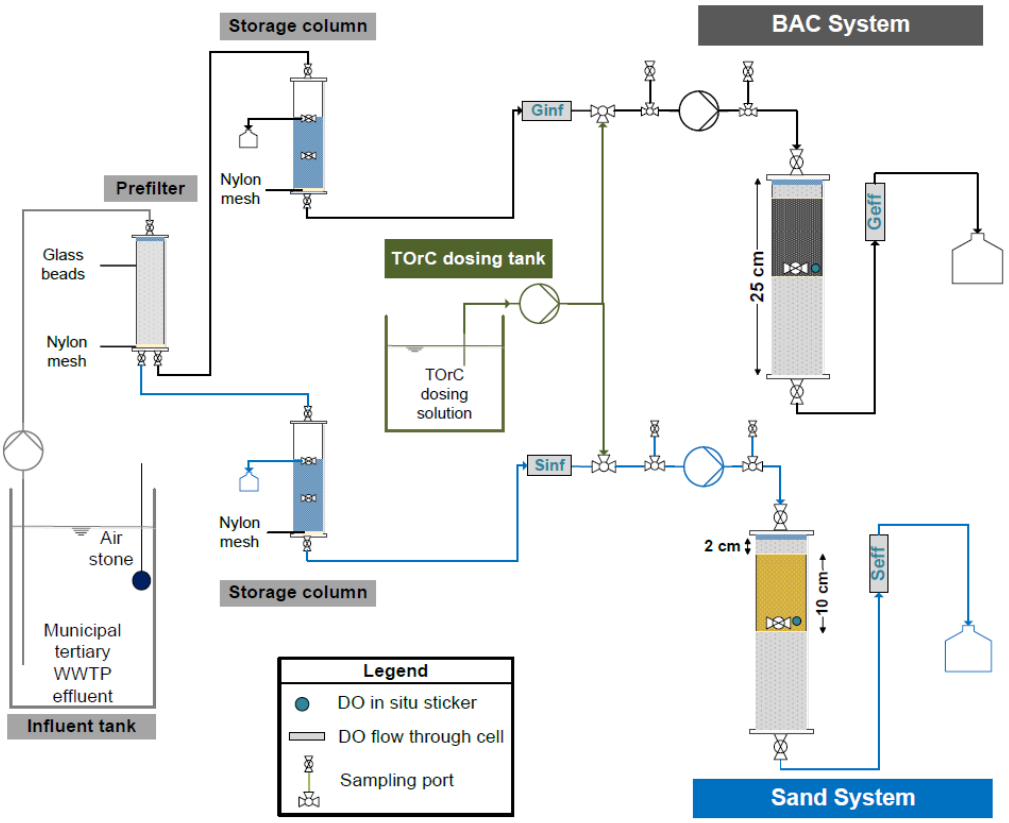


Figure 9-1: Long-term column experimental set-up.

9.2.2 High resolution sampling

Due to the inability of the RSF/Dynasand filter to consistently mitigate effluent NH_4^+-N concentrations from the WWTP to <1 mg/L, the water quality disturbances likely affected growth and composition of the column biomass, since DO was rapidly consumed in the biofilters during periods of high NH_4^+-N concentrations. Therefore, to determine TOrC removal in the columns operated over long-term with a stable influent water quality, a 300 L tank was filled with Dynasand effluent (NH_4^+-N = 1.8 mg/L) to serve as a reservoir for column operation in batch feed mode for the duration of a high resolution TOrC sampling campaign (five samples taken over 48 hours). After 7 hours of operation, the volume removed from the 300 L tank was supplemented with Dynasand effluent in which the NH_4^+-N had dropped to 1 mg/L and this mix lasted until the end of sampling. The first sample, which was taken before refilling the tank, was not included in the analysis of the high resolution results. All samples were analyzed for DOC, DO, and TOrC concentrations and UVA_{254}.

After the high resolution testing, the long-term columns continued operating for another ~3,000 BVT with TOrC spiking into continuous Dynasand effluent. However, after nearly 89,000 BVT, column operation was terminated and the media was frozen for preservation.

9.2.3 Batch biodegradation tests

Additional batch biodegradation tests were conducted in triplicate in autoclaved 100 mL glass screw-top bottles with 9 mg wet weight using BAC and sand media from the long-term column operation as inoculum. Individual batches were run with autoclaved BAC and autoclaved sand to determine abiotic TOrC removal. Tests were run with 80 mL of diluted Dynasand effluent spiked with the same TOrC concentrations as in the column influent. Dynasand effluent was diluted 1:2 with the effluent of a

sequential biofiltration set-up receiving the same WWTP effluent as feed water (Müller et al., 2017) as a measure to reduce NH_4^+-N concentration in the feed water (resulting in 1.2 mg/L in the diluted Dynasand effluent). Oxic conditions in unsealed batches, verified in a pre-experiment test, indicated that NH_4^+-N concentration did not affect TOrC removal over time. All 12 bottles were shaken at 145 rpm for 144 consecutive hours.

Samples were collected at 0, 2, 4, 7, 29, 53, 101, and 144 hours. Initial TOrC concentrations were measured from the influent mix, with and without the TOrC spike, prior to filling the bottles.

9.2.4 Analytical sampling

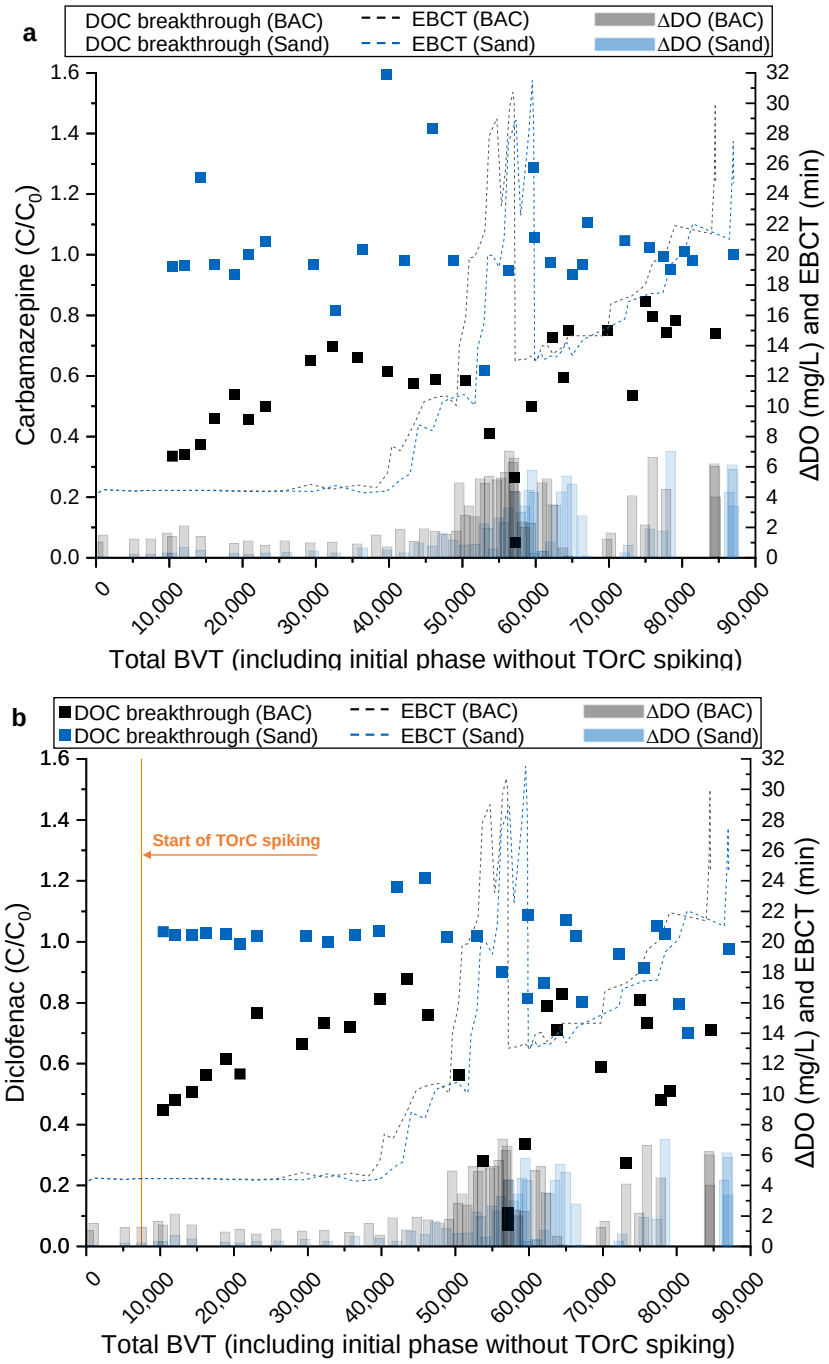
Water quality and trace organic chemical analysis was done as described in previous publications.(Müller et al., 2017; Zhiteneva et al., 2020b) Samples were analyzed for DO immediately and for DOC and UVA_{254} within 24 hours after sampling. TOrC samples were frozen at -20°C pending analysis. Until ~59,000 BVT, samples were collected in reverse order to not disturb the column flow, but afterwards they were collected synoptically according to EBCT.

9.3 Results and Discussion

9.3.1 Breakthrough behavior of sand and BAC filters during long-term operation

Sampling results over the long-term operation characterized DOC and TOrC breakthrough over nearly 89,000 BVT. While numerous mechanical and chemical disturbances affected column operation and prevented reaching a steady-state of removal, the overall breakthrough is plotted with the associated EBCT and the DO consumed to describe observed removal for every BVT. For the BAC filter, both UVA_{254} values and DOC concentrations (see Figure 11-6 and Figure 11-7, Supplementary Information (SI)) suggest more than 80% breakthrough (BT) after ~5,000 BVT. BAC breakthrough for DOC within the first 59,000 BVT was already documented in our prior work,(Zhiteneva et al., 2020b) which also indicated that biodegradation was the dominant removal mechanism. Towards the end of long-term operation, the decreasing DOC and UVA_{254} breakthroughs indicate increased removal by biodegradation in both filters, possibly also related to a steadily increasing EBCT. However, changes in feed water quality and hydraulic conditions resulted in a partially anoxic column operation (DO effluent concentrations of <0.5 mg/L at 86,000 BVT and high NH_4^+-N concentrations (2.5 mg/L) in both filters). Therefore, a quantitative assessment of DOC or UVA_{254} removal from these long-term monitoring results was not feasible.

For TOrC breakthrough, the effect of disturbances and increasing EBCT was noticeable for many compounds. Breakthrough timelines are provided for three exemplary compounds: the adsorptive and non-biodegradable anti-epileptic carbamazepine, the moderately biodegradable and adsorptive anti-inflammatory diclofenac, and the poorly adsorptive and biodegradable anti-depressant gabapentin in Figure 9-2 (other compounds illustrated in Figures 11-6 through 11-21, SI).


a
DOC breakthrough (BAC)
DOC breakthrough (Sand)
EBCT (BAC)
EBCT (Sand)
ΔDO (BAC)
ΔDO (Sand)
Carbamazepine (C/C0)
ΔDO (mg/L) and EBCT (min)
Total BVT (including initial phase without TOrC spiking)
b
DOC breakthrough (BAC)
DOC breakthrough (Sand)
EBCT (BAC)
EBCT (Sand)
ΔDO (BAC)
ΔDO (Sand)
Start of TOrC spiking
Diclofenac (C/C0)
ΔDO (mg/L) and EBCT (min)
Total BVT (including initial phase without TOrC spiking)

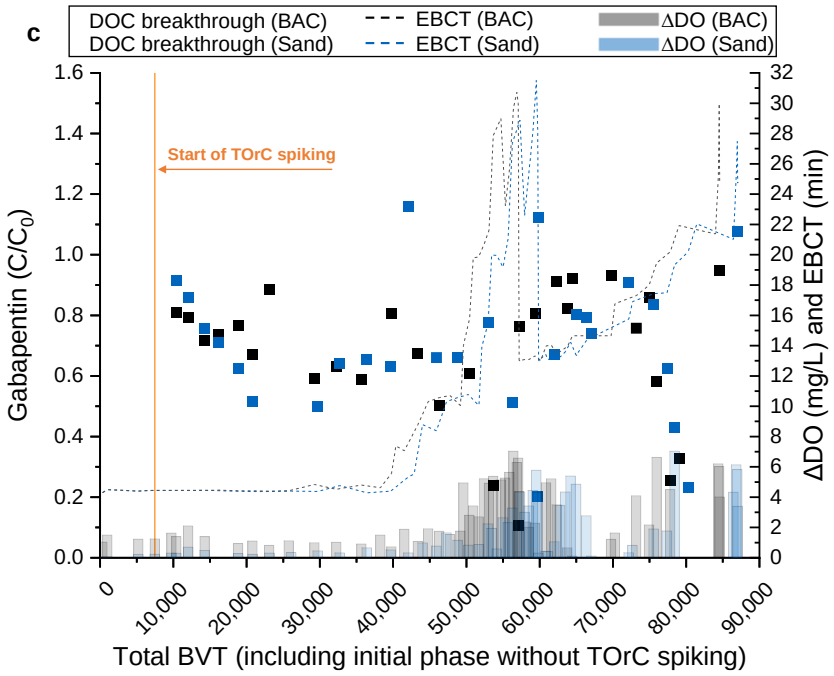


Figure 9-2: Breakthrough of carbamazepine (a), diclofenac (b) and gabapentin (c) on the primary y-axis plotted against bed volumes treated on the x-axis. Black elements represent BAC data, and blue elements represent sand data. Light black and blue bars show the consumed DO, while dashed black and blue lines show the EBCT, units for which are both on the secondary y-axis.

Prior to 40,000 BVT in the sand filter, no diclofenac or carbamazepine were removed, whereas gabapentin was removed by 40-50% due to biodegradation, demonstrating that compound-specific biodegradation was already occurring. In the BAC filter, initial removal due to GAC adsorption was evident for carbamazepine and diclofenac, with breakthrough increasing over time as available adsorption sites decreased. As gabapentin is non-adsorptive, it reached 80% breakthrough before 10,000 BVT, after which it was steadily removed up to 40%.

At approximately 40,000 BVT, the EBCT steadily increased from ~4 mins and reached ~30 mins by 60,000 BVT. This is reflected in increased gabapentin removal (80-90%) and an elevated DO consumption (5-7 mg/L) in both filters, as well as an increased carbamazepine and diclofenac removal in the BAC filter (>90%). Results from diclofenac even indicate some removal by biodegradation in the sand filter. At 60,000 BVT, both filters were repacked with glass beads on top of and below the media to allow a higher loading rate and reduce EBCT to ~14 mins (details in SI). Consequently, the reduced gabapentin and diclofenac removal in both filters and lower carbamazepine removal in the BAC filter between 60-63,000 BVT is likely due to the shorter EBCT, coupled with a slight decrease in DO consumption.

At 63,000 BVT, elevated NH_4^+-N concentrations in the feed water were first observed, which lasted until 68,000 BVT, at which point the filters were changed to recirculation mode (fed from one batch of effluent) until 70,000 BVT. This change in feed water quality is supported by the decreasing or not noticeable DO consumption of both filters from 63-68,000 BVT. Less than 30% gabapentin removal in both filters was observed during this time, possibly due to its redox dependent biodegradation,(Sperlich et al., 2017) whereas 0-50% diclofenac removal was observed. With the exception of outliers, carbamazepine removal in the BAC filter remained at 20-30% from 63,000 BVT through the end of the experimental period.

After re-establishing normal operation with fresh Dynasand effluent as feed water at 70,000 BVT, increased BAC filter removal (70%) of diclofenac was observed until 75,000 BVT, whereas gabapentin removal remained at <30% in both filters, despite increasing DO consumption. Gabapentin removal noticeably increased to 70-80% as EBCT and DO consumption rose between 75-80,000 BVT. At the same time, diclofenac was removed by 50% in the BAC filter and ~20% in the sand filter.

Another recirculation period was instituted from 80-84,000 BVT due to increasing NH_4^+-N feed water concentrations. After this, the last measurement prior to the shutdown of the systems revealed a higher breakthrough of both gabapentin and diclofenac likely due to the change in the liquid phase equilibrium concentration between the recirculation period (continuous recirculation of the same water) to normal operation (treatment of variable WWTP effluent quality).

Thus, these results reveal that elucidating the interaction of adsorption (carbamazepine), biodegradation (gabapentin), or their combination (diclofenac) explicitly in removing TOrCs was constantly compromised by the fluctuating influent water quality, which affected predominant redox conditions and prevented the long-term columns from achieving steady-state removal.

9.3.2 Removal during high resolution sampling

Removal of water quality parameters and TOrCs during high resolution sampling is depicted in Figure 9-3. As the sampling was conducted in batch operation from the same tank, no significant difference was observed in the influent values of DOC, UVA_{254}, or DO using a two-sample t-test. Based on effluent DO measurements, both filters can be characterized as fully oxic for the duration of the high resolution sampling. DOC and UVA_{254} were removed up to 20% in both systems, confirming occurrence of an active microbial community. The more efficient removal of DOC compared to UVA_{254} observed in the sand filter was reported before(Müller et al., 2019c) and was likely due to preferred biodegradation of aliphatic structures. While the removals of DOC, UVA_{254}, and DO depletion within the BAC and sand filters was significant ($p < 0.05$, two sample t-test,), there was no significant difference between the two filters.

Compounds known to be highly persistent to biodegradation, including carbamazepine, primidone, phenytoin, and tramadol, were not removed in the sand filter. The observed removal of the persistent compounds carbamazepine, primidone and phenytoin in BAC suggests that the adsorption capacity of the BAC was not yet exhausted. Similarly, poor removal of citalopram, benzotriazole and venlafaxine in sand (<5%) compared to BAC (25-50%) can mostly be attributed to the residual adsorption capacity of the activated carbon. This assumption is supported by prior results from a rapid small-scale column test conducted with the same effluent and activated carbon type,(Zhiteneva et al., 2020b) which revealed nearly the same degree of sorption for these 6 compounds, with the highest and lowest sorption efficiencies for citalopram and primidone, respectively (removal order in prior work: benzotriazole < citalopram < carbamazepine < tramadol & phenytoin < venlafaxine < primidone; removal order in this study: citalopram < tramadol < venlafaxine < carbamazepine < benzotriazole < phenytoin < primidone).

Compounds showing biodegradation in sand but 14-24% greater removal in BAC filters included atenolol, diclofenac, trimethoprim, sotalol, and climbazole. These compounds display a range of adsorption tendencies based on prior work: atenolol and trimethoprim were well adsorbed, while climbazole and diclofenac were moderately to poorly adsorbed,(Zhiteneva et al., 2020b) although diclofenac has displayed higher GAC adsorption in other studies.(Snyder et al., 2007; Müller et al., 2019a) Sotalol adsorption in GAC has not been well studied, but as it is structurally similar to atenolol and metoprolol(Golovko et al., 2020) it is expected to also be well adsorptive. Therefore, as adsorption contributes to the removal of all 5 compounds, the removal observed in the BAC filter is due to both adsorption and biodegradation, which is greater than removal due to just biodegradation in sand.

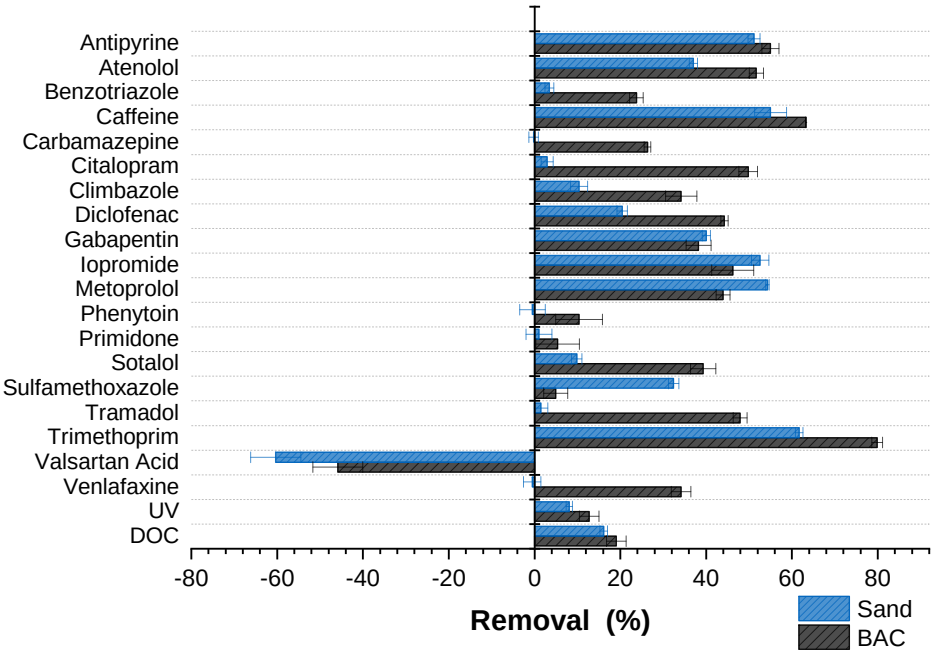


Figure 9-3: Removal of compounds and water quality parameters from the long-term filters after 48 hours of high resolution sampling (BAC caffeine n=3, all others n=4), with error bars denoting error of the sample mean.

The compounds antipyrine, caffeine, metoprolol, iopromide, gabapentin and sulfamethoxazole are similarly or even better removed in the sand filter than in the BAC filter. In an RSSCT study, metoprolol was well removed whereas antipyrine, iopromide, gabapentin, and sulfamethoxazole were poorly removed by sorption only.(Zhiteneva et al., 2020b) Caffeine has exhibited good adsorption in other GAC studies.(Snyder et al., 2007; Sun et al., 2018) As caffeine, metoprolol, antipyrine, iopromide, and gabapentin removal differences in sand and BAC were ≤10%, these compounds are either mainly removed by biodegradation with little sorption affinity, or adsorption does not notably enhance removal (metoprolol and caffeine), or removal via biodegradation is equal in both the BAC and sand filter (antipyrine, gabapentin, and iopromide).

Sulfamethoxazole was the only compound for which biodegradation in sand was clearly better than in BAC (32% vs 5% removal). However, various degrees of sulfamethoxazole biodegradation are reported in the literature, ranging from poor(Gerrity et al., 2011; Bertelkamp et al., 2014) to moderate(Müller et al., 2017; Sun et al., 2018; Karakurt-Fischer et al., 2020b) to good,(Hellauer et al., 2019; Hermes et al., 2019) with removal described as a function of EBCT, DO, and microbial communities present in studies.(Gauthier et al., 2010; Baumgarten et al., 2011; Rattier et al., 2012a; Müller et al., 2017) The presence of valsartan acid, a known transformation product of various sartan compounds(Letzel et al., 2015) under oxic conditions in both media confirms that biodegradation was occurring in both filters.

Overall, results from high resolution sampling did not confirm expected long-term benefits of BAC compared to sand as biofilter medium for weak and moderately adsorbing compounds. A final assessment of effects on better adsorbing compounds is limited as longer operation would be needed to analyze removal efficiency after full breakthrough. Results from high resolution sampling do not indicate additional long-term benefits apart from residual adsorption capacity by GAC.

9.3.3 Batch biodegradation tests

The additional batch biodegradation experiment was performed using active and autoclaved media to determine the relative contribution of adsorption to TOrC removal in the BAC filter. Frozen media from the long-term experiments was thawed to room temperature, with one half remaining 'active' after thawing, and the other autoclaved to prevent biological activity. However, the results revealed that autoclaving not only sterilized the microorganisms responsible for biodegradation, but also potentially altered the surface of the GAC, evident by increased removal of well-adsorbable compounds (known to be persistent to biodegradation under the given conditions) such as carbamazepine (Figure 11-24) in autoclaved BAC in comparison to autoclaved sand. As autoclaving has been shown to increase the adsorption of compounds(Martínez-Hernández et al., 2016; Piai et al., 2020) and did not completely inactivate the biomass, evidenced by the removal of atenolol, diclofenac, metoprolol, sotalol, and trimethoprim in sand (>10% removal) and by gabapentin removal in BAC (Figure 11-24), one round of autoclaving proved insufficient for biomass inactivation. Multiple rounds of autoclaving(Henning et al., 2018) or an alternative method for inactivating biomass could potentially provide better results.

9.3.3.1 **Calculation of removal rates**

Removal of gabapentin, sulfamethoxazole and climbazole in both media are shown in Figure 11-25, with triplicate measurements denoted by error bars. First-order biodegradation rate constants in sand were determined according to previous work(Schmidt et al., 1985) through linearization of normalized data on a logarithmic scale (see section 11.6.4) and are summarized in Table 9-1. No k values were calculated for compounds showing less than 20% overall removal. For sulfamethoxazole, an initial increase was observed in both filters, therefore the second phase k value (29-144 h) is reported as a conservative estimate. Biodegradation rates for valsartan acid were not determined due to concurrent removal and formation from degradation of sartan precursors.(Letzel et al., 2015)

In contrast to batch experiments with sand, compound removal in BAC was due to a combination of both biodegradation and adsorption. Results from high resolution monitoring demonstrated that adsorption capacity for most compounds was not exhausted even after treating more than 85,000 BVT. In addition, thawing and handling the media during the batch experiments may have affected surface properties and adsorption capacity of BAC.

Based on results from carbamazepine and other non-biodegradable compounds, adsorption equilibrium was assumed to be achieved in batch experiments for all compounds after 29 hours. To exclude the effect of adsorption, first-order biodegradation rate constants were determined from data points between 29-144 hours (1-6 days). The intercept of the linear regression provides a first estimate of removal occurring during the first 29 hours. Following this approach, however, BAC biodegradation rates could only be obtained for 4 TOrCs, as the residual concentrations for most other substances were too low to reliably determine removal rates (Table 9-1).

9.3.3.2 **Comparison of removal rates**

The batch test removal rates were compared to removal during high resolution sampling to determine how longer term removal of compounds changed. For this comparison, poor removal in the filters refers to <30%, moderate removal refers to 30-70%, and good removal refers to >70%.

For persistent compounds, high resolution sampling results were mostly confirmed, with <20% removal of carbamazepine, tramadol, primidone, benzotriazole and venlafaxine ($k < 0.035\ d^{-1}$) and 34% removal of phenytoin ($k = 0.05\ d^{-1}$) observed in batch experiments with sand. Only the effective removal of citalopram with a rate constant of $0.36\ d^{-1}$ was different from high resolution results. In BAC, tramadol, venlafaxine and citalopram were completely removed, while phenytoin, primidone and benzotriazole

Table 9-1: Removal rate constants calculated from batch biodegradation tests, ordered by decreasing removal in sand. If compound removal was <20%, the k value is denoted as <0.035 d^{-1}. Compounds which were completely removed in BAC are labeled as not detected (n.d.), rate constants for valsartan acid could not be calculated (n.c.).

	Sand				BAC			
	k, d^{-1}	r^2	n^	Total removal	k, d^{-1}	r^2	n^	Total removal
Caffeine	4.23	0.95	4	> 90%	n.d.			> 90%
Iopromide	4.01	0.82	4	> 90%	n.d.			> 90%
Atenolol	3.93	0.98	4	> 90%	n.d.			> 90%
Antipyrine	3.62	0.96	4	> 90%	n.d.			> 90%
Metoprolol	2.93	0.95	4	> 90%	< 0.035			> 90%
Trimethoprim	2.2	0.97	4	> 90%	n.d.			> 90%
Sotalol	1.16	0.96	6	> 90%	n.d.			> 90%
Gabapentin	0.76	0.98	8	> 90%	*0.21	*0.90	*4	> 90%
Valsartan acid	n.c.			90%	n.c.			*8%
Citalopram	0.36	0.67	7	> 90%	n.d.			> 90%
Climbazole	0.23	0.89	8	75%	*0.06	*0.88	*4	74%
Sulfamethoxazole	*0.23	*0.91	*4	75%	*0.10	*0.70	*4	73%
Diclofenac	0.10	0.93	8	50%	n.d.			> 90%
Phenytoin	0.05	0.82	8	34%	< 0.035			73%
Venlafaxine	< 0.035			< 20%	n.d.			> 90%
Carbamazepine	< 0.035			< 20%	*0.05	*0.92	*4	69%
Tramadol	< 0.035			< 20%	n.d.			> 90%
Primidone	< 0.035			< 20%	< 0.035			33%
Benzotriazole	< 0.035			< 20%	< 0.035			49%

*= removal normalized to day 1 concentration, ^n = the number of triplicate sets used in determining removal rate (i.e. 1 = triplicates from 1 timepoint)

were removed by <20%, with both groups confirming removal tendencies observed during high resolution sampling. A BAC removal rate could only be calculated for carbamazepine (0.05 d^{-1}). Removal observed mainly confirmed literature findings of poor biodegradation in sand filters of carbamazepine,(Bertelkamp et al., 2014; Müller et al., 2017; Hermes et al., 2019) tramadol,(Müller et al., 2017; Karakurt-Fischer et al., 2020b) and phenytoin.(Gerrity et al., 2011; Hübner et al., 2012; Bertelkamp et al., 2014; Hellauer et al., 2019; Hermes et al., 2019) Poor primidone removal in both media confirmed previous literature results.(Gerrity et al., 2011; Müller et al., 2017; Hellauer et al., 2019; Hermes et al., 2019) As benzotriazole has shown redox sensitivity,(Hellauer et al., 2017) the removal in this study is lower than reported in previous work employing biofiltration with intermittent aeration (Hellauer et al., 2017, 2018a; Müller et al., 2017) but similar to work without aeration.(Karakurt-Fischer et al., 2020b) Venlafaxine was poorly removed in sand, supporting the poor to moderate biodegradation observed in literature.(Müller et al., 2017; Hellauer et al., 2019; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) Citalopram was well removed in both BAC and sand, also confirming the moderate to good biodegradation reported in literature.(Müller et al., 2017; Hermes et al., 2019; Karakurt-Fischer et al., 2020b)

Most compounds were biodegraded in sand and can be classified as displaying fast ($k > 2\ d^{-1}$) or moderate ($0.1\ d^{-1} < k < 2\ d^{-1}$) biodegradation. Fast biodegradation of caffeine, iopromide, atenolol, antipyrine, metoprolol and trimethoprim in batch experiments was characterized by complete removal

within the first 29 hours. This observed behavior supports the good degradability of atenolol, caffeine, iopromide and trimethoprim reported in literature.(Gerrity et al., 2011; Bertelkamp et al., 2014; Müller et al., 2017; Hellauer et al., 2019; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) Good to moderate degradation of metoprolol has also been shown,(Hellauer et al., 2017; Hermes et al., 2019) whereas antipyrine was poorly degraded in BAC.(Sun et al., 2018)

Moderate biodegradation resulted in ≥50% removal of sotalol, gabapentin, citalopram, climbazole, and diclofenac within 6 days. Sotalol, climbazole, gabapentin, and citalopram have exhibited moderate to good biodegradation according to literature data.(Gerrity et al., 2011; Hellauer et al., 2017, 2019; Müller et al., 2017; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) Diclofenac is well degraded in certain systems(Hellauer et al., 2017) but not in others,(Müller et al., 2017; Hermes et al., 2019; Karakurt-Fischer et al., 2020b) and has shown good degradation in BAC.(Sun et al., 2018)

Most biodegradable compounds were efficiently removed in BAC due to initial adsorption, which prevented a comparison between filter biodegradation rates. Only four compounds (gabapentin, climbazole, carbamazepine and sulfamethoxazole) were present at high enough concentrations after initial adsorption that their removal by subsequent biodegradation could be quantified into a removal rate. The observed removal rate for carbamazepine was very low and might also be related to residual adsorption, since biodegradation under established conditions is unlikely.(Zearley and Summers, 2012; Hallé et al., 2015; Müller et al., 2017) For the remaining three compounds, the k values were greater in batch experiments with sand. This might be explained by their lower concentrations in BAC on day 1 due to initial BAC removal by adsorption. However, cumulative removal of all three compounds was the same in both filters, signifying that the active biomass in the BAC filter adapted to these concentrations and removed compounds to the same extent as in the sand filter.

Initial production of sulfamethoxazole and valsartan acid was observed in both media (Figure 11-26). For sulfamethoxazole, this could originate from sulfamethoxazole transformation products back-transforming into the parent compound, which has been observed in activated sludge.(Achermann et al., 2018) Although sulfamethoxazole showed greater removal in the sand filter during high resolution sampling, the batch results suggest that long-term removal with longer residence time is similar in both filter media.

Removal of valsartan acid was slow and also revealed initial production in both media. This generation as an intermediate from biotransformation of different sartans has been demonstrated before.(Letzel et al., 2015) Valsartan acid is better removed at high DO concentrations and longer hydraulic retention times.(Hellauer et al., 2017; Hermes et al., 2019) Its removal seemed to depend on the microbial communities present in each media, but was cumulatively greater in the sand filter. However, as this transformation product has been studied less often than most other TOrCs discussed in this study, further analysis with quantification of its parent sartan compounds (i.e. candesartan, valsartan, etc.) is recommended.

The results of this long-term, continuously fed column study and subsequent batch experiments with the filter media do not show greater TOrC removal in the BAC biofilter after adsorption capacity was exhausted. While this differs from results of prior studies investigating both media types in biofilters, which were operated until ~50,000 BVTs with ozonated WWTP effluent,(Reungoat et al., 2011; Zhu et al., 2015; Bourgin et al., 2018) these studies could not omit adsorption as a removal mechanism in their long-term observations. The high resolution results prove that less adsorptive compounds (gabapentin, iopromide, antipyrine) were not better removed in BAC. This study demonstrates that synergies between adsorption, desorption and biodegradation after BAC adsorption capacity is exhausted did not result in greater TOrC removal compared to biodegradation in technical sand. Consequently, the replacement of

technical sand by activated carbon is not a promising option to enhance long-term removal of TOrCs in SMART*plus* or other biofiltration systems.

9.4 Conclusion

This study investigated the removal of environmentally relevant TOrCs in long-term sand or BAC biofiltration while treating WWTP tertiary effluent. Through analysis of long-term removal, high resolution monitoring during steady-state conditions, and additional batch biodegradation experiments, the following conclusions can be drawn:

- While differences in initial removal of TOrCs in both biofilters were observed (see results of diclofenac and carbamazepine), a quantitative comparison of long-term removal of TOrCs in both media was not possible due to the fluctuating influent water quality affecting filter performance.
- DOC breakthrough was not a good predictor of TOrC breakthrough in sand or BAC media, as both DOC and TOrC breakthrough varied notably due to changing EBCT and changing influent water quality (i.e. high NH_4^+-N concentrations). This also affected the adsorption capacity of the BAC due to the changing adsorption equilibrium.
- The high resolution sampling proved that stable removal can be observed when influent quality and redox conditions are stable, evident by the small error bar and moderate removals of metoprolol, iopromide, gabapentin, trimethoprim, antipyrine and atenolol in the sand filter. The high resolution sampling also proved that the adsorption capacity of the BAC for TOrCs was not yet exhausted after treating >85,000 BVT, evident by the removal of carbamazepine, primidone, and phenytoin.
- Most compounds were quickly removed within the first 29 hours of the batch biodegradation tests with BAC media due to adsorption. It is hypothesized that residual adsorption capacity of BAC was further enhanced in batch experiments during thawing and experimental setup. Future batch studies should be conducted with fresh (i.e. not frozen) media from exhausted BAC filters and carefully assembled.
- After > 85,000 BVT, the BAC filter still provided greater removal of carbamazepine, tramadol, phenytoin, benzotriazole, venlafaxine, primidone and diclofenac, attributed primarily to their high adsorptive properties.
- Biodegradation removal rates could be calculated for all compounds except venlafaxine, carbamazepine, tramadol, primidone and benzotriazole in the sand filter, which showed high persistence. Although BAC filter removal rates could be calculated for gabapentin, climbazole, sulfamethoxazole, and carbamazepine, results do not suggest improved TOrC removal in the BAC filter.
- Future long-term biofiltration studies should ensure stable influent quality, which includes low turbidity, low DOC and sufficient (>1 mg/L) DO concentrations.

Competing Interests

The authors declare no competing interests.

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In conclusion, **Hypothesis 4** – Long-term BAC filtration facilitates greater TOrC removal than technical sand – **was rejected**, due to no evidence of improved BAC removal of biodegradable, non-adsorptive compounds after adsorption capacity was exhausted.

10.Discussion and future research needs

The increasing interest of cities in adopting climate-resilient, sustainable, and local water management solutions, coupled with advances in analytical detection of microbial and chemical contaminants, requires water reuse treatment schemes to demonstrate that final effluent water is within acceptable human and environmental health safety margins. To this end, this study broke down this task into 2 objectives and 5 hypotheses (**chapter 3**). The first research objective evaluated microbial and chemical risks to human health associated with the SMART*plus* potable reuse scheme. A literature study reviewing typical assumptions, programs, and methodology for conducting quantitative microbial risk assessments was conducted (**chapter 4**). Afterwards, quantitative microbial (**chapter 5**) and chemical (**chapter 6**) risk assessments were performed on the SMART*plus* based IPR treatment trains.

The second objective evaluated initial and long-term TOrC removal differences in technical sand and BAC. Initial differences between adsorption and biodegradation of compounds in BAC filters were explored in **chapter 7**. To determine which chemicals show the most removal variation during biofiltration, a literature review of TOrC removal in MAR-based biofiltration was conducted in **chapter chapter 8**. Finally, the results of long-term technical sand and BAC column studies were discussed in **chapter 9**.

Based on these results, the following discussion chapter is separated into a risk analysis section and a biofiltration section. The risk analysis discussion, combining risk assessment and risk management, covers remaining questions and improvement suggestions for more concise risk communication in future assessments. The biofiltration section is a critical discussion of factors influencing performance and improvement options for future biofiltration studies.

10.1 Risk analysis of SMART*plus*-based treatment trains

To test Hypothesis 1: Risk to human health from pathogens present in a potable reuse train employing SMART*plus* is below 10^{-6} DALYs, a literature review and a screening level QMRA were conducted.

The work presented in **chapter 4** revealed that while QMRAs have described source water concentrations in water reuse treatment trains using lognormal, uniform, and gamma PDFs, they are still often described using point values, which possibly under- or overestimate actual risk. Similarly, removal in wastewater and advanced water treatment is most often described using point values, uniform and lognormal distributions. However, when enough point value estimates of LRVs exist, a triangular distribution could provide more information on removal than a uniform distribution. Regarding the choice of dose-response model, the review showed that testing multiple models, particularly for the high-risk end of the scale, can be beneficial when a sensitivity analysis identifies dose-response model choice as a critical factor for final risk, or when model choice is insufficiently supported by literature. Assessing multiple percentiles of risk (i.e. 50^{th}, 90^{th}, 95^{th} percentiles), as well as both the 10^{-4} annual risk of infection threshold and the 10^{-6} DALYs threshold can facilitate more nuanced risk management. Identifying and/or quantifying how assumptions taken in the QMRA affect final risk is critical.

These results informed the QMRA conducted in **chapter 5**, which was a conservative assessment of human health risk stemming from the SMART*plus* IPR train. Each unit treatment was described by LRV PDFs sourced mainly from the WHO or Australian guidelines, due to the lack of empirical data for MAR and rapid sand filtration identified in chapter 4, as well as a lack of data for UV disinfection fluences of interest for the SMART*plus* treatment train. Empirical reduction data for indicator or surrogate pathogens in SMART*plus* was only available for bacteriophages and viruses, therefore *Campylobacter* and *Cryptosporidium* reductions were also adapted from the guidelines. By using a Bayesian network, a screening-level probabilistic QMRA provided estimated reductions of *Campylobacter*,

Cryptosporidium and norovirus prior to the construction and operation of the full treatment train. This BN revealed that all pathogens complied with both the 10^{-6} DALYs and 10^{-4} annual risk of infection thresholds at the 95th percentile. *Cryptosporidium* was identified as the pathogen of greatest concern, in agreement with prior QMRAs conducted on non-reverse osmosis based IPR schemes (Soller et al., 2017). Therefore, **Hypothesis 1 was accepted** when evaluating the 95% percentile benchmark of disease burden.

While the 95th percentile of disease burden for all pathogens was acceptable, the maximum *Cryptosporidium* disease burden exceeded both thresholds, with maximum *Campylobacter* risk also exceeding the 10^{-4} annual risk of infection. This was due to instances of compound failure (i.e. serial unit process treatment failure) as well as the raw sewage *Cryptosporidium* concentrations, which were the same order of magnitude as norovirus concentrations (both ~10^6 units/L, see SI 11.3). Although this study used the most recently published *Cryptosporidium* raw sewage concentrations, norovirus concentrations were not updated despite recent evidence that norovirus sewage concentrations may be 1-2 orders of magnitude greater than commonly accepted (Gerba et al., 2017). Since qPCR used for norovirus detection cannot yet distinguish living DNA from total DNA detected, updating the norovirus raw sewage concentrations could lead to an even greater LRV requirement which could be overly conservative and result in higher costs without marked public health benefits.

A sensitivity analysis of the network revealed treatment train specific CCPs for all pathogens were UV irradiation and SMART*plus*. Additionally, three (four for norovirus) operational scenarios were evaluated to determine how the pathogen reduction would respond to feasible treatment disturbances or occurences. As the Bayesian network cannot provide numerical predictions of discretized data, the scenarios can only show an increased or decreased likelihood of higher or lower LRVs. During high pathogen loading (i.e. ~10^6 units/L for *Cryptosporidium* and norovirus, and ~10^5 units/L for *Campylobacter*), no notable effect on final risk of any pathogen was seen. During SMART*plus* performance failure removal (i.e. 0 LRVs), the DALYs of all pathogens increased 2-3 log units, demonstrating that the SMART*plus* is a CCP for all pathogens. During MAR failure (i.e. 0 LRVs), pathogen DALYs exceeded the 10^{-6} threshold by 0.3-1.6 log units, but as MAR performance is difficult to influence at larger scale, MAR was not ultimately considered a CCP.

Pathogen reduction during MAR is understandably site-specific and difficult to model. The LRVs in this study were calculated as a product of residence time (50-120 days) and decay rates obtained through diffusion chamber experiments. However, MAR LRVs were capped at 4 logs due to the maximum residence time of 120 days, although *Cryptosporidium* and norovirus could also be capped at 3 logs. However, due to the likely larger magnitude of uncertainty inherent to subsurface processes in comparison to engineered unit systems, it may be pertinent to establish different cap limits for each type of system.

Although the Bayesian networks constructed in **chapter 5** identified CCPs for each pathogen, two points must be discussed. First, the networks utilized purely literature LRVs (except for SMART*plus* norovirus removal LRVs used). Second, the joint probability distributions of network nodes were sampled 100,000 times to provide simulated data for each node. However, the Bayesian networks were trained on the entire simulated dataset, with no subset of simulated data or experimental data available to validate the networks within the timeframe of the study.

A quantitative chemical risk assessment of the SMART*plus* based treatment train was conducted in chapter 6, to test Hypothesis 2: TOrC concentrations at the point of compliance of the potable reuse train employing SMART*plus* are above the corresponding MTL. By using the MEC/MTL ratio approach outlined earlier, TOrCs exceeding their MTL concentrations in the Garching WWTP effluent were considered in this assessment. Certain adjustments to the assessment in comparison to the QMRA in

chapter 5 were made: a) data from prior experiments on sequential biofiltration with intermediate aeration were adapted for the SMART*plus* biofilter; b) the train assessed in chapter 6 did not include a rapid sand filter prior to the SMART*plus* biofilter; and c) chemical removal was assumed to occur during GAC filtration based on earlier pilot- and full-scale studies. Since the point of compliance was defined at the point of groundwater injection, no additional removal during groundwater recharge or drinking water treatment was assumed, which was a rather conservative assumption as chemical advection/dispersion and dilution from landside groundwater is very likely to occur during recharge. By assigning PDFs to the SMART*plus* effluent TOrC concentrations and to the TOrC removal in subsequent treatment steps, a Bayesian network was created for each TOrC. All compounds except for valsartan acid were removed below MTL at the POC, with the probability of valsartan acid MTL exceedance ranging from 5-58%. Therefore, as valsartan acid was not sufficiently removed to below MTL, Hypothesis 2 was accepted.

The QCRA in **chapter 6** revealed the importance of selecting appropriate removal performance ranges. This was especially notable for GAC removal of valsartan acid, which was evident in the increase in probability of MTL exceedance from 5% when 90-100% GAC removal was assumed to 58% when 50-100% GAC removal was assumed. Although no sensitivity analysis was performed on the Bayesian network, GAC is likely a CCP for non-photooxidative and moderately-poorly adsorbing compounds such as gabapentin and valsartan acid. Therefore, adsorptive removal requires more careful consideration and modeling. Similarly, a scenario/failure analysis which would identify further CCPs was not undertaken for the networks.

This leaves room for improving the assessment. This includes the addition of two more nodes, for WWTP TOrC concentration and for SBF removal range, which would include the WWTP removal variability into the calculation of chemical risk. As valsartan acid is a biodegradation transformation product of various sartan compounds, its removal can be difficult to assess, as removal depends upon whether biodegradation has reached steady-state in the unit process investigated. Likewise, it is less studied in comparison to the other four TOrCs, and assumptions about its removal taken for this screening level QCRA would benefit from more site-specific data and knowledge of parent compound concentrations. Validation of the network could eventually be done using data from SMART*plus* operated with an *in situ* aeration device.

In conclusion, the investigation of **Objective 1: Evaluate microbial and chemicals risks to human health associated with the SMART*plus* potable reuse scheme** revealed that while microbial risk from the treatment train was acceptable, improvements are required prior to acceptance of chemical risk. The quantified risk is subject to change depending upon which thresholds and assumptions are used to assess it. Therefore, the importance of deciding upon both the benchmark risk level as well as assumptions about removal or reduction of contaminants with stakeholders at the beginning of the risk assessment process is particularly important. This will ensure that more focus can be placed on targeted scenario analyses to explore how a treatment train reacts, as well as if and/or which additional unit treatments are needed.

10.1.1 Future outlook for risk assessments

The difficulty of obtaining large datasets for chemical and microbial removal in IPR unit treatments complicates the establishment but even more so the validation of probabilistic QMRA/QCRA models. To this end, an open source, anonymized QMRA database or platform, where studies could deposite their empirical data, would immensely assist screening level assessments and model validation, which could be supplemented by infectivity assay data. Alternatively, expanding the suite of chemical and microbial risk assessment tools developed specifically for bank filtration during the AquaNES project

to other MAR systems would also enable future water reuse projects to test how different treatment combinations affect effluent quality and risk (AquaNES, 2016b, 2016a).

Integrated chemical and microbial risk assessments based on screening literature and testing on a site-specific basis should be adopted on a greater scale, whether for preapproval of a treatment train, scenario/failure analysis, or as validation for unit treatment inclusion or upgrade. Conducting such assessments and properly communicating the safety of a proposed IPR or DPR treatment train to the general public is critical for risk communication and public acceptance. Instead of non-intuitive distribution functions, the safety of a reuse scheme can be explained through box plots clearly comparing the LRVs required to the LRVs achieved, or through simplified but scientifically sound brochures and pamphlets. The language and images communicating the safety of the water to the public can be as important as the water quality itself when discussing public acceptance of potable reuse projects.

In terms of microbial risk assessment, multiple parameters should be agreed upon and clearly communicated at the beginning of a QMRA, including a) source water pathogen concentrations, b) origin of indicator or surrogate parameters used (i.e., empirical data, literature review, or a combination thereof), and c) the benchmark risk threshold. Raw sewage pathogen concentrations recommended used in QMRA could be updated, which will have consequences for LRVs, which are rather conservative estimates of performance and presence. Numerous unit treatments, including MAR, biologically active carbon or sand filtration are notably understudied in the literature, and would particularly benefit from an open source database. This way, more screening-level assessments could be conducted and become a more standard part of the proposal and pre-approval of potable reuse projects. To accomplish this, where possible, higher resolution sampling of ambient and challenge test pathogen, indicator and surrogate reduction should be conducted. Uniform reporting requirements, which could be outlined in the WRRMP or national regulations, would harmonize collected information so facilities and treatment trains could be more easily compared and evaluated.

As future microbial health based guidelines may become more stringent, such as Nevada's Category A+ requirement for 12/10/10 LRVs at the point of compliance (i.e., at the effluent of the environmental buffer or the AWT train) (Sundaram and Pagilla, 2019), assigning reduction credits within multi-barrier treatment system could be reconsidered. For treatment trains employing MAR systems, guidelines for evaluating and assigning reduction credits could be updated into a two-tiered approach: a MAR facility could be provided with an initial list of indicator and surrogate pathogens, after which it would determine which indicators are present in its source water and demonstrate consistent reduction, which would be conducted within the framework of a WRRMP. Then, if a facility requires more reduction credit, a second tier of analyses could be conducted, which could include QMRA, hydrogeological modeling, or a hybrid approach utilizing modeling, risk assessment, and field-scale testing. This discussion on how to soundly, effectively and correctly attribute LRVs for MAR sites is further elaborated on in a Water Research Foundation state-of-the-science report slated for publication in 2021.

As chemical monitoring is more ubiquitous and less expensive than microbial monitoring, the validation of a QCRA model should be easier to conduct at a utility level, which likely have sufficient empirical data for establishing probabilistic models. Improving probabilistic chemical risk assessment models could be done by including surrogate parameters, such as DOC and DO concentrations in the SMART*plus* biofilter, to facilitate a more comprehensive prediction of removal. Best options for handling censored data (i.e. 100% removal of carbamazepine during GAC filtration) can be determined through testing multiple approaches (i.e. substituting censored measurement with LOQ versus ½ LOQ) (World Health Organization, 2016). Future assessments will likely also benefit from the coupling of effect-based bioassays with nontarget analysis for emerging contaminants and transformation products, which can provide data on the risk of chemical mixtures in the effluents of various unit treatments

(Brunner et al., 2020). Such data could possibly be used to develop a safety factor to account for known and/or unknown mixture risk in risk assessments, similar to the mixture assessment factor currently being discussed for REACH chemicals (Drakvik et al., 2020), which could be used to protect the health of vulnerable classes of the population and of the environment when subject to long-term exposure.

10.2 Biofiltration within the SMART*plus*-based treatment train

Biofiltration was investigated in objective 2, wherein the initial and long-term TOrC removal in technical sand and BAC filters was evaluated to determine which media would provide greater TOrC removal. The following section is divided into a critical discussion of experiments undertaken to investigate the objective and includes unpublished results as well as future research recommendations.

10.2.1 Conclusions from biofiltration experiments

Hypothesis 3 states that maturation time for biodegradation in BAC will be shorter than in technical sand, which was separated into three subhypotheses for testing.

In order to test Hypothesis 3.1: Rapid small scale column tests (RSSCTs) can accurately differentiate between TOrC removal attributed specifically to biodegradation and to adsorption, RSSCT column tests with crushed GAC were conducted to quantify TOrC adsorptive capacities through 40,000 BVTs, the results of which were compared with removal seen in the BAC filter. As the RSSCT can overestimate adsorption due to the difference in particle size between the BAC filter and the RSSCT, a fouling index correction was applied. Through this correction, the TOrC breakthrough curves were reduced from 40,000 BVTs to varying BVTs. A PSDM model was used to model breakthrough back up to 40,000 BVTs, chosen as an endpoint based on the adsorptive carbamazepine not achieving notable breakthrough at 20,000 BVTs in prior RSSCT experiments (Müller et al., 2019a).

When comparing the PSDM-modeled breakthrough to the experimental BAC breakthrough, the poor agreement with experimental carbamazepine, venlafaxine and tramadol results led to the conclusion that the modeling underpredicted the adsorption capacity of compounds, and therefore differentiation between biodegradation and adsorption was not possible. This was attributed to the initial high loading rate and short EBCT, which did not allow compounds to fully adsorb to the GAC. The fouling indices calculated for each compound likely also contributed to the poor model fit for well-adsorbing compounds, as they were calculated using a general linear free energy relationship (LFER) approach instead of a LFER built on the TOrCs investigated in this study or obtained experimentally using PD-RSSCTs.

Therefore, determining removal via adsorption by comparing the breakthrough of RSSCT to BAC filter breakthrough was not possible, and therefore **Hypothesis 3.1 could not be adequately tested** as the aforementioned fouling index optimization was not feasible within the timeframe of this study.

To test **Hypothesis 3.2: Biomass establishment will be faster in BAC than in technical sand**, the biomass build-up was tested by analyzing the ATP of sand and BAC media. Samples of both media were taken at various time points from 0 – 60,000 BVTs and frozen at either -80°C or -20°C. ATP was analyzed using commercially available test kits (BacTiter-Glo Microbial Cell Viability Kit, ProMega), opaque-walles 96-well plates (Thermo Fischer Scientific), and an 2300 EnSpire Multilabel plate reader (PerkinElmer) with luminescence capabilities. The complete protocol is provided in SI 11.7.

The resulting measurements (average of two biological duplicates for each sample) suggest that while BAC biomass was greater after the first two measurements, the difference between the sand and BAC filters at each BVT was minimal (Figure 10-1). Although both the initial measurements and the lack of notable difference contradict the expectation that biomass would establish faster in BAC, the calculated ATP (0.7 – 8.5 µM) unfortunately fell outside the calibration range (0.0065 µM – 0.75 µM) and therefore

measurement values could not be confirmed with certainty. However, the inconsistent temporal gaps between the 6 measurements in Figure 10-1 likely do not provide a high enough resolution of biomass build-up, as gabapentin removal in sand was already noticed at 10,000 BVT (see Figure 9-2c) but only three ATP measurements from 0-16,000 BVTs were analyzed.

Although biomass fluctuation during biofilter lifetime is normal (Chaudhary et al., 2003; Pharand et al., 2014), sampling conditions were not always identical. Sampling from the top of a biofilter would inevitably disturb deposited particles and biomass, causing differences in ATP measurements even in biological duplicates, observed in the coefficient of variation between BAC (0.11) and sand (0.07) duplicates. As no notable change in filter operation was observed at 30,000 BVT, disturbances during sampling likely explain the ATP spike at 30,000 BVT. The results could also be discussed with more confidence if samples were analyzed in triplicate instead of duplicate (Velten et al., 2007; Hammes et al., 2010). However, due to time constraints, operational problems caused by the high ammonium conditions in the WWTP effluent affecting DO concentrations and likely also the biomass, and the limited media amount available for testing, a follow-up ATP analysis with an appropriate calibration range could not be repeated.

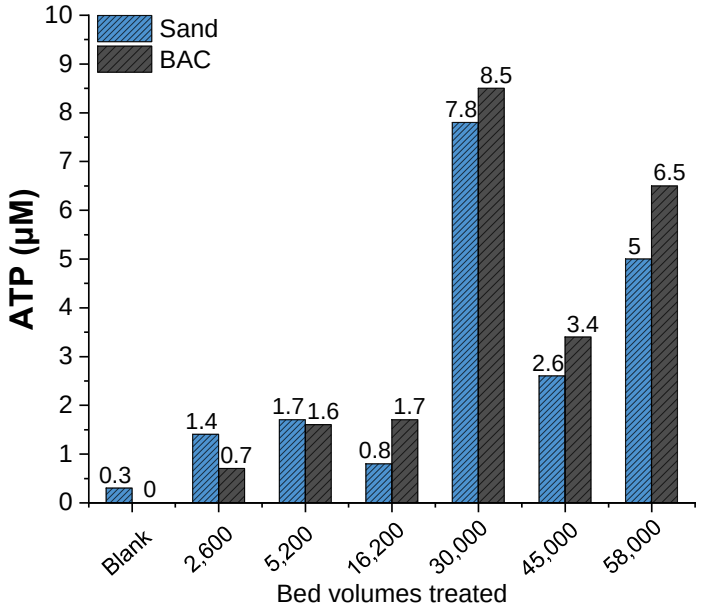

Figure 10-1: Calculated ATP concentrations for BAC and sand media.

Despite these issues, the measured ATP was anyway normalized to the BAC and sand media and ranged from $4.0x10^2$ – $3.6x10^3$ ng ATP/cm^3 media, which is within the 10^2 -10^3 ng ATP/cm^3 media for GAC and anthracite range identified as indicative of active, acclimated media in Pharand et al. (2014). These concentrations were normalized to the media density, which was 450 kg/m^3 for BAC and 1,500 kg/m^3 for sand according to manufacturer information. The resulting biomass concentrations, between $3.1x10^5$ – $1.0x10^7$ pg ATP/g media, were also similar to values reported by Greenstein et al. (2018) for virgin anthracite/sand and used BAC/sand in drinking water biofilters, which were 10^5 -10^6 pg ATP/g media. This comparison suggests that despite improper calibration range and sampling protocol inconsistencies, fine-tuning the standard operating procedure discussed in section 11.7 to ensure quality control of the ATP measurements could provide valuable information on biomass build-up in future experiments.

Although the initial ATP measurements in BAC media were not notably larger than in sand media, the improper calibration range and low sampling resolution meant that **Hypothesis 3.2 could not be adequately tested**.

In order to test **Hypothesis 3.3: TOrC biodegradation begins faster in BAC,** the sand filter breakthrough until 40,000 BVT was compared with BAC filter biodegradation determined from the comparison of RSSCT and BAC filter breakthroughs in chapter 7. This could not provide a definitive indication, as the RSSCT and BAC comparison correctly predicted significant difference for non-adsorptive and biodegradable gabapentin, but also for adsorptive and non-biodegradable carbamazepine, attributed to short EBCT and poor fouling index values. Therefore, the RSSCT-BAC filter data and the sand filter data could not be compared. From long-term column observation, a clear difference in removal in sand and BAC media for gabapentin could not be observed, neither initially nor over the entire duration of the experiment (see Figure 9-2c). Valsartan acid, a biodegradation transformation product, was only quantified in the filters after 71,000 BVT.

Consequently, an alternative workflow for assessing biodegradation was employed. Biodegradation transformation products (BTPs) in both filters were identified using a suspect-target screening approach. Triplicates of influent and effluent samples from 71,000 BVT for sand and BAC were first analyzed using the LC-MS/MS workflow mentioned in chapter 7 to determine which biodegradable spiked TOrC compounds were removed in both filters. This resulted in the identification of trimethoprim, antipyrine, metoprolol, and gabapentin, as well as non-spiked benzotriazole. Valsartan acid was not analyzed. Next, a BTP suspect list for these TOrCs was compiled from a literature review and the Eawag Biocatalysis/Biodegradation Pathway Prediction System (Eawag, 2017). Finally, the same influent and effluent samples from 71,000 BVT were sent to the University of Duisburg-Essen for LC-HRMS analysis.

Data were processed using MZmine 2.3 (MZmine Development, 2011) and compared to the BTP suspect list. Parent TOrC presence for further analysis was confirmed when a) the TOrC monoisotopic mass corresponded to the mass to charge ratio determined for the TOrC by MzMine; b) the TOrC was present in both the influent and effluent samples of the biofilters; and c) if the TOrC's LC-HRMS mass spectra agreed with the TOrC's mass spectra reported in Chemspider, MassBank or PubChem databases. BTP presence was confirmed using the same steps, but if the BTP was present in the influent biofilter sample, it was disqualified from further analysis. In summary, BTPs detected in the effluent samples were 4-hydroxyantipyrine (parent: antipyrine) in the sand filter, phenol (parent: benzotriazole), and 1-carboxycyclohexaneacetic acid (parent: gabapentin) in the BAC filter, as they were present in 2 of 3 effluent filter samples from each filter media.

However, as the samples from 71,000 BVTs were taken only 8 operating days after a 2-month shutdown of the system due to operational disturbances in the WWTP, these results are neither representative of initial biodegradation differences in the filters nor represent steady-state biodegradation. Therefore, although preliminary data shows more and different BTPs were detected in the BAC filter than the sand filter, a comprehensive temporal assessment of BTP production in both systems was not possible. Therefore, **Hypothesis 3.3 could not be adequately tested**.

In conclusion, the overall **Hypothesis 3 could not be accepted** based the inadequate analysis of subhypotheses 3.1, 3.2 and 3.3, which was severely hindered by the fluctuating WWTP water quality and the short EBCT. Quantifying initial differences in adsorption and biodegradation in the BAC filter using RSSCTs (hypothesis 3.1) proved promising but requires optimization (longer EBCT, better fouling index calculation) prior to determining the success of this approach. Likewise, quantifying biomass was hindered by improper method development and low sampling resolution, but seemed to reveal no difference in biomass establishment in BAC and sand filters (hypothesis 3.2). Lastly, if the RSSCT method described in chaper 7 was improved and the combination of the comparison between RSSCT/BAC breakthrough and sand filter breakthrough with the suspect screening of BTPs could be carried out, this would determine whether onset of biodegradation occurs faster in BAC than in technical

sand (hypothesis 3.3). Under steady WWTP effluent operating conditions, this would provide a more comprehensive assessment of initial removal differences.

To test Hypothesis 4: Long-term BAC filtration facilitates greater TOrC removal than technical sand, a few strategies were employed.

Long-term removal of TOrCs was investigated in **chapter 9**. Steady-state removal of biodegradable compounds could not be observed in the long-term sand or BAC column experiments. After roughly 86,000 BVTs, high resolution sampling conducted with a batch feed instead of continuous operation showed that removal of nearly all compounds was constant when feed water quality over 48 hours remained stable, and that removal of non-adsorptive but biodegradable compounds gapabentin, iopromide, and antipyrine was similar in both filters. Finally, a batch biodegradation test was performed to determine whether removal rates of biodegradable compounds were greater in BAC than in sand. Due to complete removal via adsorption in the BAC during the first 29 hours of the 6-day batch experiment, BAC removal rates for most adsorptive compounds, such as trimethoprim and atenolol, could not be calculated. However, compounds for which BAC removal rates were successfully calculated revealed that sulfamethoxazole, climbazole and gabapentin were removed faster in sand, possibly due to higher initial concentrations in sand compared to the lower concentrations in BAC after initial adsorption. Due to these results, **Hypothesis 4 was rejected,** as the removal seen during the high resolution campaign for non-adsorption, biodegradable compounds gabapentin, antipyrine and iopromide was similar in the BAC and sand filters.

In conclusion, the investigation of **Objective 2**: **Evaluate initial and long-term TOrC removal differences in activated carbon and technical sand** was severely affected by the variability in the WWTP effluent used as feed water to the BAC and sand filters as well as the very short EBCT at the beginning of the experiments. Initial removal differences, impacted by the EBCT not allowing full adsorption of compounds to GAC, require additional investigation. Long-term removal differences were negatively affected by WWTP effluent fluctuations, but high resolution sampling and batch biodegradation removal demonstrated that no improved TOrC removal in the BAC filter could be observed. As long-term removal without backwash or media exchange are current attributes of the SMART*plus* treatment concept, this provides support for the use of technical sand in future biofiltration applications.

10.2.2 Implications for biofiltration studies

The dynamic TOrC removal in the continuously fed biofilters could not be foreseen. Four main reasons were identified: 1) the continuous usage of real-time WWTP effluent and the initial poor pre-treatment of feed water during the first 60,000 BVTs led to high particle deposition and increasing EBCTs, requiring modification of the experimental setup; 2) variability in the WWTP effluent quality and TOrC concentrations affected the TOrC spiking in the filters (see concentrations of diclofenac and gabapentin in column influents, Table 11-12; 3) the high turbidity in the RSF effluent was mitigated with $FeCl_3$ dosing, resulting in noticeable iron hydroxide deposition in the filters; and 4) the unacceptably high NH_4^+-N concentrations in the WWTP effluent during later operation prevented the filters from reaching steady operation under oxic conditions optimal for the removal of many TOrCs. However, as this study analyzed TOrC removal with higher temporal resolution and for longer than any other published BAC study (Table 2-1), the inconsistency of long-term results was later supplemented with high resolution sampling and biodegradation rate comparison, which did not provide evidence for improved removal in BAC after adsorption capacity was exhausted.

To better assess biofilter performance in future experiments, stable and optimal feed water concentration should be ensured. Low turbidity, a stable EBCT or HRT, lower and overall more biodegradable DOC,

and stable DO providing oxic conditions in biofilters, regardless of media used, would provide optimal conditions for observing steady-state removal. Likewise, minimal changes in water quality and TOrC influent concentrations and EBCT will prevent washout of compounds, tailing, and/or desorption.

As these influential parameters are interrelated, extracting the effect of one parameter on compound removal grossly oversimplifies the relationship between the parameter and compound removal. Nevertheless, the relationship between TOrC removal and redox conditions, HRT, filter material, and ΔDOC ($DOC_{influent}$–$DOC_{effluent}$) in biofiltration based systems was investigated in **chapter 8.** The meta-analysis considered removal observed from field-, pilot- and laboratory column-scale biofiltration studies, and identified 24 compounds displaying greater than 30% variability in removal (see Figure 8-1). Correlations with HRT and ΔDOC quantitatively revealed that improved removal of nearly half of the 24 compounds were correlated with greater biological activity (ΔDOC), and a minimum of 1 day of HRT were recommended for better removal of most compounds, such as citalopram, climbazole and metoprolol. Based on the metadata, no notable differences in removal between natural (i.e. soil/aquifer media) versus technical media for individual compounds were found, as the primary removal mechanism was considered to be biodegradation (no adsorptive media was included in the meta-analysis). However, the limited data provided on DO concentrations in the studies underlined both the difficulty and the importance of adequately characterizing redox regimes in biofiltration. This is especially evident for compounds such as gabapentin (Sperlich et al., 2017; Müller et al., 2019c), acesulfame (Storck et al., 2016) and sulfamethoxazole (Baumgarten et al., 2011; Henzler et al., 2014).

To continue improving and optimizing biofiltration systems for improved chemical (as well as microbial) contaminant removal, future studies and systems should clearly describe the redox regime within the system in addition to characterizing influent and effluent water quality. Additional analysis of ATP can reveal how quickly microbial communities responsible for the biotransformation of TOrCs establish and respond to water quality changes, while more sophisticated molecular sequencing and qPCR approaches can reveal which strains or communities are present and responsible for the (co)metabolic transformation of compounds. Similarly, although DO concentrations have been used as a proxy for microbial activity, detecting BTPs in the system provides a more precise confirmation that biodegradation is occurring and expands the spectrum of TOrCs analyzed in biofiltration and therefore the knowledge of their removal in such systems.

10.2.3 Implications for SMARTplus-based IPR systems

As the results of **chapter 9** provided no evidence of the benefit of BAC versus technical sand in long-term TOrC removal, this supports the usage of technical sand as biofilter media in SMART*plus* and other biofiltration based treatment systems. Consistent removal of biodegradable TOrCs within the SMART*plus* biofilter could be achieved through ensuring optimal influent water quality composition and redox zonation within the biofilter: consistent DO concentrations above 2 mg/L with low biodegradable DOC in the influent will promote transformation of TOrCs. Ensuring low turbidity to prevent particle deposition and blockage is also critical for stable EBCT and redox zonation. As the glass bead pre-filter did not notably decrease turbidity, more appropriate pre-treatment to reduce associated biofouling could be attempted via upstream H_2O_2 oxidation (de Vera et al., 2019; Noh et al., 2019) or membrane filtration.

However, as sand does not have the adsorptive benefits of activated carbon, additional post-treatment for non- or poorly biodegradable but adsorptive TOrCs, such as carbamazepine, climbazole, tramadol, and venlafaxine, will likely be required. This will likely be achieved in the GAC filter envisioned after the SMART*plus* biofilter, although care should be taken to ensure that SMART*plus* effluent DOC concentrations do not compete with TOrCs for GAC adsorption sites. For TOrCs displaying varying removal tendencies during biodegradation, benzotriazole was removed up to 80% during sequential

biofiltration with aeration at an EBCT of 290 minutes, whereas sulfamethoxazole was removed up to 60% with aeration at EBCTs greater than 1,090 minutes (Müller et al., 2017). Benzotriazole is also well adsorbed (see **chapter 7**). For compounds which are recalcitrant to both adsorption and biodegradation, such as primidone and phenytoin (see Table 9-1 and Figure 9-3), alternative treatments could be necessary. Primidone has shown moderate removal (70%) during ozonation (Hübner et al., 2012) and phenytoin was removed up to 60% during sequential biofiltration and ozonation (Müller et al., 2019a), although both compounds primarily react with OH radicals formed during ozonation (Blackbeard et al., 2016). If using *in situ* ozonation in the SMART*plus* treatment train, monitoring removal of other chemicals will be critical (i.e., NDMA, bromate) (Sundaram and Pagilla, 2019).

One optimal SMART*plus* redox zonation and EBCT conditions have been established and subsequent GAC adsorption installed, the removal of a wider range of TOrCs could be investigated. Future research could investigate the removal of chemicals exhibiting inconsistent removal during biofiltration identified in chapter 8, such as paracetamol, climbazole and valsartan, as well as the BTPs gabapentin lactam and valsartan acid. This could be accomplished through the use of labeled compounds, as well as investigating the biodegradation pathways of compounds as has been done for trimethoprim and diclofenac (Jewell et al., 2016a, 2016b). Determining concentrations of these TOrCs at the point of compliance would also enable the selection of unit treatments targeted for more compound-specific removal when proposing and assessing future potable reuse treatment trains.

For compounds which exhibit removal under suboxic or anoxic conditions, their removal could be investigated at higher redox resolution, and whether their functional groups are correlated with removal could also be investigated. Finally, additional focus could also be placed on compounds not investigated in this dissertation but also critical for human health – namely PFOS/PFOA, which have shown promising removal via adsorption (Gagliano et al., 2020), as well as endocrine disrupting compounds such as 17ß-estradiol, which is removed by adsorption and biodegradation (Z. Li et al., 2012).

11.Supplementary information

11.1 List of publications

11.1.1 Peer reviewed journal articles

Zhiteneva, V., Ziemendorf, É., Sperlich, A., Drewes, J.E., Hübner, U. 2020. Differentiating between adsorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters. Science of the Total Environment 743., 140567 https://doi.org/10.1016/j.scitotenv.2020.140567.
Author contributions: Zhiteneva, V. (50%); Ziemendorf, É. (20%); Sperlich, A. (10%); Drewes, J.E. (5%); Hübner, U. (15%)

Zhiteneva, V., Hübner, U., Medema, G.J., Drewes, J.E. Trends in conducting quantitative microbial risk assessments for water reuse systems: a review. 2020. Microbial Risk Analysis 16, 100132. https://doi.org/10.1016/j.mran.2020.100132.
Author contributions: Zhiteneva, V. (55%); Hübner, U. (30%); Medema, G.J. (5%), Drewes, J.E. (10%)

Zhiteneva, V., Drewes, J.E., Hübner, U. Removal of trace organic chemicals in long-term biofilter operation. 2020. ACS ES&T Water 1 (2), 300-308. https://doi.org/10.1021/acsestwater.0c00072.
Author contributions: Zhiteneva, V. (70%), Drewes, J.E. (10%); Hübner, U. (20%)

Filter, J.+, **Zhiteneva, V.+**, Vick, C., Ruhl, A.S., Jekel, M., Hübner, U., Drewes, J.E. Varying attenuation of trace organic chemical in natural treatment systems – A review of key influential factors. 2021. Chemosphere 274, 129774. https://doi.org/10.1016/j.chemosphere.2021.129774.
Author contributions: Filter, J.+ (25%), Zhiteneva, V.+ (25%), Vick, C. (20%), Ruhl, A.S. (5%), Jekel, M. (5%), Hübner, U. (10%), Drewes, J.E. (10%)

Zhiteneva, V., Carvajal, G., Shehata, O., Hübner, U., Drewes, J.E. Quantitative microbial risk assessment of a non-membrane based indirect potable water reuse system using Bayesian networks. 2021. Science of the Total Environment 780, 146462. https://doi.org/10.1016/j.scitotenv.2021.146462.
Author contributions: Zhiteneva, V. (50%), Carvajal, G. (20%), Shehata, O. (15%), Hübner, U. (10%), Drewes, J.E. (5%)

11.1.2 Reports

Rauch-Williams, T., Drewes, J.E, Gerba, C., Mosher, J., **Zhiteneva, V.,** Branch, A., Davis, K. Evidence for Pathogen Removal in Managed Aquifer Recharge Systems. WRF 4957 State-of-the-Science Report. In preparation.

Cornel, P., Drewes, J.E., Firmenich, E., Fuhrmann, T., Gramel, S., Haberkamp, J., Hartmann, A. Jendrischewski, W., Karl, V., Krause, S., Lübken, M., Obermann, I., Schmidtlein, F., Sinn, J., Ziegler, D., Avellan, T., Caucci, S., Fokin, E., Grieb, A., Lahnsteiner, J., **Zhiteneva, V.**, Knitschky, R. Non-Potable Water Reuse. Development, Technologies, and International Framework for Agricultural, Urban and Industrial Uses. Report of the DWA Working Group BIZ-11.4 “Water Reuse”. June 2019.

Drewes, J. E., Hübner, U., **Zhiteneva, V.**, Karakurt, S. 2017. Characterization of Unplanned Water Reuse in the EU. Garching: Technical Univ. of Munich. Prepared for the European Commission DG Environment.

11.1.3 Conference presentations and posters

Zhiteneva, V., Rodriguez, J., Shehata, O., Ehre, M., Drewes, J.E., Hübner, U. Dealing with data scarcity in non-normally distributed environmental datasets of water treatment systems. Max-Planck-

Gesellschaft Machine Learning Summer School, August 26–September 6, 2019, Moscow, Russia. (Poster)

Zhiteneva, V., Shehata, O., Rodriguez, J., Ehre, M., Drewes, J.E., Hübner, U. Quantitative exposure and risk assessments of a potable reuse treatment train. 11th International Water & Health Seminar, June 24-26, 2019, Cannes, France.

Zhiteneva, V., Shehata, O., Rodriguez, J., Ehre, M., Drewes, J.E., Hübner, U. Quantitative exposure and risk assessments of sequential biofiltration within a potable reuse treatment train. 12th IWA International Conference on Water Reclamation and Reuse, June 16-20, 2019, Berlin, Germany.

Zhiteneva, V., Shehata, O., Rodriguez, J., Ehre, M., Drewes, J.E., Hübner, U. Quantitative exposure and risk assessments of a non-membrane based potable reuse treatment train. Annual Meeting of the German Chemistry Society (GDCh Wasser), May 27-29, 2019, Erfurt, Germany. (Poster)

Zhiteneva, V., Ziemendorf, E., Drewes, J.E., Hübner, U. Rapid small-scale column tests (RSSCTs) for differentiating between adsorption and biodegradation mechanisms removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters. Annual Meeting of the German Chemistry Society (GDCh Wasser), May 7-9, 2018, Papenburg, Germany. (Poster+)

11.2 Supplementary information for Chapter 4

Trends in applying quantitative microbial risk assessments for water reuse systems: a review

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This supplementary information for this submitted manuscript consisted of 2 items: an Excel database, which is not attached but provided thorough the DOI link, and the following Microsoft word document.

11.2.1 Supplementary information

Search string used for advanced search in Scopus, February 14, 2020:

(*wastewater* OR *"wastewater treatment"* OR *"treated wastewater"* OR *"wastewater irrigation"* OR *"irrigation"* OR *"wastewater reuse"* OR *"water recycling"* OR *"recycled water"* OR *"reclaimed water"* OR *"indirect potable reuse"* OR *"direct potable reuse"* OR *"MAR"* OR *"managed aquifer recharge"* OR *"de facto reuse" OR "water reclamation"* OR *"drinking water"* OR *"raw water"*)

AND (*"norovirus"* OR *"rotavirus"* OR *"adenovirus"* OR *"enterovirus"* OR *"cryptosporidium"* OR *"giardia"* OR *"campylobacter"* OR *"e. coli"* OR *"MS2"* OR *"PHIX 174"* OR *"Phix-174"* OR *"ΦX-174"*)

AND (*"log removal wastewater treatment"* OR *"QMRA"* OR *"quantitative microbial risk assessment"* OR *"microbial risk"* OR *"microbiological risk"*) AND (LIMIT-TO (PUBYEAR , *2020*) OR LIMIT-TO (PUBYEAR , *2019*) OR LIMIT-TO (PUBYEAR , *2018*) OR LIMIT-TO (PUBYEAR , *2017*) OR LIMIT-TO (PUBYEAR , *2016*) OR LIMIT-TO (PUBYEAR , *2015*) OR LIMIT-TO (PUBYEAR , *2014*) OR LIMIT-TO (PUBYEAR , *2013*) OR LIMIT-TO (PUBYEAR , *2012*) OR LIMIT-TO (PUBYEAR , *2011*) OR LIMIT-TO (PUBYEAR , *2010*) OR LIMIT-TO (PUBYEAR , *2009*) OR LIMIT-TO (PUBYEAR , *2008*) OR LIMIT-TO (PUBYEAR , *2007*) OR LIMIT-TO (PUBYEAR , *2006*) OR LIMIT-TO (PUBYEAR , *2005*) OR LIMIT-TO (PUBYEAR , *2004*) OR LIMIT-TO (PUBYEAR , *2003*) OR LIMIT-TO (PUBYEAR , *2002*) OR LIMIT-TO (PUBYEAR , *2001*) OR LIMIT-TO (PUBYEAR , *2000*)) AND (LIMIT-TO (LANGUAGE , *"English"*))

Search string resulted in 2669 hits. Searching for ‘qmra’ within the ‘Search within results…’ function of Scopus yielded 656 documents. These 656 hits were copied into Excel. A three tier system for deciding which papers to take into the review was then enacted. The first tier search was for the terms potable reuse, irrigation, drinking, recycled, crop, vegetable, and reclaimed, which resulted in a total of 290 papers with one of these 5 terms. Next, the second tier search was done by looking through title, abstract and keywords to assess whether they dealt with human health risk assessment of wastewater reuse systems for DPR, IPR and irrigation. Third tier search was for the terms managed aquifer recharge, open space, campylobacter, cryptosporidium, rotavirus, norovirus, adenovirus, rotavirus, giardia, e. coli, probabilistic, probability distribution, and distribution function, which yielded a final count of 108 studies from the database. Adding 9 studies from expert knowledge, this resulted in 117 full text papers assessed, of which 43 were ultimately discussed in the review.

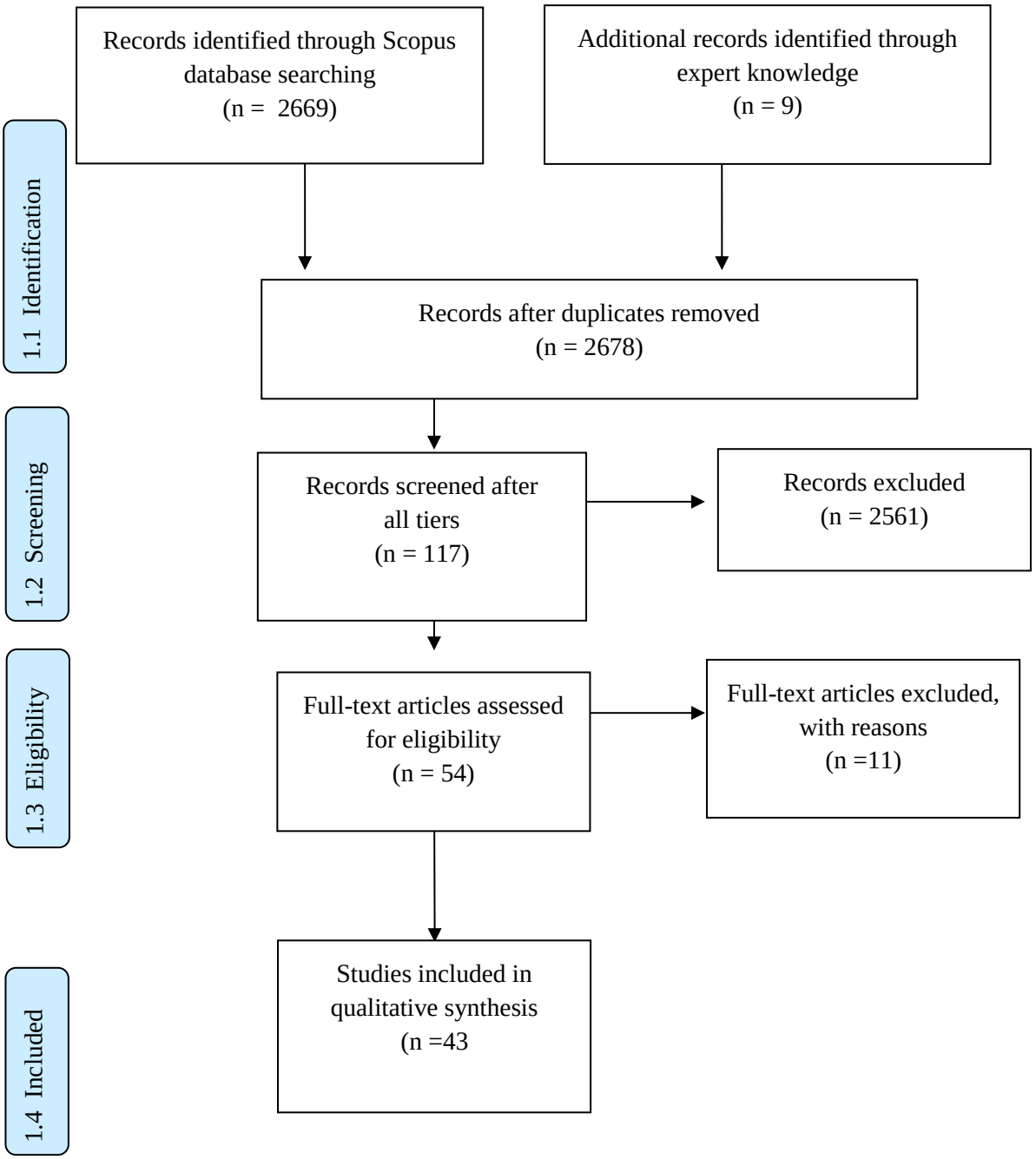

Figure 11-1: PRISMA structure for assessment of literature. Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Table 11-1: Frequency of pathogen appearance in collected literature

	Frequency	Sources
		Viruses
Norovirus	29/43	(Mara et al., 2007; Åström et al., 2007; Page et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Barker, 2013; Barker et al., 2013, 2014; Mok et al., 2014; Symonds et al., 2014; Sales-Ortells et al., 2015; Bartak et al., 2015; Beaudequin et al., 2016, 2017; Verbyla et al., 2016; Amoueyan et al., 2017, 2019a; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Ito et al., 2017; Amoueyan et al., 2019b; Owusu-Ansah et al., 2017; Pecson et al., 2017; Soller et al., 2017, 2018a, 2018b; Bergion et al., 2018; Chandrasekaran and Jiang, 2018; Gonzales-Gustavson et al., 2019)
Rotavirus	19/43	(Åström et al., 2007; Mara et al., 2007; Seidu et al., 2008; Page et al., 2010; Toze et al., 2010; Ayuso-Gabella et al., 2011; Pavione et al., 2013; Barker et al., 2013, 2014; Mok et al., 2014; Olivieri et al., 2014; Symonds et al., 2014; Mok and Hamilton, 2014; Bartak et al., 2015; Verbyla et al., 2016; Pecson et al., 2017; Beaudequin et al., 2017; Chhipi-Shrestha et al., 2017; Fuzawa et al., 2019)
Enterovirus	8/43	(Åström et al., 2007; Mara et al., 2007; Barker-Reid et al., 2010; Ayuso-Gabella et al., 2011; Symonds et al., 2014; Moazeni et al., 2017; Pecson et al., 2017; Soller et al., 2017)
Adenovirus	11/43	(Barker et al., 2013; Mok et al., 2014; Verbyla et al., 2016; Beaudequin et al., 2016; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Soller et al., 2017, 2018b, 2018a; Amoueyan et al., 2019a; Gonzales-Gustavson et al., 2019)
		Bacteria
Campylobacter	13/43	(Åström et al., 2007; Mara et al., 2007; Toze et al., 2010; Page et al., 2010; Ayuso-Gabella et al., 2011; Barker et al., 2013; Pavione et al., 2013; Soller et al., 2018a, 2018b; Beaudequin et al., 2017; Chhipi-Shrestha et al., 2017; Soller et al., 2017; Bergion et al., 2018)
E. coli	13/43	(Åström et al., 2007; Barker-Reid et al., 2010; Ayuso-Gabella et al., 2011; Agulló-Barceló et al., 2012; Pavione et al., 2013; Olivieri et al., 2014; Sales-Ortells et al., 2015; Bartak et al., 2015; Verbyla et al., 2016; Soller et al., 2017; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Owusu-Ansah et al., 2017)
		Protozoa
Cryptosporidium	22/43	(Mara et al., 2007; Åström et al., 2007; Page et al., 2010; Toze et al., 2010; Ander and Forss, 2011; Agulló-Barceló et al., 2012; Sato et al., 2013; Barker et al., 2013; Olivieri et al., 2014; Verbyla et al., 2016; Amoueyan et al., 2017; Pecson et al., 2017; Sampson et al., 2017; Soller et al., 2017, 2018a, 2018b; Amoueyan et al., 2019a; Beaudequin et al., 2017; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Xiao et al., 2018; Bergion et al., 2018)
Giardia	12/43	(Åström et al., 2007; Ander and Forss, 2011; Ferrer et al., 2012; Barker et al., 2013; Sato et al., 2013; Olivieri et al., 2014; Verbyla et al., 2016; Chhipi-Shrestha et al., 2017; Soller et al., 2017, 2018a, 2018b; Xiao et al., 2018)
		Bacteriophages
Somatic bacteriophages	7/43	(Åström et al., 2007; Ander and Forss, 2011; Agulló-Barceló et al., 2012; Bartak et al., 2015; Sales-Ortells et al., 2015; Verbyla et al., 2016; Chaudhry et al., 2017)

Table 11-2: Treatment trains utilized in studies selected for this review:

Reuse Type	Source water*	Treatment trains assessed	Reference
de facto	Raw wastewater	Primary clarification – AS – Secondary clarification – EB (surface water) – DWT (coagulation, flocculation, sedimentation, filtration, disinfection) (+ Cl_2 in 2019)	(Amoueyan et al., 2017, 2019a)
de facto	Raw wastewater	Primary clarification – AS – Secondary clarification – EB (surface water) – DWT (coagulation, flocculation, sedimentation, filtration, disinfection) – Consumer	(Amoueyan et al., 2019b)
de facto	Surface water	Coagulation – Flocculation –Sedimentation – Sand filtration – Chlorination – Fluoridation	(Sato et al., 2013)
de facto	Surface water	Flocculation – Sedimentation – Chlorine disinfection – GAC – Chlorine & chlorine dioxide disinfection	(Åström et al., 2007)
de facto	Surface water	EB (aquifer recharge) – RSF – Chlorination – (optional UV disinfection)	(Bergion et al., 2018)
de facto	Surface water	Coagulation/sedimentation – Media filtration – Cl_2	(Chaudhry et al., 2017)
IPR	Raw wastewater	Primary clarification – AS – Secondary clarification – UF – O_3 (6.9 mg/L) – BAC – O_3 (5.1 mg/L) – EB (storage time: 105 or 270 days) – SW – DWT (coagulation, flocculation, sedimentation, filtration, disinfection) (+ Cl_2 in 2019)	(Amoueyan et al., 2017, 2019a)
IPR	Raw wastewater	Primary clarification – AS – Secondary clarification – MF – RO – UV (80 mJ/cm^2) – Groundwater replenishment (60 days) – Cl_2	(Amoueyan et al., 2019a)
IPR	Raw wastewater	Primary clarification – AS – Secondary clarification – MF – RO – UV (80 mJ/cm^2) – Groundwater replenishment (60 days) – SW – DWT (coagulation, flocculation, sedimentation, filtration) – Cl_2	(Amoueyan et al., 2019a)
IPR	Raw wastewater	No treatment mentioned, only end uses: lawn, public park, golf course, agricultural irrigation	(Chhipi-Shrestha et al., 2017)
IPR	Surface water	EB (RBF, 2->88 days travel time) – NaOCl disinfection	(Bartak et al., 2015)
IPR	Surface water	EB (aquifer recharge) – RSF – Chlorination – (optional UV disinfection)	(Bergion et al., 2018)
IPR	Tula Valley: Primary WWTP effluent	EB (basalt aquifer, 20-40 days residence time) – Cl2	(Page et al., 2010)
IPR	Atlantis: Secondary WWTP effluent + stormwater in wetland	EB (unconfined sandy aquifer, ~1 year residence time) – softening – Cl_2	(Page et al., 2010)
IPR	Secondary effluent	(Cl_2) – lawn, public park, golf course, agricultural irrigation	(Chhipi-Shrestha et al., 2017)
IPR	Torreele/ St. André: Tertiary WWTP effluent	EB (unconfined sandy aquifer, 30-55 days residence time) – aeration – RSF – UV disinfection	Page et al., 2010)
DPR (th.)	Raw wastewater	LRVs determined by setting tolerable annual disease burden to $\leq 10^{-6}$ DALYs (no existing treatment steps assessed)	(Barker et al., 2013)
DPR	Raw wastewater	Primary clarification – AS – Secondary clarification – UF – O_3 (6.9 mg/L) – BAC – UV (80 or 512 mJ/cm^2) – ESB (+ Cl_2 in 2019)	(Amoueyan et al., 2017, 2019a)
DPR	Raw wastewater	Primary clarification – AS – Secondary clarification – MF – RO – UV (80 mJ/cm^2) – Surface water	(Amoueyan et al., 2019a)

		blending - DWT (coagulation, flocculation, sedimentation, filtration) - Cl_2	
DPR	Raw wastewater	Primary clarification – AS – Secondary clarification – MF – RO – UV (80 mJ/cm^2) – ESB – Cl_2	(Amoueyan et al., 2019a)
DPR	Raw wastewater	Primary clarification – AS – Secondary clarification – MF – RO – UV (80 mJ/cm^2) – ESB – Cl_2 – Consumer	(Amoueyan et al., 2019b)
DPR	Raw wastewater	Primary clarification – AS – Secondary clarification – UF O_3 – BAC – UV (80 mJ/cm^2) – ESB – Cl_2 - Consumer	(Amoueyan et al., 2019b)
DPR	Raw wastewater	Primary clarification – AS – MF – RO – UV/H_2O_2 – Cl_2	(Chaudhry et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAC - MF – RO – UV/H_2O_2 – Cl_2	(Chaudhry et al., 2017)
DPR	Raw wastewater	MBR – RO – UV/H_2O_2 – Cl_2	(Chaudhry et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAC – MF – NF – UV/H_2O_2 – BAC – Cl_2	(Chaudhry et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – MF – RO – UV/AOP (800 mJ/cm^2) or UV (12 mJ/cm^2) with H_2O_2 – ESB+Cl_2	(Soller et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAF – MF – RO – UV/ AOP (800 mJ/cm^2) or UV (12 mJ/cm^2) with H_2O_2	(Soller et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAF – UF – UV/AOP (800 mJ/cm^2) or UV (12 mJ/cm^2) with H_2O_2 – ESB+Cl_2	(Soller et al., 2017)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAF – UF – UV/AOP (800 mJ/cm^2) or UV (12 mJ/cm^2) with/without H_2O_2 – ESB+Cl_2 – Flocculation - Sedimentation - Filtration - Disinfection via chlorination	(Soller et al., 2017, 2018b)
DPR	Raw wastewater	Primary clarification – AS – MF – RO – UV disinfection (12 or 800 mJ/cm^2) – ESB+Cl_2	(Soller et al., 2018)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAF – UF – UV disinfection (12 or 800 mJ/cm^2) – ESB+Cl_2	(Soller et al., 2018a, 2018b)
DPR	Raw wastewater	Primary clarification – AS – O_3 – BAF – UF – - RO – UV (800 mJ/cm^2)	(Soller et al., 2018b)
DPR	Raw wastewater	Primary clarification – AS – UF – RO – UV (800 mJ/cm^2) – ESB+Cl_2	(Soller et al., 2018b)
DPR	Secondary WWTP effluent	(Optional PAC treatment) – Pre-O_3 – Coagulation/flocculation (HCl + $FeCl_3$) – DAF + (NaOH & MnO_4) – RGSF (anthracite + sand) – O_3 (1-1.5 mg O_3/mg DOC) + H_2O_2 – BAC – GAC – UF – Cl_2	(Ander and Forss, 2011)
DPR	Tertiary WWTP effluent; for risk assessment, raw wastewater was also evaluated	O_3 – BAC – MF/UF – RO – UV/AOP (1200 mJ/cm^2)	(Pecson et al., 2017)
Irr.	Unspecified wastewater	Restricted irrigation – Involuntary soil ingestion	(Mara et al., 2007)
Irr.	Unspecified wastewater	Unrestricted irrigation – Lettuce consumption	(Mara et al., 2007)
Irr.	Unspecified wastewater	Lettuce and cabbage irrigation – Consumption	(Owusu-Ansah et al., 2017)
Irr.	Unspecified wastewater	Lettuce and cabbage irrigation – Consumption	(Barker et al., 2014)
Irr.	Surface water	Direct lettuce irrigation – Consumption	(Verbyla et al., 2016)

Irr.	Surface water	EB (RBF extraction well) – lettuce irrigation – Consumption	(Verbyla et al., 2016)
Irr.	Surface water	Irrigation – Unintentional ingestion	(Sampson et al., 2017)
Irr.	Raw wastewater	Primary and secondary treatment – Lettuce irrigation – Consumption	(Beaudequin et al., 2016)
Irr.	Raw wastewater	Primary and secondary treatment – Lagoon storage – Surface wetlands – Subsurface wetlands – Cl_2 – Green space irrigation – Unintentional ingestion	(Beaudequin et al., 2017)
Irr.	Raw wastewater	Wastewater stabilization ponds – Actiflo – Cl_2 or UV irradiation or O_3 – Crop irrigation – Consumption	(Mok et al., 2014)
Irr.	Raw wastewater	Upflow anaerobic sludge blanket – submerged aerated biofilter – waste stabilization ponds – crop irrigation – Consumption	(Pavione et al., 2013)
Irr.	Raw wastewater	Facultative pond – 2 maturation ponds – Involuntary soil/water ingestion – Unintentional ingestion	(Symonds et al., 2014)
Irr.	Raw wastewater	UASB reactor – 2 polishing ponds – Involuntary soil/water ingestion – Unintentional ingestion	(Symonds et al., 2014)
Irr.	Raw wastewater	AS – either irrigation at the treatment plant OR UV disinfection – Cl_2 – irrigation – Consumption	(Barker, 2013)
Irr.	Raw wastewater	AS – Cl_2 – UF – irrigation – Consumption	(Barker, 2013)
Irr.	Raw wastewater	Kale/endive irrigation – Consumption	(Fuzawa et al., 2019)
Irr.	Raw wastewater	Rotating screens – aerated grit chamber – oxidation ditch – Cl_2 – Irrigation – Unintentional ingestion	(Xiao et al., 2018)
Irr.	Raw wastewater	Sedimentation – AS – Cl_2 – Flocculation (Actiflo) – Low pressure UV – Vegetable irrigation – Lettuce consumption	(Gonzales-Gustavson et al., 2019)
Irr.	Raw wastewater	Sedimentation – AS – Constructed wetland – Vegetable irrigation – Lettuce consumption	(Gonzales-Gustavson et al., 2019)
Irr.	Raw wastewater	AS – Irrigation of food crops – Lettuce consumption	(Olivieri et al., 2014)
Irr.	Raw wastewater	AS – Cl_2 – Lettuce consumption	(Olivieri et al., 2014)
Irr.	Raw wastewater	AS – Filtration – Cl_2 – Lettuce consumption	(Olivieri et al., 2014)
Irr.	Domestic untreated wastewater	Pilot-scale anoxic/oxic MBR – Crop irrigation – Unintentional and intentional consumption	(Ito et al., 2017)
Irr.	Domestic untreated wastewater	Irrigation of morning glory – Unintentional and intentional consumption	(Ferrer et al., 2012)
Irr.	Domestic wastewater	Lettuce irrigation – Unintentional and intentional consumption	(Seidu et al., 2008)
Irr.	Raw wastewater, secondary WWTP effluent, tertiary WWTP effluent	Coagulation/flocculation – sand filtration – MF – UV (18-80 mJ/cm^2) – Chlorination (1-5ppm) – Irrigation (golf course, public garden) or aquifer recharge or seawater intrusion – Unintentional consumption	(Agullo-Barcello et al., 2012)
Irr.	Secondary WWTP effluent	Crop irrigation – Lettuce consumption	(Petterson et al., 2001)
Irr.	Secondary WWTP effluent	Lettuce irrigation – Consumption	(Chandrasekaran and Jiang, 2018)
Irr.	Secondary WWTP effluent	Lettuce irrigation – Consumption	(Moazeni et al., 2017)
Irr.	Secondary WWTP effluent	$FeCl_2$ flocculation – Filtration – UV (25-30 mJ/cm^2) – Cl_2 – Irrigation – Consumption	(Sales-Ortells et al., 2015)
Irr.	Secondary WWTP effluent	Irrigation of bok choy, choi sum, gai lan, lettuce - Consumption	(Mok and Hamilton, 2014)
Irr.	Secondary WWTP effluent	Infiltration – Green space irrigation – Unintended and intended consumption	(Toze et al., 2010)

Irr.	Bolivar: Secondary WWTP effluent	DAF – Chlorination – EB (confined limestone aquifer, aerobic, ≥60 days residence time) – Crop irrigation – Consumption	(Ayuso-Gabella et al., 2011)
Irr.	Nardo: Secondary WWTP effluent	EB (unconfined karstic aquifer, nitrate reducing, 20-65 days residence time) – Crop irrigation – Consumption	(Ayuso-Gabella et al., 2011)
Irr.	Sabadell: Secondary WWTP effluent + surface water	EB (alluvial unconfined sandy aquifer, anaerobic, 7 days residence time) – UV – Cl_2 – RSF – Crop irrigation, urban irrigation & cleaning – Consumption of crops	(Ayuso-Gabella et al., 2011)
Irr.	Shafdan: Secondary WWTP effluent	EB (unconfined sandy aquifer, anaerobic, 270+ days residence time) – Cl_2 – Crop irrigation – Consumption	(Ayuso-Gabella et al., 2011)
Irr.	Western: Secondary WWTP effluent	UV disinfection – Chlorination – Vegetable irrigation – Consumption	(Barker-Reid et al., 2010)
Irr.	Eastern: Tertiary treated effluent	UF– Horticulture irrigation – Consumption	(Barker-Reid et al., 2010)

th. = theoretical assessment, EB = environmental buffer, DWT = drinking water treatment, AS = activated sludge, UF = ultrafiltration, MF = microfiltration, NF = nanofiltration, O_3 = ozone, BAC = biologically active carbon, SW = surface water, WWTP = wastewater treatment plant, PAC = powdered activated carbon, DAF = dissolved air flotation, RGSF = rapid gravity sand filtration, GAC = granular activated carbon, Cl_2 = chlorination, RBF = riverbank filtration, RSF = rapid sand filter, RO = reverse osmosis, UV/H_2O_2 = UV disinfection with hydrogen peroxide, UV/AOP = UV disinfection with advanced oxidation, UV = ultraviolet irradiation, ESB = engineered storage buffer, ESB+Cl_2 = engineered storage buffer with free chlorine disinfection, BAF = biologically active filtration Irr. = irrigation, DAF = dissolved air flotation, MBR = membrane bioreactor, UASB = upflow anaerobic sludge blanket. *Secondary WWTP effluent = biological process plus sedimentation.

Table 11-3: Disease burdens used in various water reuse studies, with some studies using both classifications

Tolerable disease/health burden	Frequency	Guideline documents	Studies
$\leq 10^{-4}$ infections per year ($\leq$ 1 illness per 10,000 people)	23/43	(U.S. Environmental Protection Agency, 1998; WaterReuse Research Foundation, 2011, 2015)	(Petterson et al., 2001; Mara et al., 2007; Åström et al., 2007; Seidu et al., 2008; Barker-Reid et al., 2010; Ander and Forss, 2011; Agulló-Barceló et al., 2012; Pavione et al., 2013; Sato et al., 2013; Olivieri et al., 2014; Beaudequin et al., 2016; Amoueyan et al., 2017; Chaudhry et al., 2017; Ito et al., 2017; Owusu-Ansah et al., 2017; Pecson et al., 2017; Amoueyan et al., 2019a; Soller et al., 2017, 2018a, 2018b; Amoueyan et al., 2019b; Bergion et al., 2018; Chandrasekaran and Jiang, 2018)
$\leq 10^{-6}$ DALYs per person per year ($\leq$ 1 illness per 1,000,000 people)	27/43	Table 7.4 in (World Health Organization, 2011), (World Health Organization, 2017b)	(Page et al., 2010; Toze et al., 2010; Ayuso-Gabella et al., 2011; Ferrer et al., 2012; Barker, 2013; Barker et al., 2013, 2014; Mok and Hamilton, 2014; Mok et al., 2014; Symonds et al., 2014; Sales-Ortells et al., 2015; Bartak et al., 2015; Verbyla et al., 2016; Beaudequin et al., 2016, 2017; Amoueyan et al., 2017, 2019a; Chhipi-Shrestha et al., 2017; Ito et al., 2017; Moazeni et al., 2017; Owusu-Ansah et al., 2017; Sampson et al., 2017; Chandrasekaran and Jiang, 2018; Xiao et al., 2018; Bergion et al., 2018; Fuzawa et al., 2019; Gonzales-Gustavson et al., 2019)

Table 11-4: Frequency of applied mathematical and statistical approaches in QMRA studies.

Type	Frequency	Sources
Sensitivity analysis	32/43	(Page et al., 2010; Barker-Reid et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Pavione et al., 2013; Sato et al., 2013; Barker, 2013; Barker et al., 2013, 2014; Mok et al., 2014; Olivieri et al., 2014; Symonds et al., 2014; Sales-Ortells et al., 2015; Beaudequin et al., 2017; Verbyla et al., 2016; Beaudequin et al., 2016; Amoueyan et al., 2017, 2019a; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Ito et al., 2017; Moazeni et al., 2017; Amoueyan et al., 2019b; Owusu-Ansah et al., 2017; Pecson et al., 2017; Sampson et al., 2017; Soller et al., 2017, 2018a; Chandrasekaran and Jiang, 2018; Xiao et al., 2018; Fuzawa et al., 2019; Gonzales-Gustavson et al., 2019)
Monte Carlo simulations	31/43	(Petterson et al., 2001; Mara et al., 2007; Seidu et al., 2008; Page et al., 2010; Toze et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Ferrer et al., 2012; Pavione et al., 2013; Barker, 2013; Barker et al., 2013; Mok and Hamilton, 2014; Mok et al., 2014; Olivieri et al., 2014; Sales-Ortells et al., 2015; Bartak et al., 2015; Verbyla et al., 2016; Beaudequin et al., 2016, 2017; Moazeni et al., 2017; Pecson et al., 2017; Sampson et al., 2017; Soller et al., 2017, 2018a, 2018b; Chhipi-Shrestha et al., 2017; Xiao et al., 2018; Bergion et al., 2018; Amoueyan et al., 2019b; Fuzawa et al., 2019; Gonzales-Gustavson et al., 2019)
(Spearman) rank order correlation	13/43	(Barker-Reid et al., 2010; Barker, 2013; Barker et al., 2013; Sato et al., 2013; Barker et al., 2014; Pavione et al., 2013; Mok et al., 2014; Verbyla et al., 2016; Chaudhry et al., 2017; Moazeni et al., 2017; Owusu-Ansah et al., 2017; Xiao et al., 2018; Bergion et al., 2018)

Factor sensitivity	7/43	(Page et al., 2010; Ayuso-Gabella et al., 2011; Symonds et al., 2014; Beaudequin et al., 2016; Amoueyan et al., 2017, 2019a; Pecson et al., 2017)
Latin Hypercube sampling	7/43	(Seidu et al., 2008; Barker-Reid et al., 2010; Toze et al., 2010; Ayuso-Gabella et al., 2011; Pavione et al., 2013; Sampson et al., 2017; Fuzawa et al., 2019)
Bayesian network	4/43	(Beaudequin et al., 2016, 2017; Verbyla et al., 2016; Ito et al., 2017)
Markov Chain Monte Carlo	3/43	(Åström et al., 2007; Verbyla et al., 2016; Soller et al., 2018a)
Wilcoxon tests & Mann-Whitney	5/43	(Barker, 2013; Barker et al., 2014; Verbyla et al., 2016; Owusu-Ansah et al., 2017; Soller et al., 2017)
Analysis of variance	2/43	(Barker et al., 2013; Owusu-Ansah et al., 2017)
Other (Tukey test, Fligner-Killeen, Shapiro Wilk, Kruskal Wallis, Anderson Darling)	5/43	(Barker, 2013; Barker et al., 2013, 2014; Sales-Ortells et al., 2015; Owusu-Ansah et al., 2017)
Evaluated or mentioned alternate PDFs	22/43	(Petterson et al., 2001; Seidu et al., 2008; Barker-Reid et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Agulló-Barceló et al., 2012; Sato et al., 2013; Barker, 2013; Barker et al., 2013; Mok et al., 2014; Symonds et al., 2014; Verbyla et al., 2016; Amoueyan et al., 2017; Chaudhry et al., 2017; Ito et al., 2017; Owusu-Ansah et al., 2017; Pecson et al., 2017; Soller et al., 2017, 2018a; Amoueyan et al., 2019a; Bergion et al., 2018; Chandrasekaran and Jiang, 2018)
Conducted both sensitivity analysis and evaluate/mentioned alternative PDFs	18/43	(Barker-Reid et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Sato et al., 2013; Barker, 2013; Barker et al., 2013; Mok et al., 2014; Symonds et al., 2014; Verbyla et al., 2016; Amoueyan et al., 2017, 2019a; Owusu-Ansah et al., 2017; Pecson et al., 2017; Soller et al., 2017, 2018a; Chaudhry et al., 2017; Ito et al., 2017; Chandrasekaran and Jiang, 2018)
Failures	7/43	(Ayuso-Gabella et al., 2011; Agulló-Barceló et al., 2012; Amoueyan et al., 2017, 2019a, 2019b; Pecson et al., 2017; Soller et al., 2018b)
Empirical data	27/43	(Petterson et al., 2001; Åström et al., 2007; Toze et al., 2010; Ander and Forss, 2011; Ayuso-Gabella et al., 2011; Agulló-Barceló et al., 2012; Ferrer et al., 2012; Pavione et al., 2013; Sato et al., 2013; Mok and Hamilton, 2014; Symonds et al., 2014; Barker et al., 2014; Sales-Ortells et al., 2015; Bartak et al., 2015; Verbyla et al., 2016; Ito et al., 2017; Moazeni et al., 2017; Owusu-Ansah et al., 2017; Pecson et al., 2017; Chaudhry et al., 2017; Chhipi-Shrestha et al., 2017; Soller et al., 2018b; Xiao et al., 2018; Bergion et al., 2018; Chandrasekaran and Jiang, 2018; Gonzales-Gustavson et al., 2019)
Discussed effect on final risk	12/43	(Agulló-Barceló et al., 2012; Barker, 2013; Barker et al., 2013; Symonds et al., 2014; Verbyla et al., 2016; Amoueyan et al., 2017, 2019a; Chaudhry et al., 2017; Ito et al., 2017; Soller et al., 2017, 2018a; Chandrasekaran and Jiang, 2018)

11.2.2 References

Agulló-Barceló, M., Casas-Mangas, R., Lucena, F., 2012. Direct and indirect QMRA of infectious cryptosporidium oocysts in reclaimed water. J. Water Health 10, 539–548. https://doi.org/10.2166/wh.2012.082

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Gerrity, D., 2019a. Equivalency of Indirect and Direct Potable Reuse Paradigms based on a Quantitative Microbial Risk Assessment Framework. Microb. Risk Anal. https://doi.org/10.1016/j.mran.2019.06.003

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Gerrity, D., 2019b. A dynamic quantitative microbial risk assessment for norovirus in potable reuse systems. Microb. Risk Anal. https://doi.org/10.1016/j.mran.2019.100088

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Pecson, B., Gerrity, D., 2017. Quantifying pathogen risks associated with potable reuse: A risk assessment case study for Cryptosporidium. Water Res. 119, 252–266. https://doi.org/10.1016/j.watres.2017.04.048

Ander, H., Forss, M., 2011. Microbiological Risk Assessment of the Water Reclamation Plant in Windhoek , Namibia. Chalmers University of Technology.

Åström, J., Petterson, S., Bergstedt, O., Pettersson, T.J.R., Stenström, T.A., 2007. Evaluation of the microbial risk reduction due to selective closure of the raw water intake before drinking water treatment closure of the raw water intake before drinking water. J. Water Health. https://doi.org/10.2166/wh.2007.139

Ayuso-Gabella, N., Page, D., Masciopinto, C., Aharoni, A., Salgot, M., Wintgens, T., 2011. Quantifying the effect of Managed Aquifer Recharge on the microbiological human health risks of irrigating crops with recycled water. Agric. Water Manag. 99, 93–102. https://doi.org/10.1016/j.agwat.2011.07.014

Barker-Reid, F., Harper, G.A., Hamilton, A.J., 2010. Affluent effluent: growing vegetables with wastewater in Melbourne , Australia — a wealthy but bone-dry city. Irrig. Drain. Syst. 79–94. https://doi.org/10.1007/s10795-009-9082-x

Barker, S.F., 2013. Risk of norovirus gastroenteritis from consumption of vegetables irrigated with highly treated municipal wastewater-evaluation of methods to estimate sewage quality. Risk Anal. 34, 803–817. https://doi.org/10.1111/risa.12138

Barker, S.F., Amoah, P., Drechsel, P., 2014. A probabilistic model of gastroenteritis risks associated with consumption of street food salads in Kumasi, Ghana: Evaluation of methods to estimate pathogen dose from water , produce or food quality. Sci. Total Environ. 487, 130–142. https://doi.org/10.1016/j.scitotenv.2014.03.108

Barker, S.F., Packer, M., Scales, P.J., Gray, S., Snape, I., Hamilton, A.J., 2013. Pathogen reduction requirements for direct potable reuse in Antarctica : Evaluating human health risks in small communities. Sci. Total Environ. 461–462, 723–733. https://doi.org/10.1016/j.scitotenv.2013.05.059

Bartak, R., Page, D., Sandhu, C., Grischek, T., Saini, B., Mehrotra, I., Jain, C.K., Ghosh, N.C., 2015. Application of risk-based assessment and management to riverbank filtration sites in India. J. Water Health 13, 174–189. https://doi.org/10.2166/wh.2014.075

Beaudequin, D., Harden, F., Roiko, A., Mengersen, K., 2017. Potential of Bayesian networks for adaptive management in water recycling. Environ. Model. Softw. 91, 251–270. https://doi.org/10.1016/j.envsoft.2017.01.016

Beaudequin, D., Harden, F., Roiko, A., Mengersen, K., 2016. Utility of Bayesian networks in QMRA-based evaluation of risk reduction options for recycled water. Sci. Total Environ. 541, 1393–1409. https://doi.org/10.1016/j.scitotenv.2015.10.030

Bergion, V., Lindhe, A., Sokolova, E., Ros, L., 2018. Risk-based cost-benefit analysis for evaluating microbial risk mitigation in a drinking water system. Water Res. 132. https://doi.org/10.1016/j.watres.2017.12.054

Chandrasekaran, S., Jiang, S.C., 2018. A dynamic transport model for quantification of norovirus internalization in lettuce from irrigation water and associated health risk. Sci. Total Environ. 643, 751–761. https://doi.org/10.1016/j.scitotenv.2018.06.158

Chaudhry, R.M., Hamilton, K.A., Haas, C.N., Nelson, K.L., 2017. Drivers of microbial risk for direct potable reuse and de facto reuse treatment schemes: The impacts of source water quality and blending. Int. J. Environ. Res. Public Health 14, 1–20. https://doi.org/10.3390/ijerph14060635

Chhipi-Shrestha, G., Hewage, K., Sadiq, R., 2017. Microbial quality of reclaimed water for urban reuses: Probabilistic risk-based investigation and recommendations. Sci. Total Environ. 576, 738–751. https://doi.org/10.1016/j.scitotenv.2016.10.105

Ferrer, A., Nguyen-viet, H., Zinsstag, J., 2012. Quantification of Diarrhea Risk Related to Wastewater Contact in Thailand Quantification of Diarrhea Risk Related to Wastewater Contact in Thailand. Ecohealth. https://doi.org/10.1007/s10393-012-0746-x

Fuzawa, M., Smith, R.L., Ku, K., Shisler, J.L., Feng, H., Juvik, J.A., Nguyen, T.H., 2019. Roles of Vegetable Surface Properties and Sanitizer Type on Annual Disease Burden of Rotavirus Illness by Consumption of Rotavirus-Contaminated Fresh Vegetables : A Quantitative Microbial Risk Assessment. Risk Anal. 1. https://doi.org/10.1111/risa.13426

Gonzales-Gustavson, E., Rusinol, M., Medema, G., Calvo, M., Girones, R., 2019. Quantitative risk assessment of norovirus and adenovirus for the use of reclaimed water to irrigate lettuce in Catalonia. Water Res. 153, 91–99. https://doi.org/10.1016/j.watres.2018.12.070

Ito, T., Kitajima, M., Kato, T., Ishii, S., Segawa, T., Okabe, S., Sano, D., 2017. Target virus log10 reduction values determined for two reclaimed wastewater irrigation scenarios in Japan based on tolerable annual disease burden Water Research Target virus log 10 reduction values determined for two reclaimed wastewater irrigation scena. Water Res. 125, 438–448. https://doi.org/10.1016/j.watres.2017.08.057

Mara, D.D., Sleigh, P.A., Blumenthal, U.J., Carr, R., 2007. Health risks in wastewater irrigation: Comparing estimates from quantitative microbial risk analyses and epidemiological studies. J. Water Health 5, 39–50. https://doi.org/10.2166/wh.2006.055

Moazeni, M., Nikaeen, M., Hadi, M., Moghim, S., Mouhebat, L., Hatamzadeh, M., Hassanzadeh, A., 2017. Estimation of health risks caused by exposure to enteroviruses from agricultural application of wastewater effluents. Water Res. https://doi.org/10.1016/j.watres.2017.08.028

Mok, H.-F., Hamilton, A.J., 2014. Exposure Factors for Wastewater-Irrigated Asian Vegetables and a Probabilistic Rotavirus Disease Burden Model for Their Consumption. Risk Anal. 34, 602–613. https://doi.org/10.1111/risa.12178

Mok, H.F., Barker, S.F., Hamilton, A.J., 2014. A probabilistic quantitative microbial risk assessment model of norovirus disease burden from wastewater irrigation of vegetables in Shepparton, Australia. Water Res. 54, 347–362. https://doi.org/10.1016/j.watres.2014.01.060

Olivieri, A.W., Seto, E., Cooper, R.C., Cahn, M.D., Colford, J., Crook, J., Debroux, J., Mandrell, R., Suslow, T., 2014. Risk-Based Review of California's Water-Recycling Criteria for Agricultural Irrigation. J. Environ. Eng. https://doi.org/10.1061/(ASCE)EE.1943-7870.0000833

Owusu-Ansah, E. de G.J., Sampson, A., Amponsah, S.K., Abaidoo, R.C., Dalsgaard, A., Hald, T., 2017. Probabilistic quantitative microbial risk assessment model of norovirus from wastewater irrigated vegetables in Ghana using genome copies and fecal indicator ratio conversion for estimating exposure dose. Sci. Total Environ. 601–602, 1712–1719. https://doi.org/10.1016/j.scitotenv.2017.05.168

Page, D., Dillon, P., Toze, S., Bixio, D., Genthe, B., Jiménez Cisneros, B.E., Wintgens, T., 2010. Valuing the subsurface pathogen treatment barrier in water recycling via aquifers for drinking supplies. Water Res. 44, 1841–1852. https://doi.org/10.1016/j.watres.2009.12.008

Pavione, D.M.., Bastos, R.K.X., Bevilacqua, P.D., 2013. Quantitative microbial risk assessment applied to irrigation of salad crops with waste stabilization pond effluents. Water Sci. Technol. https://doi.org/10.2166/wst.2013.674

Pecson, B.M., Triolo, S.C., Olivieri, S., Chen, E.C., Pisarenko, A.N., Yang, C., Olivieri, A., Haas, C.N., Trussell, R.S., Trussell, R.R., 2017. Reliability of pathogen control in direct potable reuse : Performance evaluation and QMRA of a full-scale 1 MGD advanced treatment train. Water Res. 122, 258–268. https://doi.org/10.1016/j.watres.2017.06.014

Petterson, S.R., Ashbolt, N.J., Sharma, A., 2001. Microbial Risks from Wastewater Irrigation of Salad Crops: a Screening-Level Risk Assessment. Water Environ. Res. 72. https://doi.org/10.2175/106143002X140161

Sales-Ortells, H., Fernandez-Cassi, X., Timoneda, N., Dürig, W., Girones, R., Medema, G., 2015. Health risks derived from consumption of lettuces irrigated with tertiary ef fl uent containing norovirus. Food Res. Int. 68, 70–77. https://doi.org/10.1016/j.foodres.2014.08.018

Sampson, A., Owusu-Ansah, E.J., Mills-Robertson, F.C., Ayi, I., Abaidoo, R.C., Hald, T., Permin, A., 2017. Probabilistic quantitative microbial risk assessment model of farmer exposure to Cryptosporidium spp . in irrigation water within Kumasi. Microb. Risk Anal. 6, 1–8. https://doi.org/10.1016/j.mran.2017.06.001

Sato, M.I.Z., Galvani, A.T., Padula, J.A., Nardocci, A.C., Lauretto, M. de S., Razzolini, M.T.P., Hachich, E.M., 2013. Assessing the infection risk of Giardia and Cryptosporidium in public drinking water delivered by surface water systems in Sao Paulo State, Brazil. Sci. Total Environ. 442, 389–396. https://doi.org/10.1016/j.scitotenv.2012.09.077

Seidu, R., Heistad, A., Amoah, P., Drechsel, P., Jenssen, P.D., Stenström, T.A., 2008. Quantification of the health risk associated with wastewater reuse in Accra, Ghana: A contribution toward local guidelines. J. Water Health 6, 461–471. https://doi.org/10.2166/wh.2008.118

Soller, J.A., Eftim, S.E., Nappier, S.P., 2018a. Direct potable reuse microbial risk assessment methodology: Sensitivity analysis and application to State log credit allocations. Water Res. 128, 286–292. https://doi.org/10.1016/j.watres.2017.10.034

Soller, J.A., Eftim, S.E., Warren, I., Nappier, S.P., 2017. Evaluation of microbiological risks associated with direct potable reuse. Microb. Risk Anal. 5, 3–14. https://doi.org/10.1016/j.mran.2016.08.003

Soller, J.A., Parker, A.M., Salveson, A., 2018b. Public Health Implications of Short Duration, Off-Specification Conditions at Potable Reuse Water Treatment Facilities. Environ. Sci. Technol. https://doi.org/10.1021/acs.estlett.8b00470

Symonds, E.M., Verbyla, M.E., Lukasik, J.O., Kafle, R.C., Breitbart, M., Mihelcic, J.R., 2014. A case study of enteric virus removal and insights into the associated risk of water reuse for two wastewater treatment pond systems in Bolivia. Water Res. 65, 257–270. https://doi.org/10.1016/j.watres.2014.07.032

Toze, S., Bekele, E., Page, D., Sidhu, J., Shackleton, M., 2010. Use of static Quantitative Microbial Risk Assessment to determine pathogen risks in an unconfined carbonate aquifer used for Managed Aquifer Recharge. Water Res. 44, 1038–1049. https://doi.org/10.1016/j.watres.2009.08.028

U.S. Environmental Protection Agency, 1998. National Primary Drinking Water Regulations: Disinfectants and Disinfection Byproducts: 40 CFR 9, 141, 142, Federal Register.

Verbyla, M.E., Symonds, E.M., Kafle, R.C., Cairns, M.R., Iriarte, M., Mercado Guzmán, A., Coronado, O., Breitbart, M., Ledo, C., Mihelcic, J.R., 2016. Managing Microbial Risks from Indirect Wastewater Reuse for Irrigation in Urbanizing Watersheds. Environ. Sci. Technol. 50, 6803–6813. https://doi.org/10.1021/acs.est.5b05398

WaterReuse Research Foundation, 2015. Framework for Direct Potable Reuse.

WaterReuse Research Foundation, 2011. Direct Potable Reuse-a path forward. Alexandria, VA.

World Health Organization, 2017. Guidelines for Drinking-Water Quality: Fourth edition incorporating the first addendum, WHO Library Cataloguing-in-Publication Data. https://doi.org/10.1016/S1462-0758(00)00006-6

World Health Organization, 2011. Guidelines for Drinking-water Quality. https://doi.org/10.1016/S1462-0758(00)00006-6

Xiao, S., Hu, S., Zhang, Y., Zhao, X., Pan, W., 2018. Influence of sewage treatment plant effluent discharge into multipurpose river on its water quality: A quantitative health risk assessment of Cryptosporidium and Giardia. Environ. Pollut. 233, 797–805. https://doi.org/10.1016/j.envpol.2017.11.010

11.3 Supplementary information for Chapter 5

Quantitative microbial risk assessment of a non-membrane based indirect potable water reuse system using Bayesian networks

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11.3.1 Selection of PDFs

Pathogen occurrence in raw sewage

While it is critical to use correct units when comparing results of different enumeration or plating tests, for this study most probable number (MPN) and colony forming units (CFU) were considered to be interchangeable. As studies used a variety of point values as well as varying distributions to describe presence of pathogens in raw sewage, selecting one PDF was difficult. Therefore, all raw sewage distributions were adapted from Beaudequin et al. (2017), who used triangular distributions for all pathogens based on recommendation from guidelines (NRMMC–EPHC–AHMC, 2006). The use of triangular distributions to describe removal in treatment steps has also been mentioned by in other works (Page et al., 2010a; Smeets et al., 2006; Smeets, 2008; World Health Organization, 2016).

Campylobacter occurrence in raw sewage ranged from <1 to 105 CFU/L to a default value of 7,000 CFU/L (NRMMC–EPHC–AHMC, 2006; World Health Organization, 2017a). The triangular distribution of Beaudequin et al. (2017) (min 100, most likely 7,000, max 100,000, units CFU/L) was adapted by updating the minimum to 0 CFU/L (World Health Organization, 2017a).

Cryptosporidium presence in raw sewage revealed geographical and country specific variability, with concentrations ranging from <1 to 105 oocysts/L and a default value of 2,700 oocysts/L (World Health Organization, 2017a), whereas other guidelines reported 101 to 104 oocysts/L (NRMMC–EPHC–AHMC, 2006; Rose et al., 2005) and others provide a maximum of 2,000 oocysts/L (NRMMC-EPHC-NHMR, 2008). Though some studies adapted a lognormal distribution with low parameter values to describe the lower concentrations (Amoueyan et al., 2017; Chaudhry et al., 2017; Ottoson et al., 2006; Pecson et al., 2017), this approach fails to cover higher concentrations. A more conservative and wide ranging assumption of a triangular distribution with min, most likely, and max of 0, 2,000, and 10,000 oocysts/L used by Beaudequin et al. (2017) could feature higher concentrations more accurately. Therefore, this study adapted the triangular distribution and updated the most likely value to 2,700 oocysts/L and the maximum value to 105 oocysts/L (World Health Organization, 2017a).

Norovirus concentrations in raw sewage displayed noticeable seasonality (Eftim et al., 2017), with higher concentrations reported in winter months. Guidelines reported a range of <1 to 106 units/L, with a default value of 20,000 units/L (World Health Organization, 2017a), or 101 to 104 (NRMMC–EPHC–AHMC, 2006). Beaudequin et al. (2017) used a triangular distribution (min 1 * 104, most likely 5 * 106, max 1 * 107, PCR units/mL) to describe concentrations in raw wastewater, which were high due to a novel method of calculating norovirus concentrations from epidemiological data. Improvements of analytical methods over the last 25 years, such as quantitative polymerase chain reaction (qPCR) have revealed that virus concentrations in raw sewage could be 2-3 logs greater than assumed by older guideline values, on the order of 107 to 109 units per L (Gerba et al., 2017). However, as qPCR cannot detect the difference between infective and non-infective genome copies, these higher concentrations could overestimate the infective potential in raw sewage. Therefore, the older guideline values were used for this study, and a triangular distribution was fit to the World Health Organization (2017a) values (min 0, most likely 20,000, max 106 units/L).

Pathogen removal during secondary treatment

Studies which used uniform distributions to characterize *Campylobacter* removals reported LRVs between 0.6-3 (Asano et al., 2007; Beaudequin et al., 2017; NRMMC–EPHC–AHMC, 2006; Soller et al., 2017, 2018; US EPA, 2017; World Health Organization, 2016). (Ayuso-Gabella et al., 2011) used a triangular distribution with min, most likely and max values of 1, 2 and 3.5 LRVs, citing the 1-3 LRVs from the Australian guidelines (NRMMC–EPHC–AHMC, 2006). This study adopted the triangular distribution of Ayuso-Gabella et al. (2011) but changed the minimum value to 0.6.

Reported uniformly distributed *Cryptosporidium* removals ranged from 0.5 to 3.5 LRVs (Ander and Forss, 2011; NRMMC–EPHC–AHMC, 2006). One triangular distribution was found: the Australian reuse guidelines provide a range of 0.5 to 1 LRV (NRMMC–EPHC–AHMC, 2006), which was adapted into a triangular distribution with min, most likely and max values of 0.5, 1.0 and 1.5 (Ayuso-Gabella et al., 2011). Two studies used normal distributions with (2.1, 0.78) (Amoueyan et al., 2019; Chaudhry et al., 2017), citing prior work (Ottoson et al., 2006). This study adopted the triangular distribution of (Ayuso-Gabella et al., 2011) which provides a more conservative removal estimate.

Reported uniformly distributed norovirus removals in the literature ranged from 0 to 4 LRVs (Mok et al., 2014). Australian guidelines give an estimate of 0.5 to 2 LRVs of enteric viruses via secondary treatment (NRMMC–EPHC–AHMC, 2006). Normal PDFs to describe norovirus removal during secondary treatment were used in two studies: (Chaudhry et al., 2017) used (μ=2.1, σ=0.78), while (Amoueyan et al., 2019) used (μ=1.2, σ=0.78), both citing (Lodder et al., 2005). This study adapted a uniform distribution to the ambient removal range of phages reported in Karakurt-Fischer et al. (2021) (0.5, 2) to better encompassthe removal range reported on site, and to take a wider range than the values reported for human norovirus (0.8, 1). The 0.8-1 LRVs were later investigated through scenario analysis.

Pathogen removal during rapid sand filtration

Of three studies which gave LRVs of *Campylobacter* reduction during rapid sand filtration, two used min/max values and one used a triangular distribution. Of the studies which used min/max values, 0.2-1 LRVs (Hijnen and Medema, 2007) and 0.6 to 2.8 LRVs (Mohammed and Seidu, 2019) were found. (Ayuso-Gabella et al., 2011) used a triangular distribution with 0, 0, and 0.5 as the minimum, most likely and maximum parameters based on the Australian reuse guidelines (NRMMC–EPHC–AHMC, 2006), which provided values for dual media filtration with coagulation. WHO guidelines recommend 0.2 to 4.4 LRVs for granular high rate filtration (World Health Organization, 2017b). Smeets et al. (2006) provided minimum, average and maximum LRVs of 0.1, 0.6, and 1.5 for rapid sand filtration of bacteria in a DWTP. Due to lack of studies on rapid sand filtration with wastewater, and overwhelming lack of specification of operational parameters, although the LRVs in Mohammed and Seidu (2019) were obtained in a DWTP, a uniform distribution was fit to their values (0.6, 2.8).

Cryptosporidium removal in rapid sand filtration ranged from 0 to 5.7 LRVs (Emelko, 2003; Smeets et al., 2006). Studies which used min/max values found 0 to 2.3 LRVs (Hijnen and Medema, 2007), and 0.1 to 0.7 LRVs (Mohammed and Seidu, 2019) for rapid sand filtration, and 4.7 to 5.7 LRVs for dual media filtration (Emelko, 2003). WHO guidelines recommend 0.4 to 3.3 LRVs for granular high rate filtration (World Health Organization, 2017b). Ayuso-Gabella et al. (2011) utilized a triangular distribution (0, 0, 0.5) adapted to Australian guidelines, which actually recommended 1-5 to 2.5 LRVs for dual media filtration with coagulation (NRMMC–EPHC–AHMC, 2006). Smeets et al. (2006) provided minimum, average and maximum LRVs of 0, 2, and 3.1 for rapid sand filtration in a DWTP. Due to lack of studies on rapid sand filtration with wastewater, this study used a triangular distribution fit to the values of Smeets et al. (2006).

Norovirus removal in rapid sand filtration ranged from 0 to 3.8 LRVs. Studies which used min/max values found 0.1 to 3.8 LRVs (Hijnen and Medema, 2007; Smeets et al., 2006) and 0.06 to 0.3 LRVs (Mohammed and Seidu, 2019). WHO guidelines found 0 to 3.5 LRVs for granular high rate filtration (World Health Organization, 2017b). This study adapted a uniform distribution to the ambient removal range of human norovirus reported in Karakurt-Fischer et al. (2021) (0, 0.3) as this encompassed the removal reported on site (and was wider than 0.2 LRVs).

Pathogen removal during SMARTplus

Campylobacter removal during slow sand filtration ranged from 1.2 to 6 LRVs. WHO guidelines found 2 to 6 LRVs for slow sand filtration (no loading rates reported) (World Health Organization, 2017b), while Hijnen and Medema (2007) and Smeets et al. (2006) reported LRVs of 1.2 to 4.8, which is a range for bacteria compiled from many SSF studies and attributed to loading rates of 0.1-1 m/hr with a filter bed depth of 0.5-1 m. This study will adapt a uniform distribution to the values from the WHO.

Cryptosporidium removal during slow sand filtration ranged from 0.3 to 6 LRVs. WHO guidelines found 0.3 to >5 LRVs for slow sand filtration (no loading rates reported) (World Health Organization, 2017b), while Hijnen and Medema, (2007) found 2.7 to >6.5 LRVs and Smeets et al. (2006) reported 0.3 to >6.5 LRVs, both of which are ranges of values from numerous studies. This study will adapt a uniform distribution to the values from the WHO.

Ambient average removal of phages demonstrated in Karakurt-Fischer et al., (2021) (2.2, 3) were adapted to a uniform distribution to characterize norovirus removal. The ambient average norovirus removal reported (2.5, 2.7) was too narrow for the distribution, and was instead tested during the scenario analysis.

Pathogen removal during UV disinfection

As the target fluence for adenovirus inactivation is 180 mJ/cm^2 (Sherchan et al., 2014), the UV irradiation results summarized here will address studies which are closest to this target value. The WHO Potable Reuse Guidelines recommend 6 LRVs for bacteria, viruses and protozoa through UV irradiation, which was adapted as the maximum LRV for Campylobacter and Cryptosporidium (World Health Organization, 2017a).

Reported *Campylobacter* LRVs ranged depending on the study and guideline, with many sources providing LRVs at undisclosed fluences. The WHO Guidelines for Drinking Water Quality assign 4 LRVs for fluences between 0.65 to 230 mJ/cm^2 (World Health Organization, 2017b). However, the WHO Potable Reuse Guidelines assign 6 LRVs and the Australian guidelines assign 2 to >4 LRVs, both at undisclosed fluences (but assuming a standard irradiation dose of 40-60 mJ/m^2) (NRMMC–EPHC–AHMC, 2006; World Health Organization, 2017a). Other studies have reported 5.3 LRVs for bacteria and bacterial spores already at low fluences of 0.5 to 6 mJ/cm^2 (Hijnen et al., 2006). Therefore, this study adapted a uniform distribution from 4-6 LRVs to encompass the most updated guidelines and the higher end of removal.

Reported *Cryptosporidium* LRVs likewise ranged depending on the chosen guidance document. The WHO Guidelines for Drinking Water Quality assigned 4 LRVs for a fluence range from <1 to 60 mJ/cm^2 (World Health Organization, 2017b), while the Potable Reuse Guidelines recommend 6 LRVs for an undisclosed fluence (World Health Organization, 2017a). However, 4 LRVs have already been shown at 22 mJ/cm^2 (Sherchan et al., 2014), therefore assigning only 4 LRVs is likely too conservative to accurately describe removal (Chaudhry et al., 2017). Therefore, the removal used for this study was a uniform distribution between 4 to 6 LRVs.

Reported norovirus LRVs for UV irradiation varied widely, with many studies describing irradiation without stating the applied fluence. The WHO Guidelines for Drinking Water Quality specify 4 LRVs for 7 to 186 mJ/cm² (World Health Organization, 2017b), which is also confirmed by the WHO Potable Reuse Guidelines (World Health Organization, 2017a) and was based on the work of Sherchan et al. (2014). This study will therefore adopt a uniform distribution of 3.9 to 4 for norovirus irradiation.

Pathogen removal through groundwater recharge

Removal rates or point estimates during groundwater recharge were difficult to obtain from literature, due to varying hydraulic retention times and redox conditions in subsurface treatment systems. It is also

important to note that the provided estimates are usually conservative, as pathogen recovery greatly depends on the detection method used. The LRVs for groundwater recharge were modeled as the product of residence time and pathogen decay, and were capped at a maximum of 4 LRVs, to provide a conservative estimate for human health risk based on the assumed subsurface residence time of 50-120 days and decay rates reported for MS2 in Regnery et al. (2017). Pathogen decay rates are discussed below. According to the most recent issue of the WHO Guidelines for Drinking Water Quality, bank filtration can achieve 2 to >6 LRVs for bacteria, >1 to >2 LRVs for protozoa, and >2.1 to 8.3 LRVs for viruses (World Health Organization, 2017b).

Campylobacter subsurface pathogen decay rate in a sandy aquifer was described using a triangular distribution (0.02, 0.08, 1.5, log10 d^{-1}) (Ayuso-Gabella et al., 2011). Page et al. (2010b) used a point value (5.6) to describe decay rate in log10 d^{-1} adapted from values reported in (NRMMC–EPHC–AHMC, 2006). To include more variability in the assessment, this study used the triangular distribution from Ayuso-Gabella et al. (2011).

Cryptosporidium removals in subsurface treatment varied. The lowest decay values were used by Sidhu et al. (2010) and Ayuso-Gabella et al. (2011) with a normal mean and a normal standard deviation of 0.012 log10 d^{-1} and 0.003 log10 d^{-1}. Toze et al. (2010) reported an average decay rate of 0.0254 log10 d^{-1}, and when using a broken stick model, described decay from days 0-12 as 0.0824 log10 d^{-1} and from days 12-40 with 0.0682 log10 d^{-1}. Sidhu and Toze (2012) found point values ranging from 0.025 to 0.032 log10 d^{-1}. This study adapted a uniform distribution to the values reported in Toze et al. (2010) (0.025, 0.082).

Norovirus decay during subsurface treatment was not found, therefore studies from MS2 bacteriophage decay were substituted instead, although utilizing MS2 removal as norovirus removal could overestimate norovirus removal (Regnery et al., 2017; Shirasaki et al., 2010). MS2 decay was calculated to be 0.093-0.174 log10 d^{-1} (Sidhu and Toze, 2012), although higher removals of MS2 are seen in the unsaturated zone, as MS2 is extremely hydrophobic and interacts with the air-water interface (Jin et al., 2000) and therefore does not reach the saturated zone. Despite these limitations, MS2 has been shown to be an acceptable surrogate for norovirus in groundwater (Bae and Schwab, 2008). This study adapted a uniform distribution for the rates reported by Sidhu and Toze (2012).

Pathogen removal during aeration and dual media filtration

As the operation of filtration within conventional drinking water treatment varies based on factors such as source water and national/state regulations, studies performing only aeration and filtration were not found. Therefore, literature data on dual media filtration (without coagulation) was selected for this treatment step.

Removal of pathogens in dual media filtration was credited with 0 to 1 LRVs for Campylobacter, 1.5 to 2.5 LRVs for Cryptosporidium, and 0.5-2 LRVs for norovirus in the Australian guidelines (NRMMC-EPHC-NHMR, 2008). The U.S. Surface Water Treatment Rule credits conventional filtration with > 2 LRVs for Cryptosporidium and 2 LRVs for viruses (US EPA, 2005). The Australian ranges were adapted to a uniform distribution for each pathogen to provide more variability in the assessment..

11.3.2 Selection of dose-response models

Campylobacter

The first model tested for *Campylobacter* was the beta Poisson model of Medema et al. (1996), applied to adults, with Equation 11-1 adapted from World Health Organization (2016),

$$P_{inf} = 1 - \left(1 + \frac{N}{\beta}\right)^{-\alpha} \quad \textit{Equation 11-1}$$

where α =0.145 and β =7.59 are model parameters and N is the number of ingested organisms.

The same model was updated by Teunis et al. (2005) by combining observations of illnesses from two outbreak cases and updating the parameter values (α=0.024, β=0.011). This equation and parameters are recommended for a mixed population (World Health Organization, 2016) and this model was therefore tested as an alternative model.

Cryptosporidium

The prevalence of dose response models for Cryptosporidium in the literature ranged widely: the Center for Advancing Microbial Risk Assessment (CAMRA) lists beta Poisson as the recommended dose-response model (CAMRA, 2020), the U.S. Environmental Protection Agency uses an exponential model (US EPA, 2006), and a recent study by Messner and Berger (2016) showed that exponential with immunity, beta Poisson and fractional Poisson were the best choices, according to their deviance information criterion (DIC). As the difference in DIC for the latter three models was <3 and evaluating the beta Poisson model was computationally intensive, the authors chose to test the simpler fractional Poisson and the exponential models from Messner and Berger (2016). The fractional Poisson is the upper bound on risk, whereas the exponential model is the lowest risk dose-response model. It is worth noting that mechanistic assumptions of immunity among experimental dose-response subjects is controversial on biological grounds (Schmidt and Chappell, 2016).

The first dose-response model evaluated was the exponential model depicted in Equation 11-2,

$$P_{inf} = \mathrm{P}(1 - e^{-D*r}) \quad \textit{Equation 11-2}$$

where D is the pathogen dose, P = 0.737 is the fraction of hosts perfectly susceptible to infection, and r = 0.0022 is the probability of an oocyst initiating infection (Messner and Berger, 2016).

Additionally, the fractional Poisson model in Equation 3, which is considered to be an even more conservative model as it assumes all oocysts are capable of causing an infection and covers lower doses better than the exponential with immunity model, was also evaluated,

$$P_{inf} = P\left(1 - e^{-D}\right) \quad \textit{Equation 11-3}$$

where P= 0.737. The fractional Poisson model is a special case of the exponential with immunity model, and when r approaches 1, the models will be the same.

Norovirus

The first model tested was the approximated fractional Poisson dose-response model (Messner et al., 2014) depicted in Equation 11-4,

$$P_{inf} = P * (1 - e^{-\frac{d}{\mu}}) \quad \textit{Equation 11-4}$$

where P = 0.722 represents the maximum likelihood estimate of fraction of perfectly susceptible individuals, and μ = 1106 represents the estimate of the mean aggregate size (Messner et al., 2014). This model uses pooled data from numerous studies investigating both GI.1 and GII.4 norovirus genotypes.

The majority of published QMRAs use the 1F1 hypergeometric model of Teunis et al. (2008), which predicts high risks at low doses (Van Abel et al., 2017). This model was developed via a challenge study and the hypergeometric distribution has previously been applied in the assessment of water reuse scenarios (Soller et al., 2017; Symonds et al., 2014). However, when α << ß and ß >> 1 (Teunis and

Havelaar, 2000), a beta Poisson approximation can be used for the hypergeometric model for computational simplicity Van Abel et al. (2017), and was the second model tested in this study. The beta Poisson approximation shows the same linear behavior at low doses as the hypergeometric model, and as the discrepancy between the model results is low (Teunis et al., 1999), the parameter values calculated for the disaggregated distribution using maximum likelihood estimates using both the 8fIIa and 8fIIb strains from Teunis et al. (2008) in Van Abel et al. (2017) were used (α=0.104, ß=32.3). Although Van Abel et al. (2017) suggests modeling an aggregated and disaggregated model when aggregation state of the water is unknown, this disaggregated approximate beta Poisson model provided a slightly more conservative estimate of risk at low concentrations (1-~100 genomic equivalent copies/L) than the most conservative aggregated fractional Poisson model. As use of the aggregated model requires either a mechanistic or empirical approach to norovirus dose-response, and studies are inconclusive about which approach is more suitable under which conditions, the disaggregated model was ultimately settled on. The utilized approximate beta Poisson equation is depicted in Equation 11-5.

$$P_{inf} = 1 - \left[1 + \left\{\frac{\mathbf{dose}}{\boldsymbol{\beta}}\right\}\right]^{-\alpha} \qquad \textit{Equation 11-5}$$

where β = 32.3 and α = 0.104 (Van Abel et al., 2017).

11.3.3 Sensitivity tornado plots

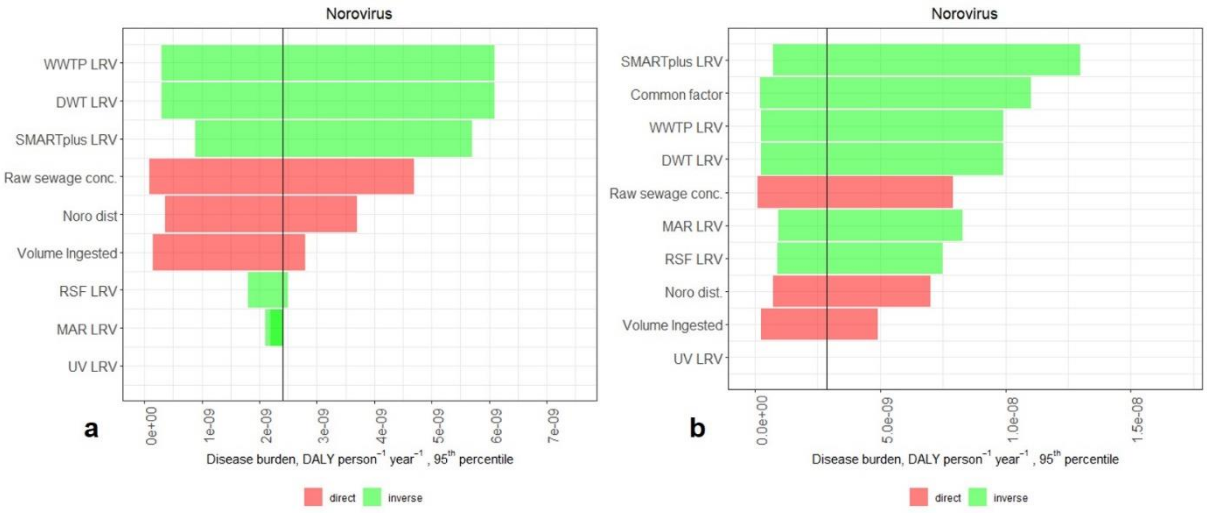

Figure 11-2: Tornado plot showing the range of norovirus DALYs achieved when minimum and maximum values of each node are used in the normal network (a) and correlation network (b).

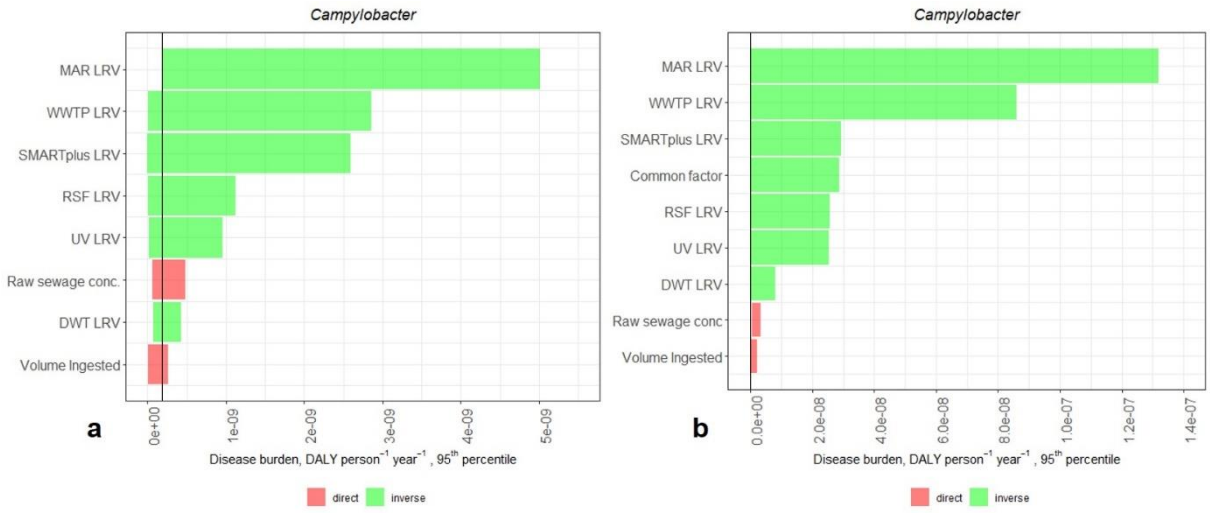

Figure 11-3: Tornado plot showing the range of Campylobacter DALYs achieved when minimum and maximum values of each node are used in the normal network (a) and correlation network (b).

11.3.4 Comparison between BN and Monte Carlo analysis

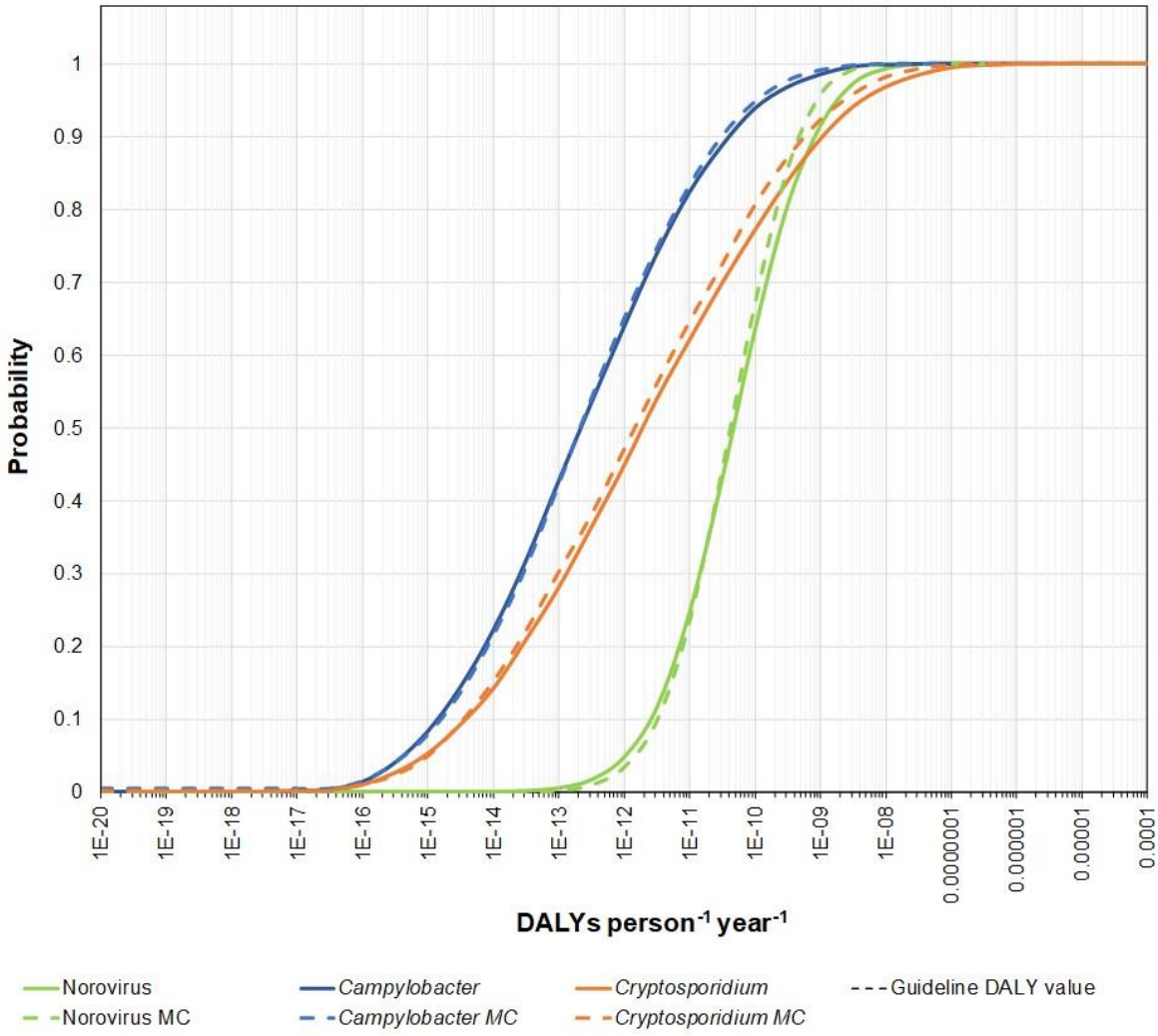

Figure 11-4: CDFs of DALYs generated by the Bayesian network and a Monte Carlo simulation, both run for n=10,000 samples.

To determine plausibility of the BN, a Monte Carlo simulation was conducted as a confidence check. For comparison of the BN and the Monte Carlo simulation, the mean absolute error (MAE) between the CDFs of both models was calculated. Although the difference between MC and BN results widened as MAR residence time increased to 115-120 days, the BN was always more conservative at the higher percentiles (i.e. 95^{th}). MAE was small for all 3 pathogens (norovirus = $3 * 10^{-10}$, *Cryptosporidium* $2 * 10^{-8}$, and *Campylobacter* $5 * 10^{-11}$).

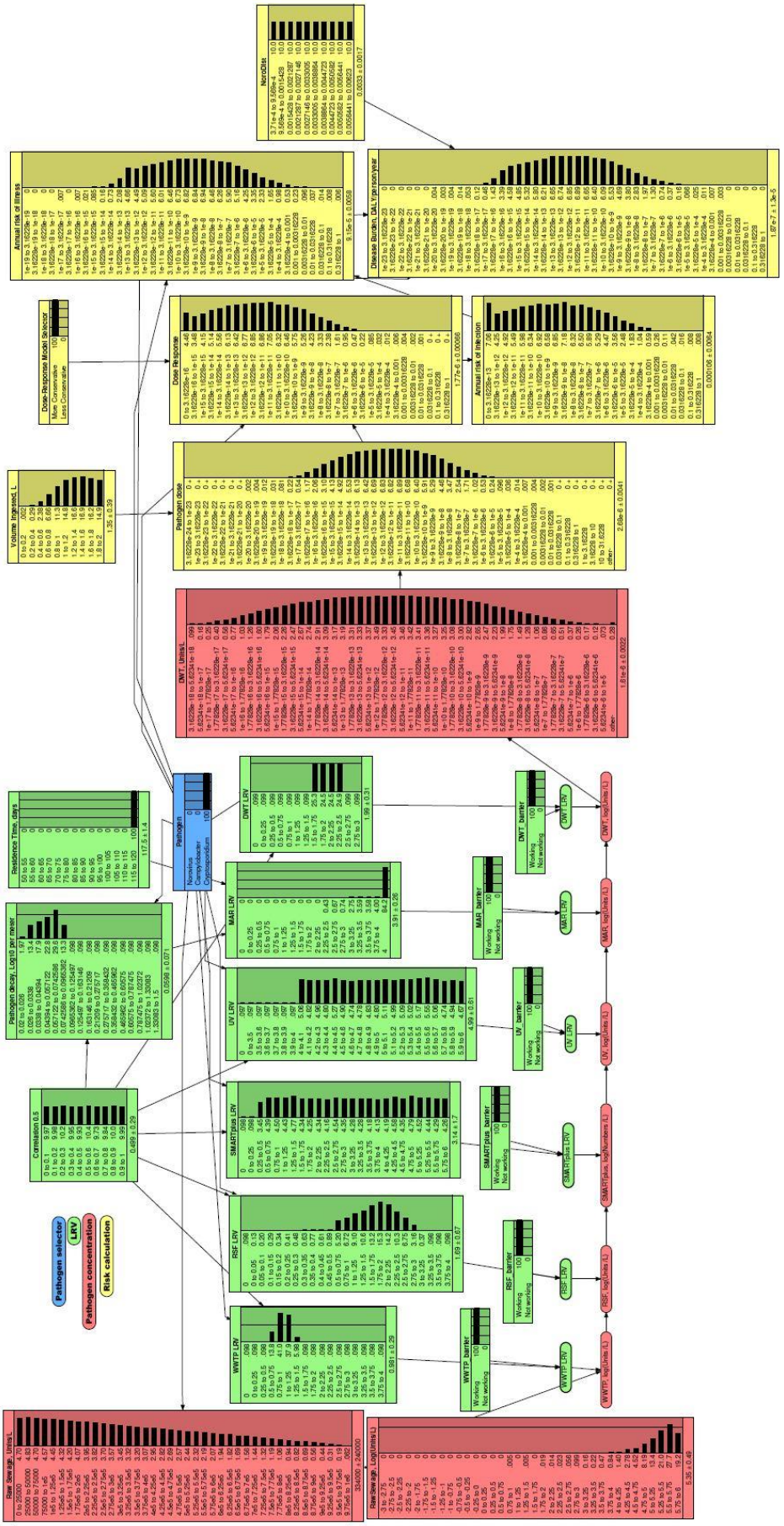

Figure 11-5: The continuous correlation factor network for all pathogens in Netica, showing the case for Cryptosporidium.

11.3.5 References

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Gerrity, D., 2019. Equivalency of Indirect and Direct Potable Reuse Paradigms based on a Quantitative Microbial Risk Assessment Framework. Microb. Risk Anal. https://doi.org/10.1016/j.mran.2019.06.003

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Pecson, B., Gerrity, D., 2017. Quantifying pathogen risks associated with potable reuse: A risk assessment case study for Cryptosporidium. Water Res. 119, 252–266. https://doi.org/10.1016/j.watres.2017.04.048

Ander, H., Forss, M., 2011. Microbiological Risk Assessment of the Water Reclamation Plant in Windhoek, Namibia. Chalmers University of Technology.

Asano, T., Burton, F.L., Leverenz, H.L., Tsuchihashi, R., Tchobanoglous, G., 2007. Water Reuse: Issues, Technologies, and Applications.

Ayuso-Gabella, N., Page, D., Masciopinto, C., Aharoni, A., Salgot, M., Wintgens, T., 2011. Quantifying the effect of Managed Aquifer Recharge on the microbiological human health risks of irrigating crops with recycled water. Agric. Water Manag. 99, 93–102. https://doi.org/10.1016/j.agwat.2011.07.014

Bae, J., Schwab, K.J., 2008. Evaluation of Murine Norovirus, Feline Calicivirus, Poliovirus, and MS2 as Surrogates for Human Norovirus in a Model of Viral Persistence in Surface Water and Groundwater. Appl. Enviromental Microbiol. 74, 477–484. https://doi.org/10.1128/AEM.02095-06

Beaudequin, D., Harden, F., Roiko, A., Mengersen, K., 2017. Potential of Bayesian networks for adaptive management in water recycling. Environ. Model. Softw. 91, 251–270. https://doi.org/10.1016/j.envsoft.2017.01.016

CAMRA, 2020. QMRA Wiki [WWW Document]. URL http://qmrawiki.org/ (accessed 2.5.20).

Chaudhry, R.M., Hamilton, K.A., Haas, C.N., Nelson, K.L., 2017. Drivers of microbial risk for direct potable reuse and de facto reuse treatment schemes: The impacts of source water quality and blending. Int. J. Environ. Res. Public Health 14, 1–20. https://doi.org/10.3390/ijerph14060635

Eftim, S.E., Hong, T., Soller, J., Boehm, A., Warren, I., Ichida, A., Nappier, S.P., 2017. Occurrence of norovirus in raw sewage – A systematic literature review and meta-analysis. Water Res. 111, 366–374. https://doi.org/10.1016/j.watres.2017.01.017

Emelko, M.B., 2003. Removal of viable and inactivated Cryptosporidium by dual- and tri-media filtration. Water Res. 37, 2998–3008. https://doi.org/10.1016/S0043-1354(03)00113-1

Gerba, C.P., Betancourt, W.Q., Kitajima, M., 2017. How much reduction of virus is needed for recycled water: A continuous changing need for assessment? Water Res. 108, 25–31. https://doi.org/10.1016/j.watres.2016.11.020

Hijnen, W., Medema, G., 2007. Elimination of Micro-organisms by Drinking Water Treatment Processes: A review. https://doi.org/10.2166/9781780401584

Hijnen, W.A.M., Beerendonk, E., Medema, G.J., 2006. Inactivation credit of UV radiation for viruses, bacteria and protozoan (oo)cysts in water: a review. Water Res. 40, 3–22.

Jin, Y., Chu, Y., Li, Y., 2000. Virus removal and transport in saturated and unsaturated sand columns. J. Contam. Hydrol. 111–128.

Karakurt-Fischer, S., Rien, C., Sanz-Prat, A., Szewzyk, R., Drewes, J.E., Hübner, U., Selinka, H.C., 2020. Fate and Transport of Viruses within a High Infiltration Rate Plug Flow Biofilter Designed for Non-Membrane Based Potable Reuse Applications.

Lodder, W.J., Maria, A., Husman, D.R., 2005. Presence of Noroviruses and Other Enteric Viruses in Sewage and Surface Presence of Noroviruses and Other Enteric Viruses in Sewage and Surface Waters in The Netherlands. https://doi.org/10.1128/AEM.71.3.1453-1461.2005

Medema, G.J., Teunis, P.F.M., Havelaar, A.H., Haas, C.N., 1996. Assessment of the dose-response relationship of Campylobacter jejuni. Int. J. Food Microbiol. 30, 101–111.

Messner, M.J., Berger, P., 2016. Cryptosporidium Infection Risk: Results of New Dose-Response Modeling. Risk Anal. 000. https://doi.org/10.1111/risa.12541

Messner, M.J., Berger, P., Nappier, S.P., 2014. Fractional Poisson — A Simple Dose-Response Model for Human Norovirus. Risk Anal. 34, 1820–1829. https://doi.org/10.1111/risa.12207

Mohammed, H., Seidu, R., 2019. Climate-driven QMRA model for selected water supply systems in Norway accounting for raw water sources and treatment processes. Sci. Total Environ. 660, 306–320. https://doi.org/10.1016/j.scitotenv.2018.12.460

Mok, H.F., Barker, S.F., Hamilton, A.J., 2014. A probabilistic quantitative microbial risk assessment model of norovirus disease burden from wastewater irrigation of vegetables in Shepparton, Australia. Water Res. 54, 347–362. https://doi.org/10.1016/j.watres.2014.01.060

NRMMC-EPHC-NHMR, 2008. Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 2) Augmentation of Drinking Water Supplies.

NRMMC–EPHC–AHMC, 2006. Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 1) National Water Quality Management Strategy. Canberra, Australia.

Ottoson, J., Hansen, A., Bjo, B., Norder, H., Stenstro, T.A., 2006. Removal of viruses , parasitic protozoa and microbial indicators in conventional and membrane processes in a wastewater pilot plant 40, 1449–1457. https://doi.org/10.1016/j.watres.2006.01.039

Page, D., Dillon, P., Toze, S., Bixio, D., Genthe, B., Jiménez Cisneros, B.E., Wintgens, T., 2010a. Valuing the subsurface pathogen treatment barrier in water recycling via aquifers for drinking supplies. Water Res. 44, 1841–1852. https://doi.org/10.1016/j.watres.2009.12.008

Page, D., Dillon, P., Toze, S., Sidhu, J., 2010b. Characterising aquifer treatment for pathogens in managed aquifer recharge. Water Sci. Technol. 62, 2009–2015. https://doi.org/10.2166/wst.2010.539

Pecson, B.M., Triolo, S.C., Olivieri, S., Chen, E.C., Pisarenko, A.N., Yang, C., Olivieri, A., Haas, C.N., Trussell, R.S., Trussell, R.R., 2017. Reliability of pathogen control in direct potable reuse : Performance evaluation and QMRA of a full-scale 1 MGD advanced treatment train. Water Res. 122, 258–268. https://doi.org/10.1016/j.watres.2017.06.014

Regnery, J., Gerba, C.P., Dickenson, E.R. V, Drewes, J.E., 2017. The importance of key attenuation factors for microbial and chemical contaminants during managed aquifer recharge: A review. Crit. Rev. Environ. Sci. Technol. 47, 1409–1452. https://doi.org/10.1080/10643389.2017.1369234

Rose, J.B., Farrah, S.R., Harwood, V.J., Levine, A.D., Lukasik, J., Menendez, P., Scott, T.M., 2005. Reduction of Pathogens, Indicator Bacteria, and Alternative Indicators by Wastewater Treatment and Reclamation Processes, Water Environment Research Foundation.

Schmidt, P.J., Chappell, C.L., 2016. Comment on “Cryptosporidium Infection Risk: Results of New Dose-Response Modeling” — Discussion of Underlying Assumptions and Their Implications. Risk Anal. 36, 2189–2192. https://doi.org/10.1111/risa.12731

Sherchan, S.P., Snyder, S.A., Gerba, C.P., Pepper, I.L., 2014. Inactivation of MS2 coliphage by UV and hydrogen peroxide: Comparison by cultural and molecular methodologies. J. Environ. Sci. Heal. , Part A Toxic/Hazardous Subst. Environ. Eng. 37–41. https://doi.org/10.1080/10934529.2014.854607

Shirasaki, N., Matsushita, T., Matsui, Y., Oshiba, A., Ohno, K., 2010. Estimation of norovirus removal performance in a coagulation – rapid sand filtration process by using recombinant norovirus VLPs. Water Res. 44, 1307–1316. https://doi.org/10.1016/j.watres.2009.10.038

Sidhu, J., Toze, S., Hodgers, L., Shackelton, M., Barry, K., Page, D., Dillon, P., 2010. Pathogen inactivation during passage of stormwater through a constructed reedbed and aquifer transfer , storage and recovery. Water Sci. Technol. https://doi.org/10.2166/wst.2010.398

Sidhu, J.P.S., Toze, S., 2012. Assessment of pathogen survival potential during managed aquifer recharge with diffusion chambers. J. Appl. Microbiol. https://doi.org/10.1111/j.1365-2672.2012.05360.x

Smeets, P., 2008. Stochastic Modelling of Drinking Water Treatment in Quantitative Microbial Risk Assessment. https://doi.org/10.2166/9781780401591

Smeets, P., Rietveld, L., Hijnen, W., Medema, G., Stenström, T.A., 2006. Efficacy of water treatment processes.

Soller, J.A., Eftim, S.E., Nappier, S.P., 2018. Direct potable reuse microbial risk assessment methodology: Sensitivity analysis and application to State log credit allocations. Water Res. 128, 286–292. https://doi.org/10.1016/j.watres.2017.10.034

Soller, J.A., Eftim, S.E., Warren, I., Nappier, S.P., 2017. Evaluation of microbiological risks associated with direct potable reuse. Microb. Risk Anal. 5, 3–14. https://doi.org/10.1016/j.mran.2016.08.003

Symonds, E.M., Verbyla, M.E., Lukasik, J.O., Kafle, R.C., Breitbart, M., Mihelcic, J.R., 2014. A case study of enteric virus removal and insights into the associated risk of water reuse for two wastewater treatment pond systems in Bolivia. Water Res. 65, 257–270. https://doi.org/10.1016/j.watres.2014.07.032

Teunis, P., van der Brandhof, W., Nauta, M., Wagenaar, J., van den Kerkhof, H., van Pelt, W., 2005. A reconsideration of the Campylobacter dose – response relation. Epidemiol. Infect. 583–592.

Teunis, P.F.M., Havelaar, A.H., 2000. The Beta Poisson Dose-Response Model Is Not a Single-Hit Model. Risk Anal. 20. https://doi.org/10.1111/0272-4332.204048

Teunis, P.F.M., Moe, C.L., Liu, P., Miller, S.E., Lindesmith, L., Baric, R.S., Le Pendu, J., Calderon, R.L., 2008. Norwalk Virus: How Infections is it? J. Med. Virol. 80, 1468–1476. https://doi.org/10.1002/jmv

Teunis, P.F.M., Nagelkerke, N.J.D., Haas, C.N., 1999. Dose Response Models For Infectious Gastroenteritis. Risk Anal. 19.

Toze, S., Bekele, E., Page, D., Sidhu, J., Shackleton, M., 2010. Use of static Quantitative Microbial Risk Assessment to determine pathogen risks in an unconfined carbonate aquifer used for Managed Aquifer Recharge. Water Res. 44, 1038–1049. https://doi.org/10.1016/j.watres.2009.08.028

US EPA, 2017. 2017 Potable Reuse Compendium. Washington, D.C.

US EPA, 2006. National primary drinking water regulations: Long term 2 enhanced surface water treatment rule: Final Rule.

US EPA, 2005. SWTR Fact Sheet.

Van Abel, N., Schoen, M.E., Kissel, J.C., Meschke, J.S., Van Abel, N., Schoen, M.E., Kissel, J.C., Meschke, J.S., 2017. Comparison of Risk Predicted by Multiple Norovirus Dose – Response Models and Implications for Quantitative Microbial Risk Assessment. Risk Anal. 37, 245–264. https://doi.org/10.1111/risa.12616

World Health Organization, 2017a. Potable reuse: Guidance for producing safe drinking-water. Geneva.

World Health Organization, 2017b. Guidelines for Drinking-Water Quality: Fourth edition incorporating the first addendum, WHO Library Cataloguing-in-Publication Data. https://doi.org/10.1016/S1462-0758(00)00006-6

World Health Organization, 2016. Quantitative Microbial Risk Assessment: Application for Water Safety Management. https://doi.org/10.1002/9781118910030

11.4 Supplementary information for Chapter 7

Differentiating between sorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in biological activated carbon (BAC) filters

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11.4.1 Experimental setup and properties

11.4.1.1 GAC properties

Table 11-5: Configurations and properties of BAC filter and RSSCT column.

	BAC	RSSCT
Particle size, mm	1.2	0.15
Column inner ⌀, mm	71	10
Cross sectional area, cm²	39.6	0.785
Bed length, cm	23	2.9
Bed volume, cm³	910	2.26
Hydraulic loading rate (HLR), m/h	3.41	27.3
Flowrate mL/min	225	35.7
EBCT, s	243	3.79
Scaling factor	--	8

Carbon used was Chemviron Cyclecarb 401, with a bed density of 450 kg/m^3. GAC for the BAC filter was initially flushed in tap water to dispel oxygen sorbed onto the material prior to loading into filter, with flush water and particles discarded until flush water ran clear.

11.4.2 Particle size analysis

11.4.2.1 Imaging

A particle size analysis was carried out using static image analysis technique to determine the GMD of the virgin Cyclecarb 401. The principle of static image analysis is to take a picture of particles and to determine their size by processing the picture.

Pictures were taken with an EOS 100D camera (Canon, Japan) in raw format (*.CR2). Approximately 1,078 particles were analyzed in four batches. The particles were spread, without touching, on a blurred surface, and lit from below with a halogen lamp, resulting in a uniformly bright background behind the GAC particles. The camera was fixed at minimum focus distance to maximize the resolution of the GAC particles in the picture, and picture taking command is sent via an external intervalometer to prevent shaking. A ruler was added on the same plane as the particles for scale.

Pictures were analyzed with ImageJ (ImageJ 1.51i, National Institutes of Health, USA), according to a protocol for particle sizing ("Particle Analysis Using ImageJ," n.d.). Each CR2 image was loaded with the DCRaw Reader plugin, pixel units were converted into metric units using the scale, the image was converted to 8-bit grayscale and then to black and white by selecting the right threshold, which makes the GAC particles appear black and the background appear white. Finally, the integrated Analyze Particles tool was used to delineate each particle and to calculate its area in metric units. Calculated areas were reported in mm² to an excel sheet.

As GAC particles are not round, this should be considered in the calculations. To attribute a representative diameter to each particle, the projected area diameter, which is the diameter of a disc with the same projected area as the particle, was adopted, as it is easier to compute and it converges to a statistically significant measurement faster (Fan and Zhu, 1998). However, this method could have introduced bias as the GAC particles were not randomly oriented but laid flat, therefore this assumption may have overestimated the true diameter.

11.4.2.2 Calculations

To derive the scaling factor, a unique representative particle diameter is required for both the virgin and crushed GAC. The geometric mean diameter (GMD) was used as a representative particle diameter (Chowdhury et al., 2013), as it is more robust to outliers in comparison to the arithmetic mean. GMD was calculated using equation S1, with the following equation,

$$GMD = \left(\prod_{i=1}^{n} d_i\right)^{\frac{1}{n}} \quad \textit{Equation S1}$$

with d_i representing the diameters of a set of particles, and n the number of particles.

For the RSSCT particles, virgin carbon was first crushed with a mortar and pestle and then sieved. The diameter was estimated using equation S2, with d_i and d_{i+1} representing the diameter of two sieve sizes used (Baker and Herrman, 2002). Sizes used were a 125 μm sieve and a 180 μm sieve (DIN-ISO 3310-1 200x50mm, Retsch GmbH, Germany) and what was collected between them corresponded to a mean particle size of 150 μm.

$$GMD \approx \sqrt{d_i * d_{i+1}} \quad \textit{Equation S2}$$

Table 11-6: Dimensionless parameters and equations used to size RSSCT columns.

Number	Description	Equation	Reference
S2.1	Solid material density	$\rho_M = \frac{m_A}{V_{wet} - \frac{m_{wet} - m_A}{\rho_w}}$	(Worch, 2012)
S2.2	Particle density	$\rho_P = \frac{m_A}{V_{wet}}$	(Worch, 2012)
S2.3	Intraparticle porosity	$\varepsilon_p = 1 - \frac{\rho_p}{\rho_m}$	(Worch, 2012)
S2.4	Apparent particle density	$\rho_P = \frac{\rho_b}{1 - \varepsilon_b}$	(Worch, 2012)
S2.5	Pore solute distribution parameter, $\boldsymbol{D_g}$	$D_g = \frac{q_0 \rho_b}{C_0 \varepsilon_b}$	(Worch, 2012)
S2.6	Pore diffusion modulus, $\boldsymbol{Ed}$	$Ed = \frac{D_p (EBCT * \varepsilon)(1-\varepsilon)\varepsilon_p}{R^2 \varepsilon}$	(Crittenden et al., 2012)
S2.7	Surface diffusion modulus, $\boldsymbol{Ed_s}$	$Ed_s = \frac{D_s D_g (EBCT * \varepsilon)}{R^2}$	(Crittenden et al., 2012)
S2.8	Capacity factor, $\boldsymbol{C_F}$	$C_F = \frac{q_0 \rho_b}{C_0 \varepsilon}$	(Harada, 2014)
S2.9	Peclet number, $\boldsymbol{Pe}$	$Pe = \frac{Lv}{E}$	(Crittenden et al., 2012)
S2.10	Stanton number, **St**	$\mathrm{St} = \frac{k_f (1-\varepsilon)(EBCT * \varepsilon)}{\varepsilon R}$	(Crittenden et al., 2012)
S2.11	Scaling factor	$SF = \left(\frac{d_{p,BAC}}{d_{p,RSSCT}}\right) = \frac{v_{RSSCT}}{v_{BAC}}$	(Worch, 2012)
S2.12	Empty bed contact time	$EBCT = \frac{h}{V_v}$	(Worch, 2012)
S2.13	Average linear velocity	$v = \frac{HLR}{\varepsilon_b}$	(Worch, 2012)
S2.14	Integral mass balance	$C_0 \dot{V} \int_{t=0}^{t=\infty} \left(1 - \frac{C}{C_0}\right) dt \approx q_0 m_A$	(Worch, 2012)

Where ρ_P denotes apparent particle density, ρ_m denotes solid material density, ρ_w is the density of water, V_{wet} is the volume of wet carbon, ε_p denotes intraparticle porosity, ε_b denotes bulk porosity, D_p denotes the pore diffusion coefficient, D_g denotes the pore solute distribution parameter, t denotes fluid residence time in the adsorber, D_s denotes surface diffusion coefficient, C_F denotes the capacity factor, q_0 denotes solid phase equilibrium concentration, C_0 denotes influent phase concentration, ε denotes bed porosity, h denotes the bed length, v denotes average linear velocity, D_x denotes the longitudinal dispersion coefficient, k_f denotes the film mass transfer coefficient, d_p denotes particle diameter, v denotes average linear velocity, SC denotes RSSCT column and LC denotes BAC column, $\dot{V}$ is the volumetric flow rate, R is the radius of the adsorbent particle, V_v is filter velocity, h is adsorber height, HLR is the hydraulic loading rate, and E is the dispersion coefficient.

Note that the scaling factor calculated for the design of the RSSCTs was calculated from the data available at the time, where the GAC filter had an average flowrate of 225 mL/min (EBCT = 243 s, HLR = 3.41 m/h) and had only seen ~15,000 BVT. In the paper, the results of the RSSCTs are compared with experimental results of the GAC filter through ~40,000 BVT.

11.4.3 Chemical parameters and fouling correction

Molecular descriptors for calculating the molar volume at normal boiling point were calculated using SMILES downloaded from internet available locations in .smi format, converted to MDL SFD format by OpenBabel 2.4.1., then input into PaDEL-Descriptor (PaDEL-Descriptor 2.21, National University of Singapore, Singapore).

PaDEL computed values included the following: McGowan's characteristic volume (V), overall hydrogen bond acidity (A), overall hydrogen bond basicity (B), combined dipolarity/polarizability (S), and excess molar refraction (E). Equations used were S3 and S4.

$$Y = 0.165 * PC1 + 0.883 \qquad \textit{Equation S3}$$

$$PC1 = -0.612 * S - 0.247 * A - 0.370 * B - 0.341 * V - 0.558 * E \qquad \textit{Equation S4}$$

Equations used to calculate the compound specific descriptors can be found in (Reinert, 2013). Carbamazepine and benzotriazole SMILES files were downloaded from Zinc database (http://zinc.docking.org/) in SDF format, and directly put into PaDEL.

Table 11-7: Desired spiking concentrations of chemicals into BAC filter and RSSCT column for PSDM model. These concentrations were used as influent concentrations in AdDesignS™.

Compound	CAS registry number	Molecular weight (g/mo)]	Target influent concentration (ng/L)	Average influent BAC concentration (mg/L) n=11-14	Average influent RSSCT concentration (mg/L) n=18
Antipyrine	60-80-0	188	500	4.53 e-4	5.21 e-4
Atenolol	29122-68-7	266	500	4.48 e-4	5.46 e-4
Benzotriazole	Not spiked	119	Not spiked	3.84 e-3	5.33 e-3
Caffeine	58-08-2	194	2000	Not assessed	Not assessed
Carbamazepine	Not spiked	236	Not spiked	4.30 e-4	4.02 e-4
Citalopram	59729-32-7	324	500	4.97 e-4	6.28 e-4
Climbazole	38083-17-9	293	100	1.22 e-4	1.46 e-4
Diclofenac	15307-79-6	296	500	1.35 e-3	1.42 e-3
Erythromycin	114-07-8	734	500	Not assessed	Not assessed
Gabapentin	60142-96-3	171	500	1.26 e-3	1.09 e-3
Iopromide	73334-07-3	791	2000	1.03 e-3	1.07 e-4
Metoprolol	37350-58-6	267	500	3.88 e-4	3.88 e-4
Phenytoin	57-41-0	252	100	6.1 e-5	7.5 e-5
Primidone	125-33-7	218	500	3.49 e-4	3.45 e-4
Sulfamethoxazole	723-46-6	253	500	4.13 e-4	5.66 e-4
Tramadol	27203-92-5	263	500	6.98 e-4	7.55 e-4
Trimethoprim	738-70-5	290	500	4.04 e-4	2.31 e-4
Venlafaxine	93413-69-5	277	500	7.06 e-4	9.69 e-4

Table 11-8: Structural properties of TOrCs used to calculate molar volume at normal boiling point.

TOrC	McGowan molecular volume V	Hydrogen bonding acidity A	Hydrogen bonding basicity B	Dipolarity or Polarizability S	Excess molar fraction E	PC1	Fouling factor Y	Fouling index FI	MV @ NBP (cm^3/mol)
Antipyrine	1.48	0.00	0.25	1.00	1.01	-1.78	0.59	3.41	198.45
Atenolol	2.18	0.55	1.74	1.88	1.35	-3.42	0.32	1.94	347.72
Benzotriazole	1.81	0.46	0.63	1.45	1.76	-2.83	0.42	2.37	261.31
Carbamazepine	0.86	0.20	0.44	1.16	1.40	-2.00	0.55	3.16	177.58
Caffeine	1.36	0.00	1.31	1.00	1.59	-2.45	0.48	2.71	192.01
Citalopram	2.53	0.00	1.31	1.99	1.65	-3.48	0.31	1.90	345.97
Climbazole	2.19	0.00	1.24	1.85	1.35	-3.09	0.37	2.17	290.04
Diclofenac	2.02	0.59	1.34	2.10	2.06	-3.77	0.26	1.72	302.49
Erythromycin	5.77	0.41	4.71	3.54	1.87	-7.02	-0.28	0.56	244.60
Gabapentin	1.44	0.77	0.92	0.83	0.53	-1.82	0.58	3.35	195.40
Iopromide	3.82	1.08	3.21	4.84	4.15	-8.04	-0.44	0.40	476.31
Metoprolol	2.26	0.10	1.43	1.17	1.03	-2.62	0.45	2.56	353.56
Phenytoin	1.87	1.17	1.05	1.06	2.10	-3.13	0.37	2.14	251.78
Primidone	1.68	1.21	1.46	1.90	1.53	-3.42	0.32	1.94	229.11
Sulfamethoxazole	1.72	0.61	1.17	2.73	1.82	-3.86	0.25	1.67	353.73
Tramadol	2.23	0.35	1.49	1.32	1.14	-2.84	0.41	2.37	302.27
Trimethoprim	2.18	0.50	1.32	3.57	2.42	-4.89	0.08	1.17	299.60
Venlafaxine	2.37	0.35	1.36	1.32	1.14	-2.84	0.41	2.37	332.03

11.4.4 AdDesignS™ modeling parameters

Table 11-9: PSDM input parameters.

Type	Parameter	RSSCT	BAC
Water properties	Temperature (°C)	15	15
	Pressure (atm)	1	1
Fixed bed properties	Bed length (m)	0.029	0.23
	Bed diameter (m)	0.01	0.071
	Bed mass (g)	1.016	410
	Flowrate (mL/min)	36	192
Adsorbent properties	Apparent particle density (kg/m^3)	1250	1250
	Particle radius (m)	7.5 e-5	6 e-4
	Intraparticle porosity (-)	0.81	0.81
	Particle shape factor (-)	1	1
Component properties	Molar volume at NBP (cm^3/mol)	TOrC dependent	TOrC dependent
	Initial concentration	Same as for influent concentration	Same as for influent concentration
	Freundlich K (mg/g)*(L/mg)^(1/n)	TOrC dependent. Calibration parameter	TOrC dependent. See Equation 25
	Freundlich 1/n (-)	1	1
	Tortuosity (-)	1	1.81
	SPDFR (-)	0	0
Simulation parameters	Total run time	42 hours	155 days
	First point displayed	0 hour	0 day
	Time step	1 hour	1 day
	Number of axial elements	10-12	10-12
	Number of collocation points in the axial direction	8	8
	Number of collocation points in the radial direction	5	5
Input file	Influent concentration	TOrC dependent	TOrC dependent

Table 11-10: AdDesignS™ governing equations for TOrC-specific kinetic parameters.

Pore diffusion coefficient D_p, cm²/s	$\boldsymbol{D_p = \frac{D_L}{\tau}}$
Liquid diffusion coefficient	$D_L = \frac{13.26 * 10^{-5}}{\mu^{1.14} * V_{m,NBP}^{0.589}}$
Film mass transfer coefficient k_f, cm/s	$k_f = \frac{(1 + 1.5(1-\varepsilon)D_L}{d_p}\left[2 + 0.644\, Re^{\frac{1}{2}}\, Sc^{\frac{1}{3}}\right]$
Surface diffusion coefficient D_s, cm²/s	$D_s = SPDFR + f(D_p)$
Tortuosity (when run time >70 days), calculated by AdDesignS™	$\tau = 0.334 + 0.009518 * t_{op}$

Where μ is the liquid viscosity, V is the molar volume at the normal boiling point, τ is tortuosity (set to 1 when run length <70 days), t_{op} is time of operation in days, $Re = (d_p * V_v)/(\varepsilon \upsilon)$ and $Sc = \upsilon / D_L$, for which υ is kinematic viscosity.

11.4.5 Root mean squared error calculation (RMSE)

To quantify the fit between PSDM simulated values and experimental data, the root mean squared error was used. The lowest RMSE is associated with the K value for the model which most closely fits to the adjusted RSSCT breakthrough (Jachner and Petzoldt, 2007).

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n} \left(Y_i^{RSSCT} - Y_i^{PSDM}\right)^2}{n}} \qquad \textit{Equation S5}$$

In the RMSE equation, $Y = \frac{C}{C_0}$ and n is equal to the number of RSSCT breakthrough points. A K_{RSSCT} value was first estimated for each compound from the RSSCT experimental data (not adjusted, using days instead of BVTs due to program requirements), then used to calculate PSDM model values. The K_{RSSCT} value was iteratively refined by running a Matlab script to find the K value with the lowest corresponding RMSE.

Table 11-11: Comparison of adsorption removal with prior literature.

TOrC	Sorption prediction this study	Sorption potential in literature	Characteristics of literature studies	Sources
Atenolol	Good	Good	EBCT higher (17 – 120 min) Lower DOC (3.8 – 7.3 mg/L) Mostly WWTP effluent	(Reungoat et al., 2011, 2012; Sbardella et al., 2018; Sun et al., 2018; Müller et al., 2019a; Guillossou et al., 2020)
Trimethoprim	Good	Good	EBCT higher (7 min – 72 hours) DOC variable (1.7 – 7.3 mg/L) Surface water, WWTP effluent	(Snyder et al., 2007; Rossner et al., 2009; Reungoat et al., 2011; Chowdhury et al., 2013; Kennedy et al., 2015; Greenstein et al., 2018; Sbardella et al., 2018; Sun et al., 2018; Müller et al., 2019a; Guillossou et al., 2020)
Metoprolol	Good	Good	EBCT higher (30 – 120 min) Lower DOC (3.8 – 6.6 mg/L) WWTP effluent	(Reungoat et al., 2011; Sbardella et al., 2018; Müller et al., 2019a)
Citalopram	Good	Good	EBCT higher (17 – 45 min) Similar DOC (4.7 – 6.6 mg/L) WWTP effluent	(Reungoat et al., 2012; Müller et al., 2019a)
Benzotriazole	Good	Good	EBCT higher (15 min – 54 days) Similar DOC (4.6 – 6.6 mg/L) Drinking water, groundwater, demineralized water, WWTP effluent	(Sperlich et al., 2017; Müller et al., 2019a; Piai et al., 2020)
Phenytoin	Moderate	Good	EBCT higher (30 – 120 mins) Lower/similar DOC (3.8 – 7.2 mg/L) WWTP effluent	(Gerrity et al., 2011; Reungoat et al., 2011; Müller et al., 2019a)
		Poor	EBCT higher (17 – 45 mins) Similar DOC (5.8 – 6.6 mg/L) WWTP effluent	(Reungoat et al., 2012)
Venlafaxine	Moderate	Good	EBCT higher (17 – 120 min); Lower DOC (3.8 – 6.6 mg/L)	(Reungoat et al., 2011, 2012; Sbardella et al., 2018)
Carbamazepine	Moderate	Moderate	EBCT higher (7 – 30 min) Lower DOC (1.7 – 4.6 mg/L) Surface water, drinking water, groundwater	(Chowdhury et al., 2013; Kennedy et al., 2015; Sperlich et al., 2017)
		Poor	EBCT generally higher (7.6 min – 3 weeks) Variable DOC (2.5 – 7.3 mg/L) WWTP effluent, surface water	(Snyder et al., 2007; Rossner et al., 2009; Reungoat et al., 2011; Sbardella et al., 2018; Sun et al., 2018; Müller et al., 2019a; Guillossou et al., 2020)
Primidone		Moderate	EBCT higher (15 & 30 min)	(Sperlich et al., 2017; Sun et al., 2018)

	Moderate-Poor		Lower DOC (4.6 mg/L) WWTP effluent, drinking water, groundwater	
		Moderate	EBCT higher (24 min) Similar DOC (5.8 ± 1.1mg/L) Used effluent of same WWTP	(Müller et al., 2019a)
Diclofenac	Moderate-Poor	Good	EBCT higher (7 min – 54 days) Lower DOC (1.7 – 6.6 mg/L) Surface water, WWTP effluent, drinking water	(Snyder et al., 2007; Reungoat et al., 2011; Kennedy et al., 2015; Sun et al., 2018; Müller et al., 2019a; Piai et al., 2020)
		Moderate-poor	EBCT higher (7.6 min – 3 weeks) Lower DOC (2.5 mg/L) Surface water	(Snyder et al., 2007; Rossner et al., 2009; Chowdhury et al., 2013)
Climbazole	Moderate	No studies found		
Tramadol	Moderate	Good	EBCT higher (17 – 120 min) Lower DOC (3.8 – 6.9) mg/L WWTP effluent	(Reungoat et al., 2011, 2012; Müller et al., 2019a)
Gabapentin	Poor	Poor	EBCT higher (15 – 30 min) Similar DOC (4.7 – 6.6 mg/L) WWTP effluent, drinking water, groundwater	(Sperlich et al., 2017; Müller et al., 2019a)
Antipyrine	Poor	Good	EBCT higher (23 min) Lower DOC (4.2 mg/L) WWTP effluent	(Sun et al., 2018)
Iopromide	Poor	Moderate-poor	EBCT higher (7 min – 54 days) Lower DOC (2.5 – 6.6 mg/L) Surface water, WWTP effluent, drinking water	(Snyder et al., 2007; Rossner et al., 2009; Chowdhury et al., 2013; Kennedy et al., 2015; Müller et al., 2019a; Piai et al., 2020)
Sulfamethoxazole	Poor	Good	EBCT higher (17 – 50 min) Lower DOC (3.8 – 4.6 mg/L) WWTP effluent	(Reungoat et al., 2011; Sbardella et al., 2018; Sun et al., 2018)
		Good-moderate	EBCT higher (24 min) Similar DOC (5.8 ± 1.1mg/L) Used effluent of same WWTP	(Müller et al., 2019a)
		Moderate-poor	EBCT higher (7 min – 3 weeks) DOC variable (1.7 – 6.6 mg/L) Surface water, WWTP effluent	(Snyder et al., 2007; Rossner et al., 2009; Reungoat et al., 2012; Chowdhury et al., 2013; Kennedy et al., 2015; Greenstein et al., 2018; Sbardella et al., 2018)

11.4.6 References

Baker, S., Herrman, T., 2002. Evaluating Particle Size, Kansas State University.

Chowdhury, Z.K., Summers, R.S., Westerhoff, G.P., Leto, B.J., Nowack, K.O., Corwin, C.J., 2013. Activated Carbon: Solutions for Improving Water Quality, Activated Carbon: Solutions for Improving Water Quality. American Water Works Association. https://doi.org/10.1021/ed023p98

Crittenden, J.C., Trussell, R.R., Hand, D.W., Howe, K. j., Tchobanoglous, G., 2012. MWH's Water Treatment Principles and Design, Third. ed. John Wiley & Sons, Inc., Hoboken, New Jersey.

Fan, L.-S., Zhu, C., 1998. Principles of Gas-Solid Flows. Cambridge University Press.

Gerrity, D., Gamage, S., Holady, J.C., Mawhinney, D.B., Quiñones, O., Trenholm, R.A., Snyder, S.A., 2011. Pilot-scale evaluation of ozone and biological activated carbon for trace organic contaminant mitigation and disinfection. Water Res. 45, 2155–2165. https://doi.org/10.1016/j.watres.2010.12.031

Greenstein, K.E., Lew, J., Dickenson, E.R.V., Wert, E.C., 2018. Investigation of biotransformation, sorption, and desorption of multiple chemical contaminants in pilot-scale drinking water biofilters. Chemosphere 200, 248–256. https://doi.org/10.1016/j.chemosphere.2018.02.107

Guillossou, R., Roux, J. Le, Mailler, R., Pereira-Derome, C.S., Varrault, G., Bressy, A., Vulliet, E., Morlay, C., Nauleau, F., Rocher, V., Gasperi, J., 2020. Influence of dissolved organic matter on the removal of 12 organic micropollutants from wastewater effluent by powdered activated carbon adsorption. Water Res. https://doi.org/10.1016/j.watres.2020.115487

Harada, B.K., 2014. Comparative Evaluation of Six Different Activated Carbon for TCP Removal Using Rapid Small Scale Column Test. University of Hawai'i at Manoa.

Jachner, S., Petzoldt, T., 2007. Statistical Methods for the Qualitative Assessment of Dynamic Models with Time Delay (R Package qualV). J. Stat. Softw. 22.

Kennedy, A.M., Reinert, A.M., Knappe, D.R.U., Ferrer, I., Summers, R.S., 2015. Full- and pilot-scale GAC adsorption of organic micropollutants. Water Res. 68, 238–248. https://doi.org/10.1016/j.watres.2014.10.010

Müller, J., Drewes, J.E., Hübner, U., 2019. Investigating synergies in sequential biofiltration- trace organic chemicals from wastewater. Environ. Sci. Water Res. Technol. https://doi.org/10.1039/c9ew00181f

Particle Analysis Using ImageJ [WWW Document], n.d. URL http://www.nuance.northwestern.edu/docs/epic-pdf/Particle Analysis Using ImageJ.pdf

Piai, L., Blokland, M., Wal, A. Van Der, Langenhoff, A., 2020. Biodegradation and adsorption of micropollutants by biological activated carbon from a drinking water production plant. J. Hazard. Mater. https://doi.org/10.1016/j.jhazmat.2020.122028

Reinert, A.M., 2013. Granular Activated Carbon Adsorption of Micropollutants from Surface Water: Field- Scale Adsorber Performance and Scale-Up of Bench-Scale Data. North Carolina State University.

Reungoat, J., Escher, B.I., Macova, M., Argaud, F.X., Gernjak, W., Keller, J., 2012. Ozonation and biological activated carbon filtration of wastewater treatment plant effluents. Water Res. 46, 863–872. https://doi.org/10.1016/j.watres.2011.11.064

Reungoat, J., Escher, B.I., Macova, M., Keller, J., 2011. Biofiltration of wastewater treatment plant effluent: Effective removal of pharmaceuticals and personal care products and reduction of toxicity. Water Res. 45, 2751–2762. https://doi.org/10.1016/j.watres.2011.02.013

Rossner, A., Snyder, S.A., Knappe, D.R.U., 2009. Removal of emerging contaminants of concern by alternative adsorbents. Water Res. 43, 3787–3796. https://doi.org/10.1016/j.watres.2009.06.009

Sbardella, L., Comas, J., Fenu, A., Rodriguez-Roda, I., Weemaes, M., 2018. Advanced biological activated carbon filter for removing pharmaceutically active compounds from treated wastewater. Sci. Total Environ. 636, 519–529. https://doi.org/https://doi.org/10.1016/j.scitotenv.2018.04.214

Snyder, S.A., Adham, S., Redding, A.M., Cannon, F.S., DeCarolis, J., Oppenheimer, J., Wert, E.C., Yoon, Y., 2007. Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. Desalination 202, 156–181. https://doi.org/10.1016/j.desal.2005.12.052

Sperlich, A., Harder, M., Zietzschmann, F., Gnirß, R., 2017. Fate of Trace Organic Compounds in Granular Activated Carbon (GAC) Adsorbers for Drinking Water Treatment. Water 9. https://doi.org/10.3390/w9070479

Sun, Y., Angelotti, B., Brooks, M., Dowbiggin, B., Evans, P.J., Wang, Z., 2018. A pilot-scale investigation of disinfection by-product precursors and trace organic removal mechanisms in ozone-biologically activated carbon treatment for potable reuse. Chemosphere 210. https://doi.org/10.1016/j.chemosphere.2018.06.162

Worch, E., 2012. Adsorption Technology in Water Treatment: Fundamentals, Processes, and Modeling. De Gruyter. https://doi.org/10.1515/9783110240238

11.5 Supplementary information for Chapter 8

Varying attention of trace organic chemicals in natural treatment systems –

A review of key influential factors

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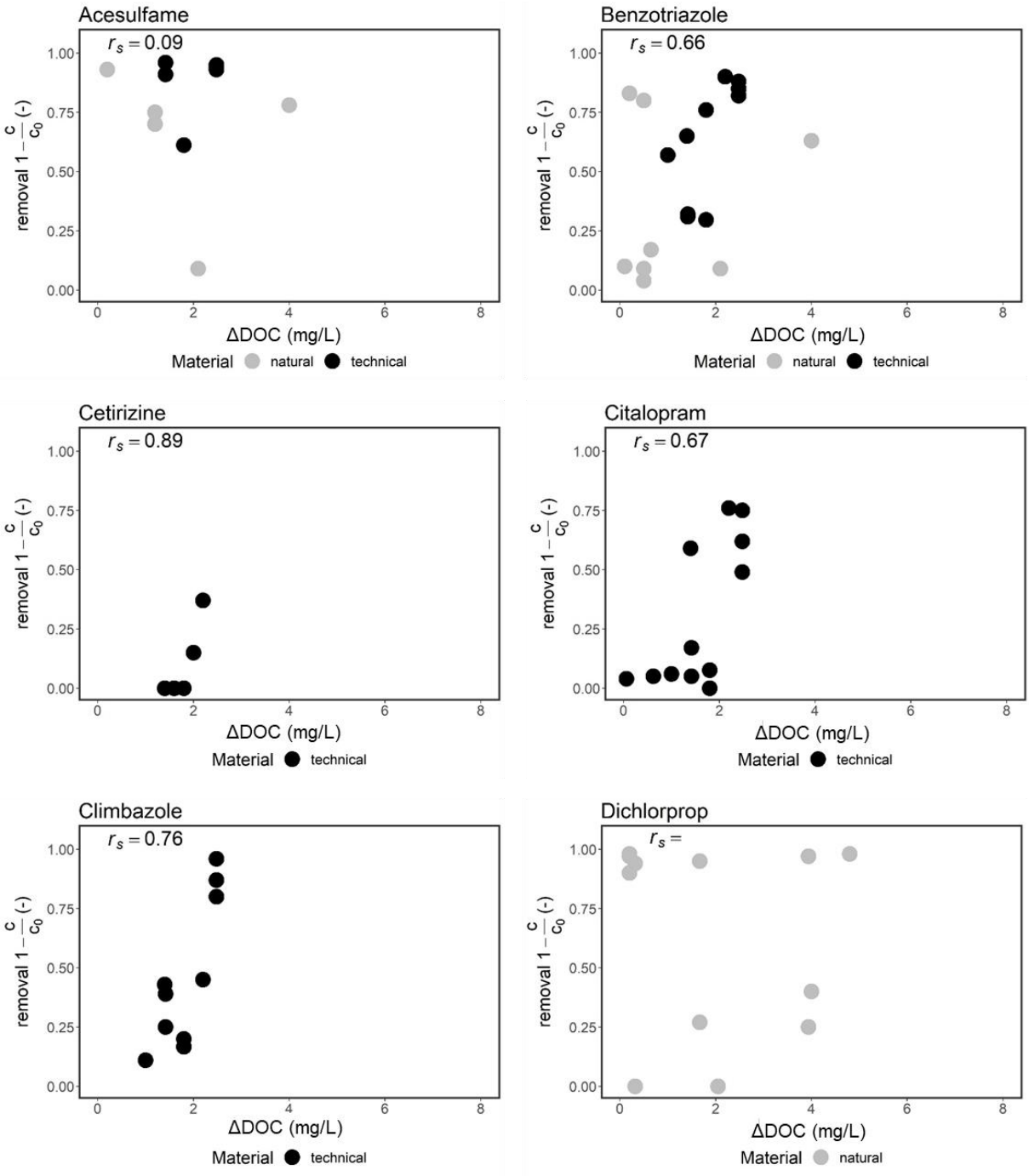
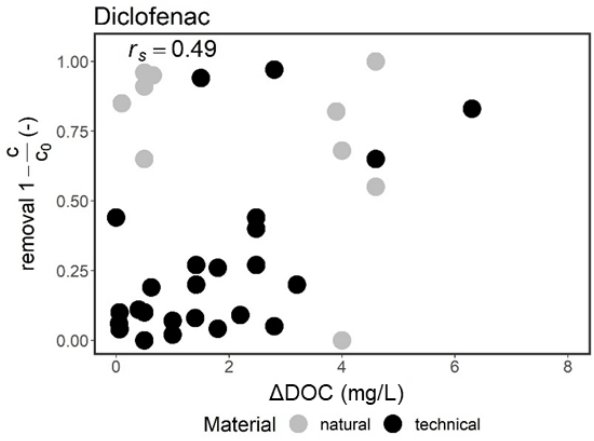
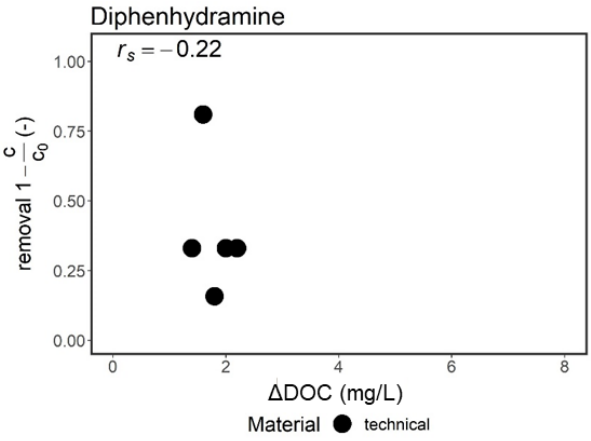
This supplementary information for this manuscript consists of 2 items: an Excel database, which is not attached but provided thorough the DOI link, and the following graphs depicting correlations between parameters and TOrC removal.

1. Correlations between ΔDOC and TOrC removal




Diclofenac
$r_s = 0.49$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical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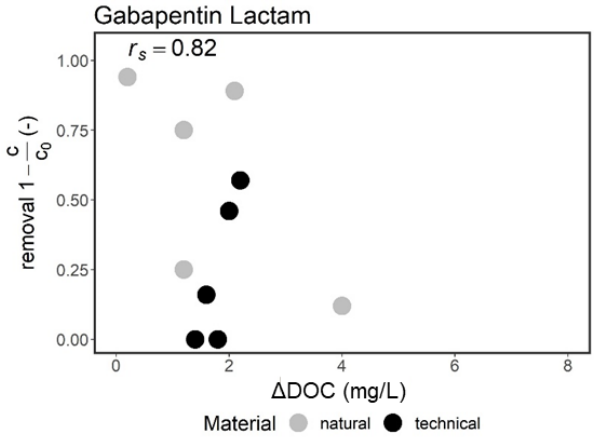
ΔDOC (mg/L)
Material technical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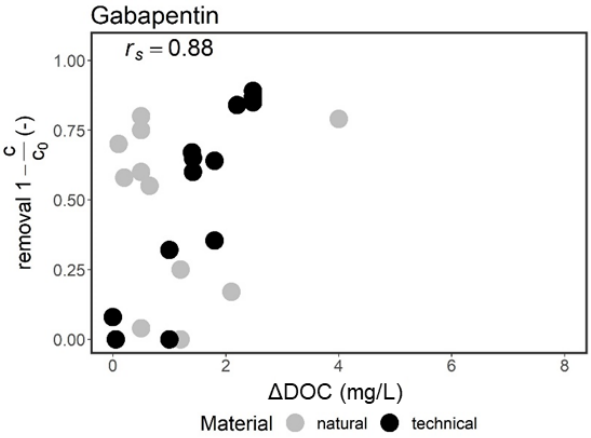
$r_s = 0.82$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical


Gabapentin
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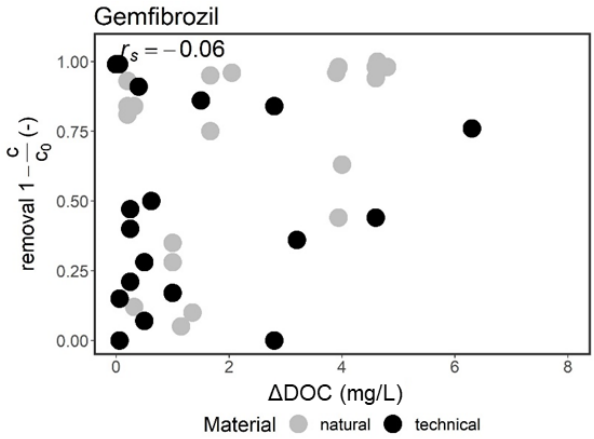
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical


Gemfibrozil
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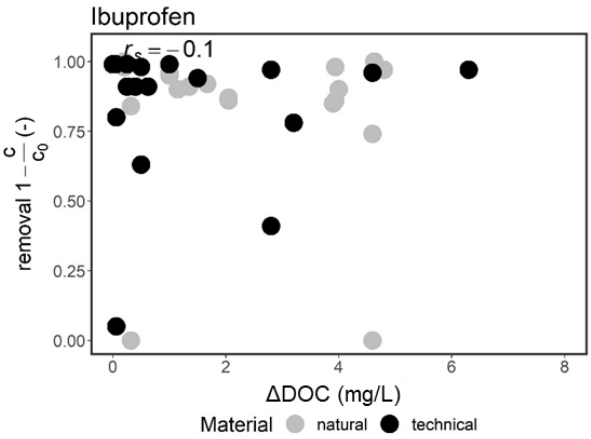
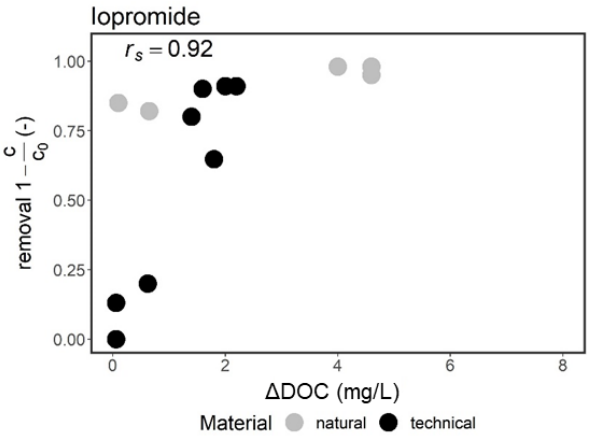
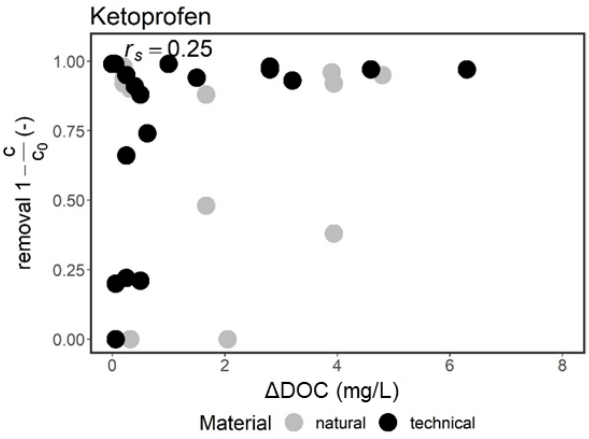
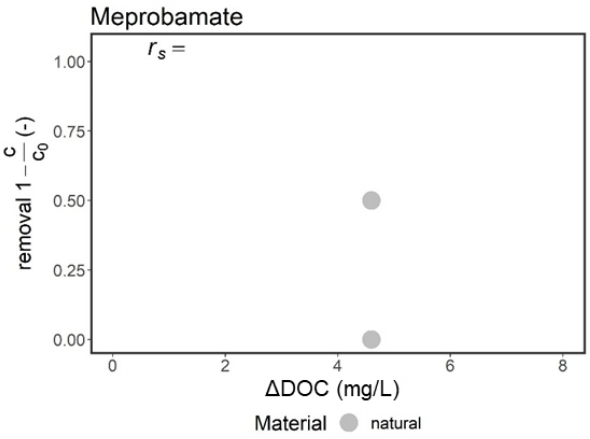
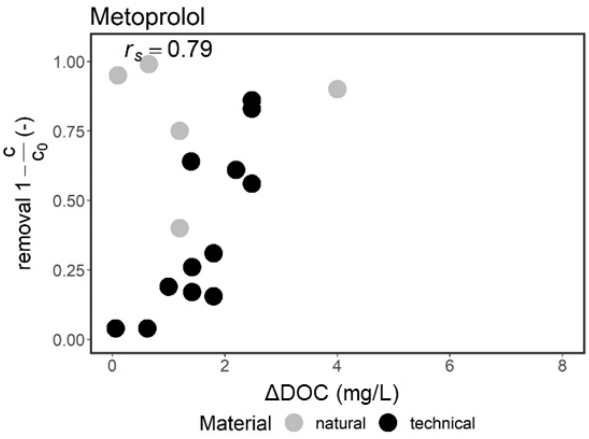
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical

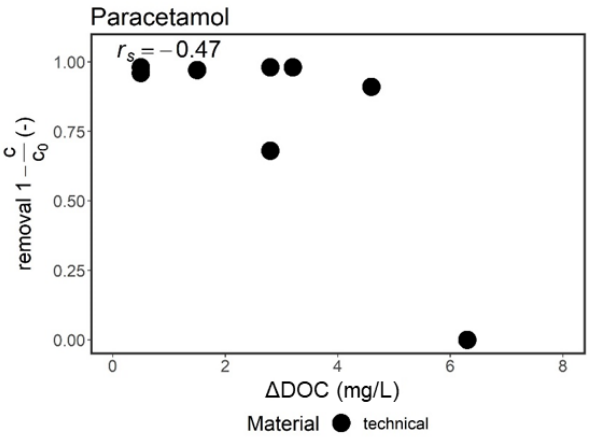

Ibuprofen
$r_s = -0.1$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical

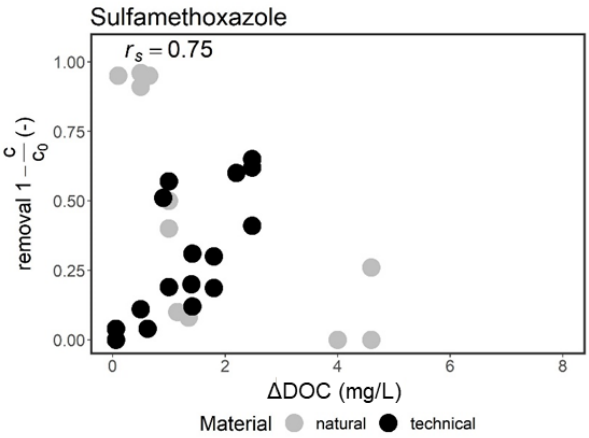

Iopromide
$r_s = 0.92$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical

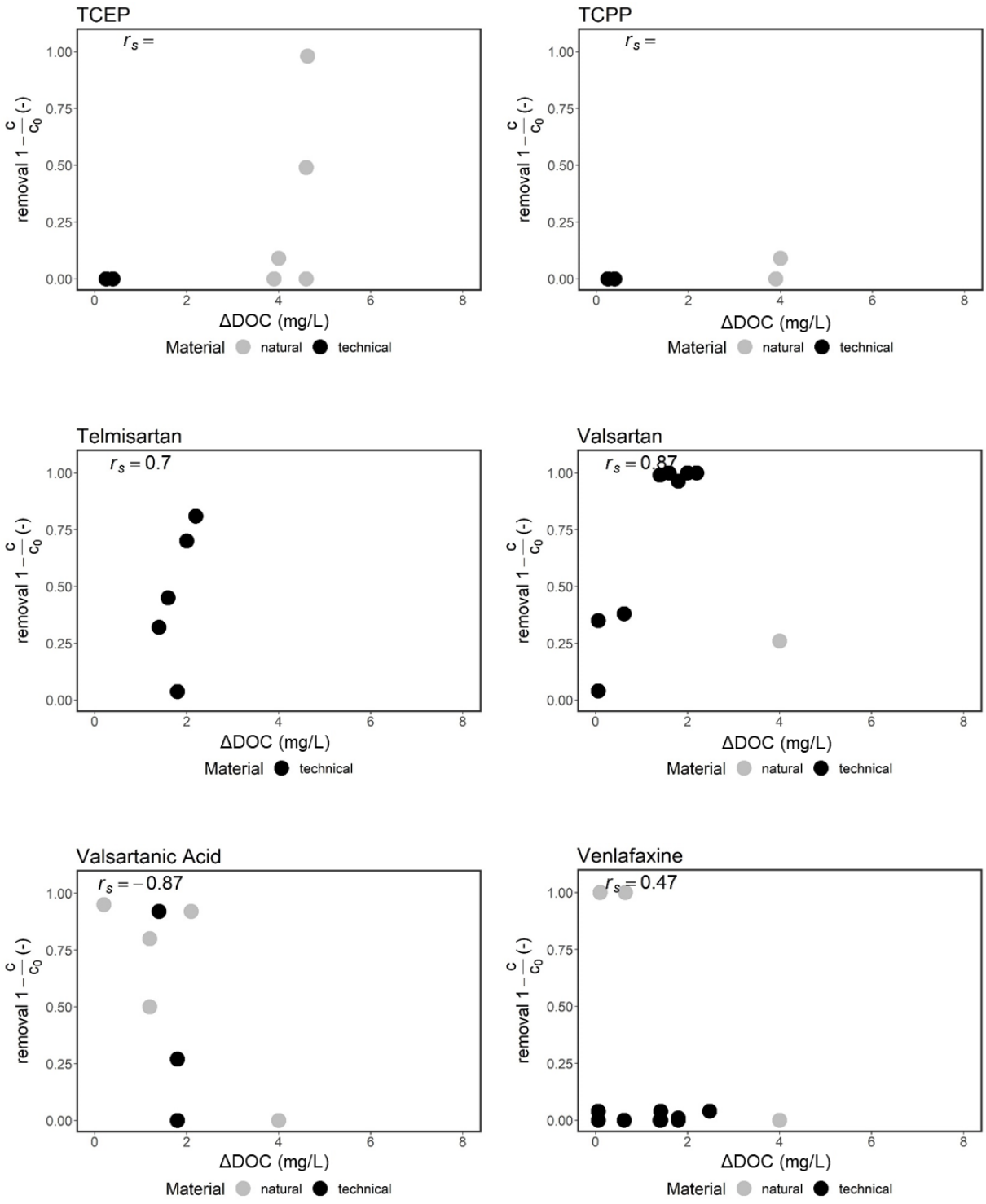

Ketoprofen
$r_s = 0.25$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical


Meprobamate
$r_s =$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural

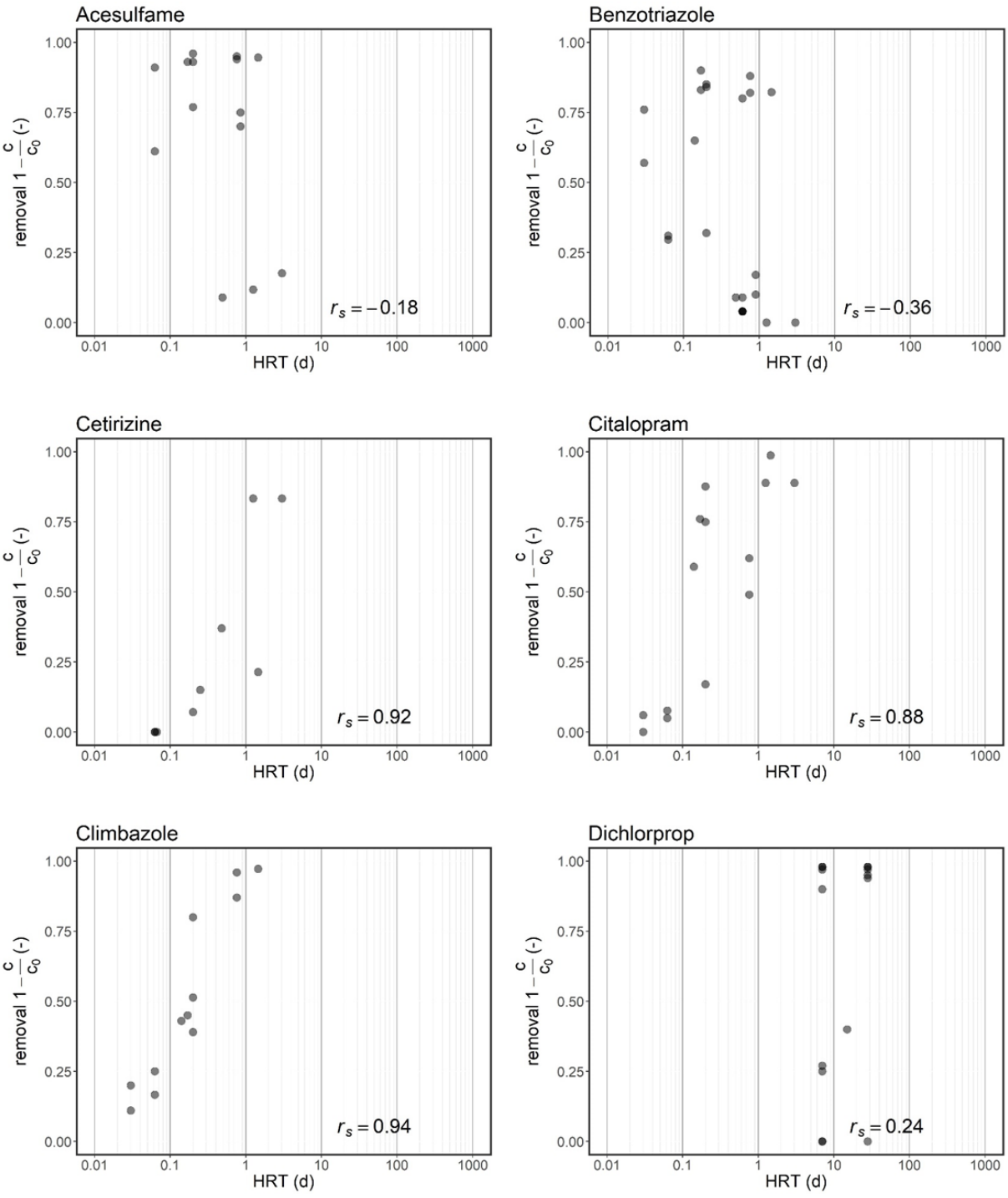

Metoprolol
$r_s = 0.79$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical

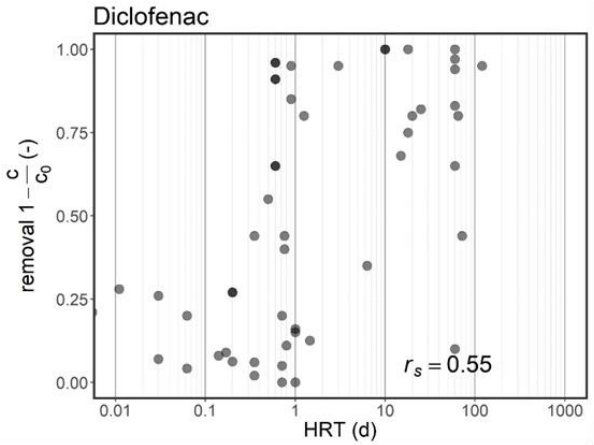

Paracetamol
$r_s = -0.47$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material technical

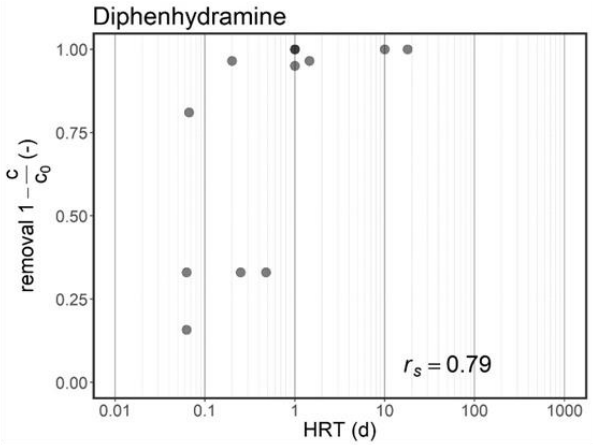

Sulfamethoxazole
$r_s = 0.75$
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical

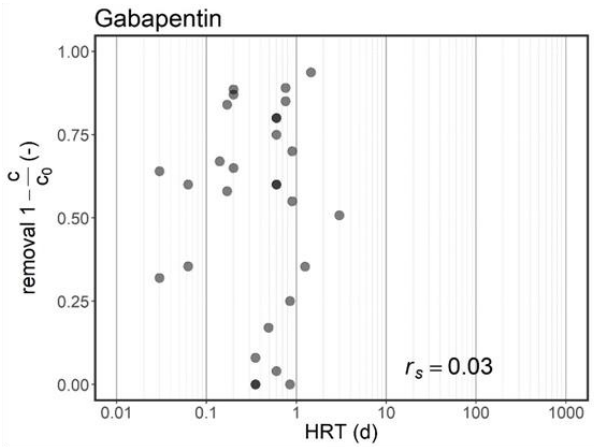

TCEP
r_s =
TCPP
r_s =
Telmisartan
r_s = 0.7
Valsartan
r_s = 0.87
Valsartanic Acid
r_s = −0.87
Venlafaxine
r_s = 0.47
removal $1 - \frac{c}{c_0}$ (-)
ΔDOC (mg/L)
Material natural technical
Material technical

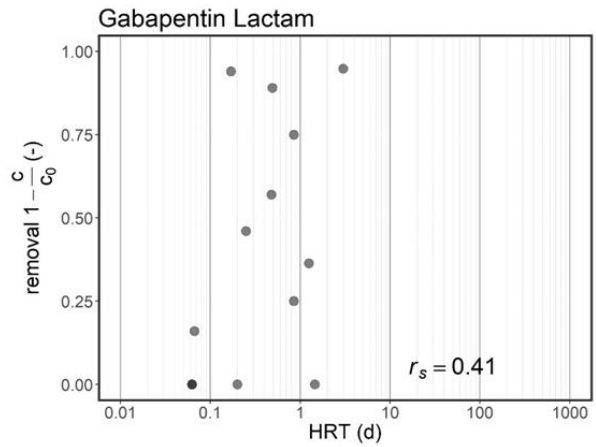
2. Correlations between HRT and TOrC removal

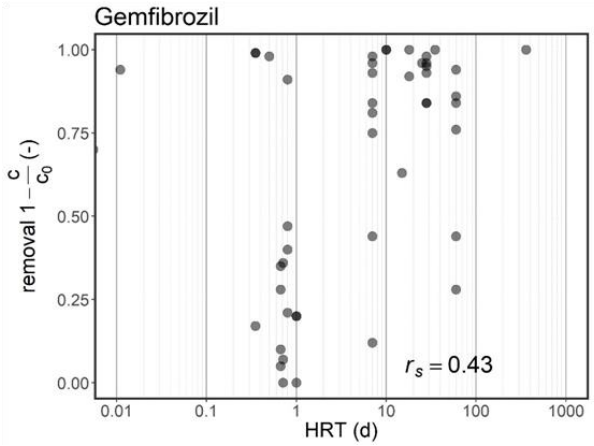


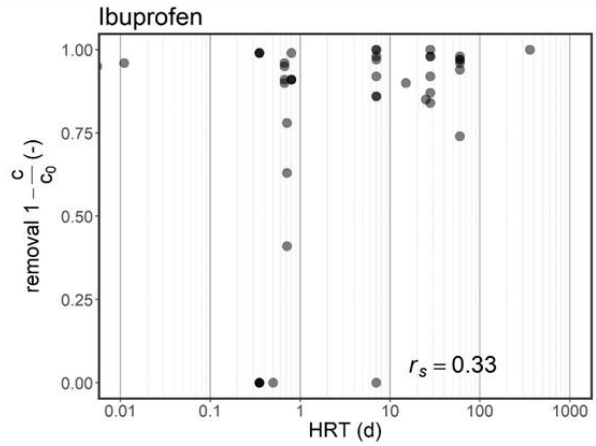

Diclofenac
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.55$

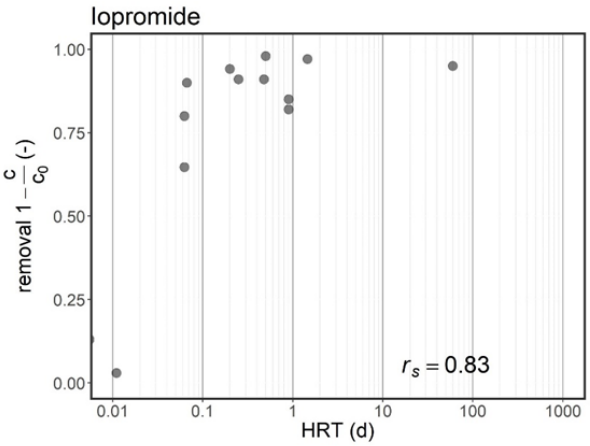

Diphenhydramine
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.79$

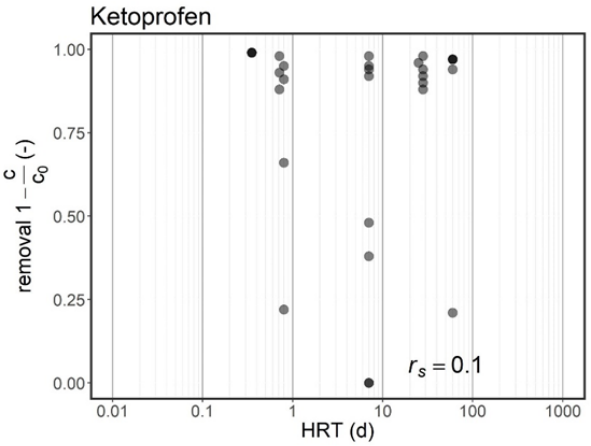

Gabapentin
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.03$

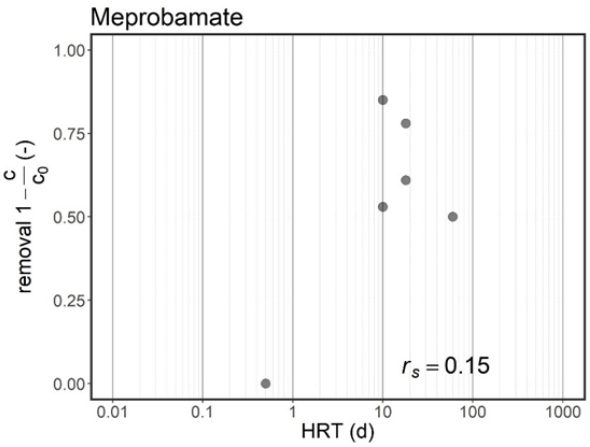

Gabapentin Lactam
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.41$

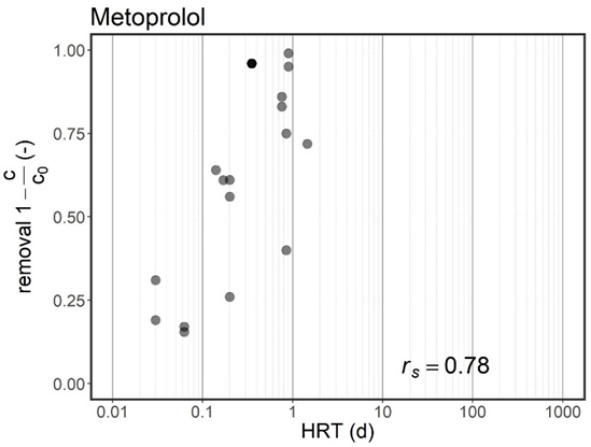

Gemfibrozil
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.43$

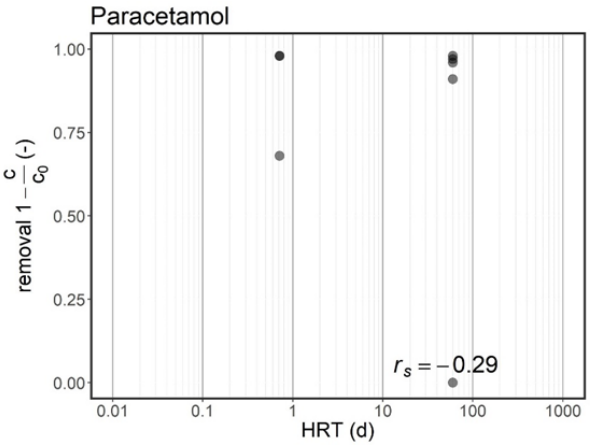

Ibuprofen
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.33$

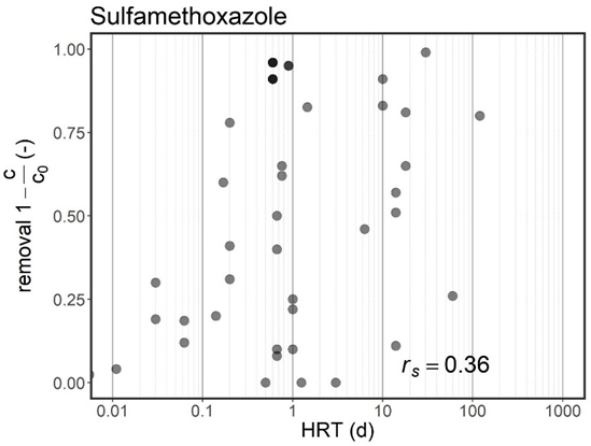

Iopromide
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.83$

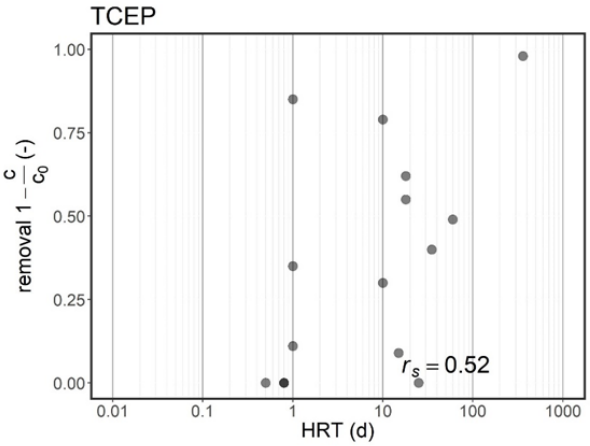

Ketoprofen
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.1$

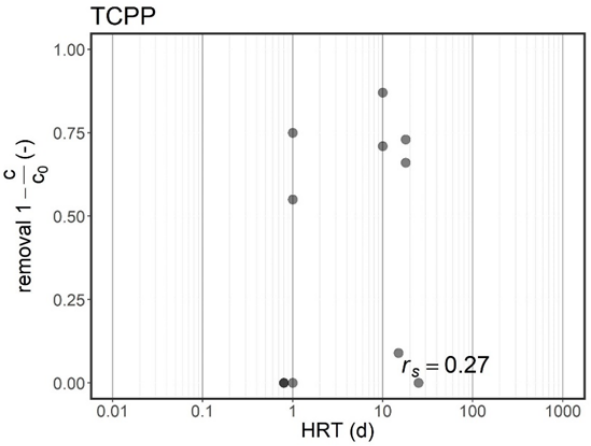

Meprobamate
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.15$

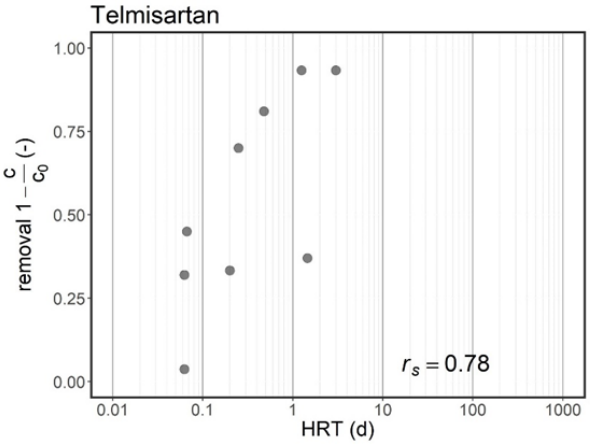

Metoprolol
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.78$

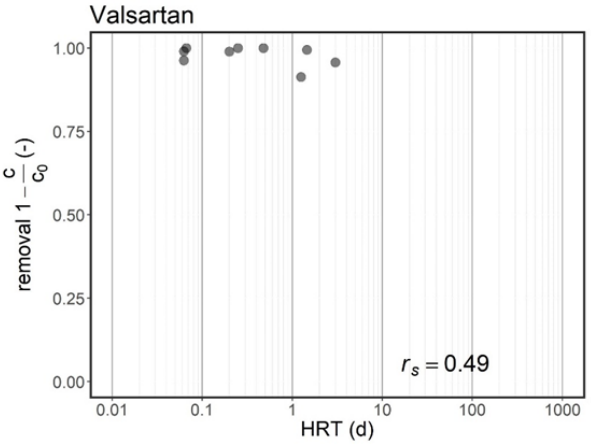

Paracetamol
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = -0.29$

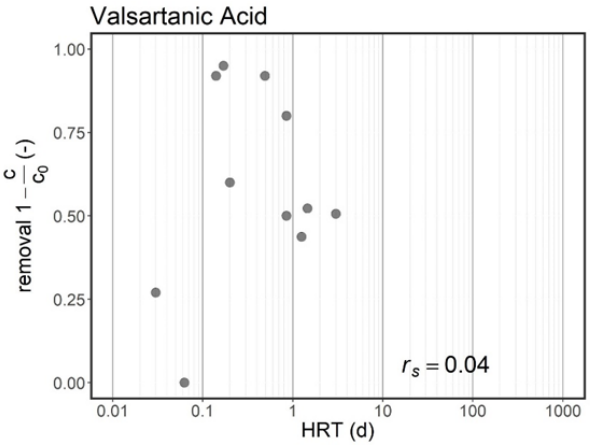

Sulfamethoxazole
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.36$

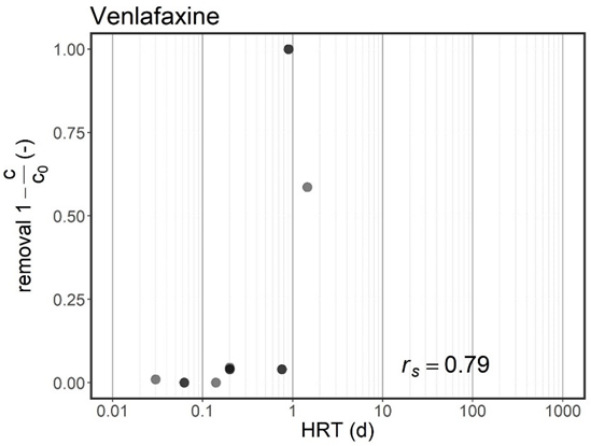

TCEP
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.52$


TCPP
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.27$

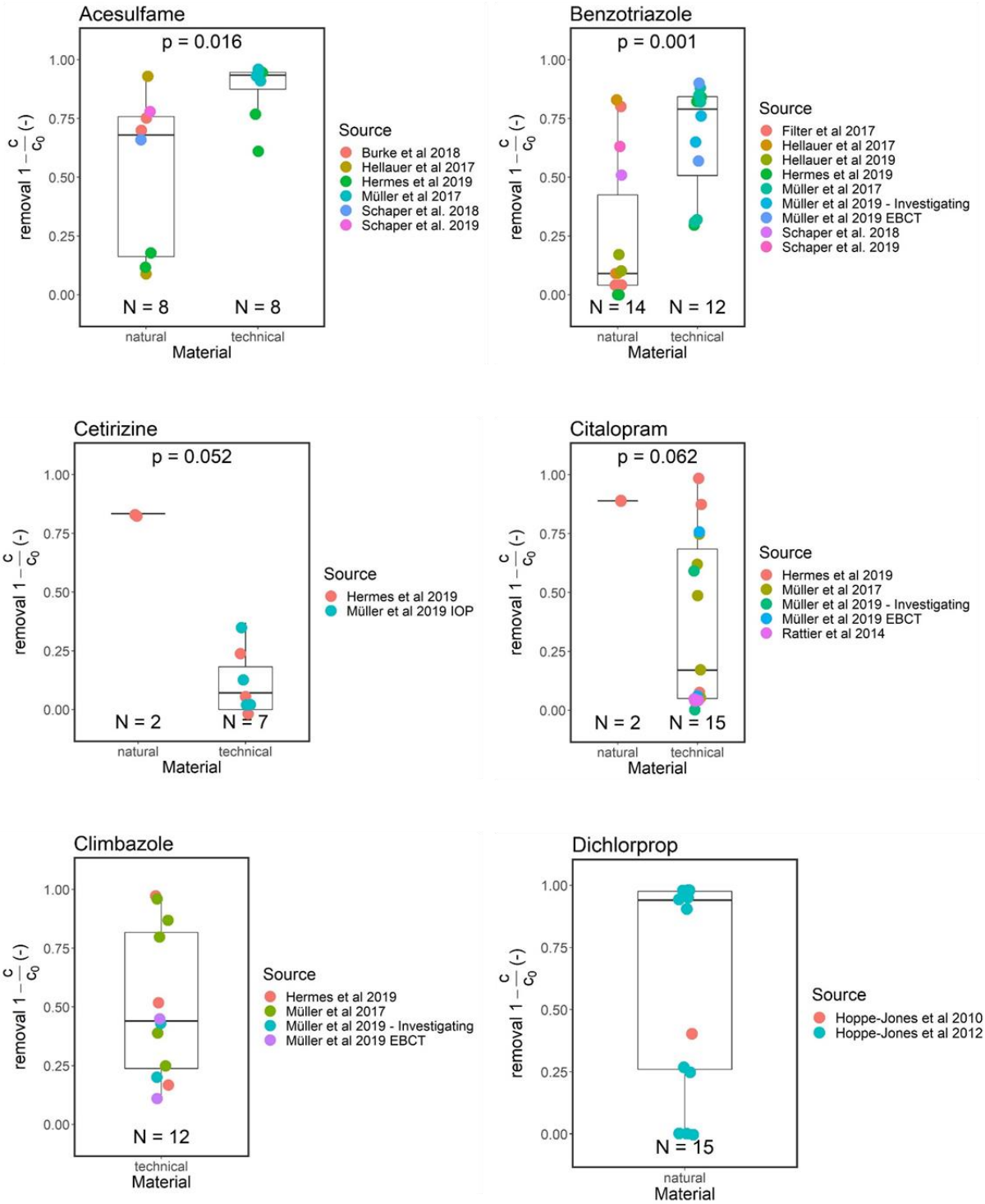

Telmisartan
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.78$

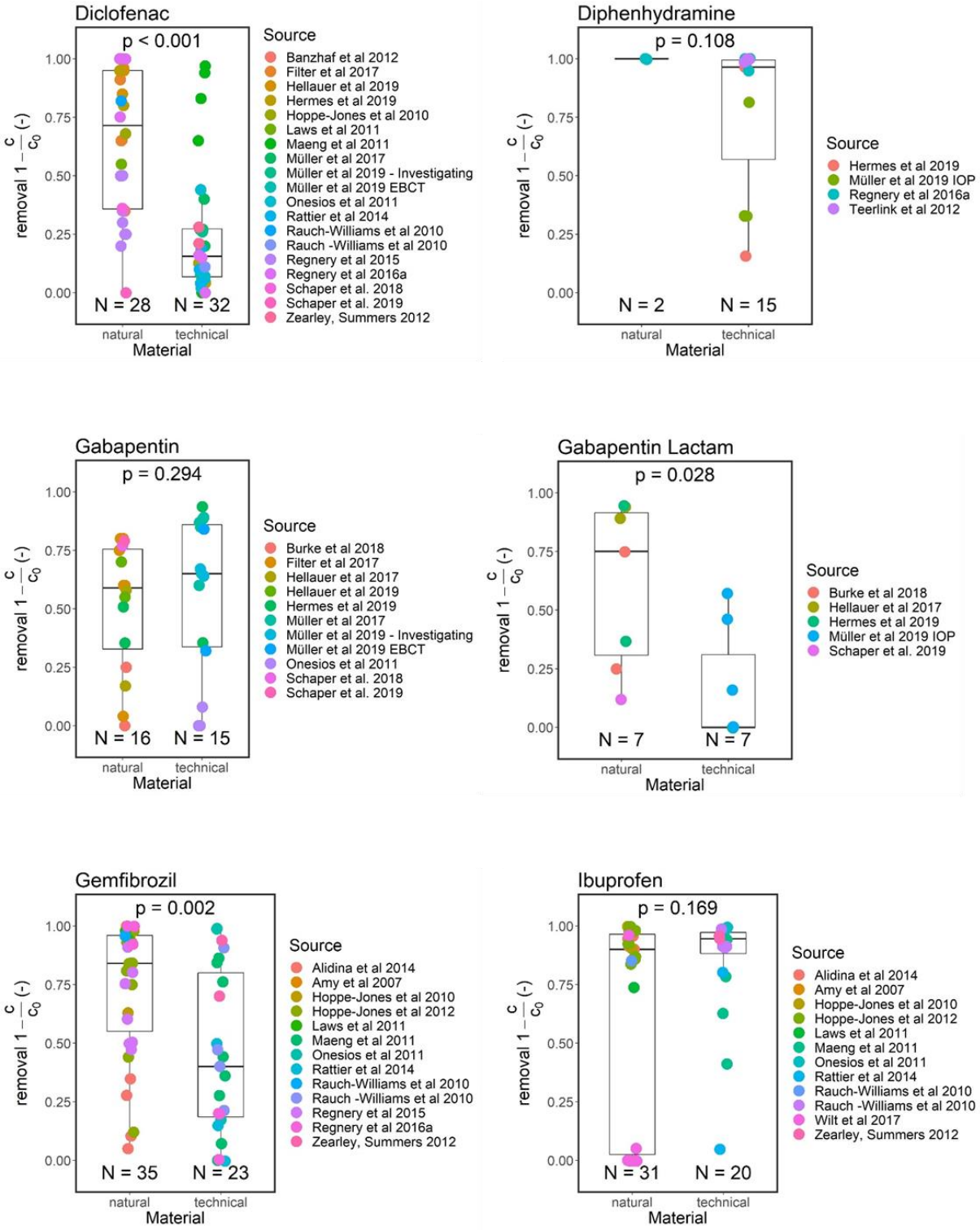

Valsartan
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.49$

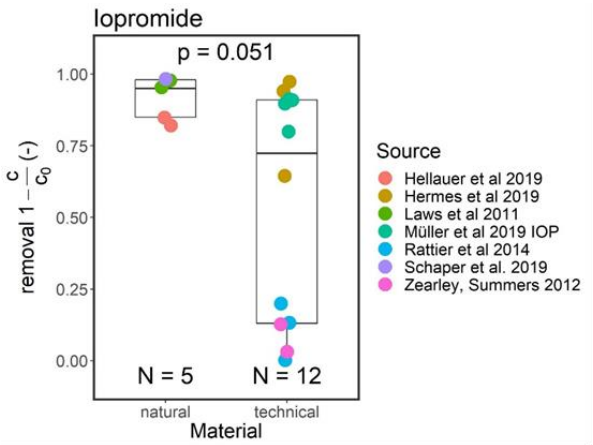

Valsartanic Acid
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.04$

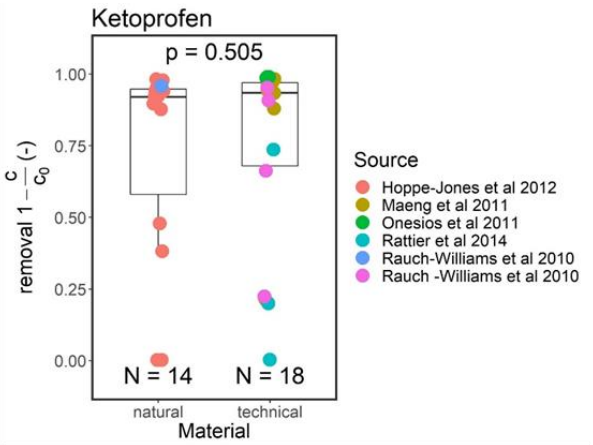

Venlafaxine
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
0.01
0.1
1
10
100
1000
HRT (d)
$r_s = 0.79$

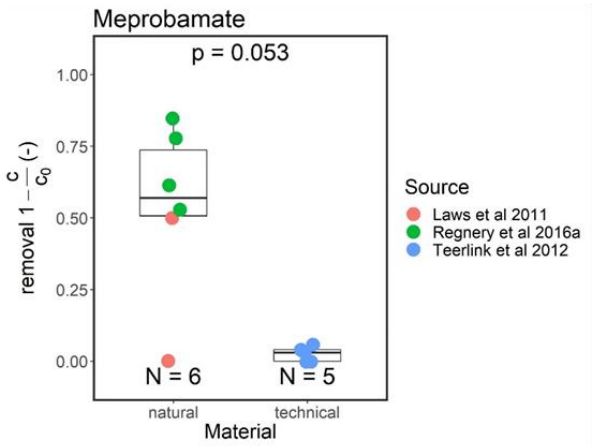
3. Correlations between filter material and TOrC removal

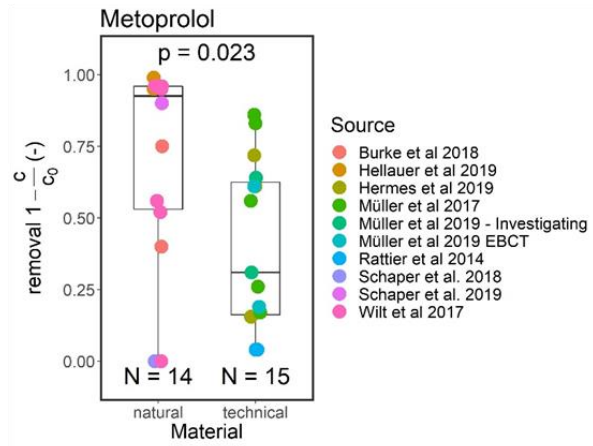


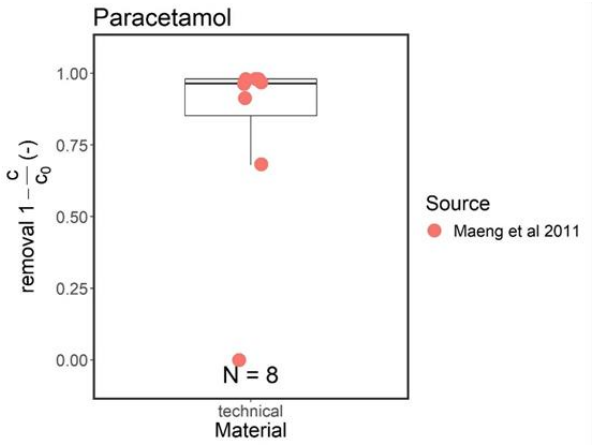

Diclofenac
p < 0.001
N = 28
N = 32
natural
technical
Material
removal $1 - \frac{c}{c_0}$ (-)
Source
Banzhaf et al 2012
Filter et al 2017
Hellauer et al 2019
Hermes et al 2019
Hoppe-Jones et al 2010
Laws et al 2011
Maeng et al 2011
Müller et al 2017
Müller et al 2019 - Investigating
Müller et al 2019 EBCT
Onesios et al 2011
Rattier et al 2014
Rauch-Williams et al 2010
Rauch -Williams et al 2010
Regnery et al 2015
Regnery et al 2016a
Schaper et al. 2018
Schaper et al. 2019
Zearley, Summers 2012
Diphenhydramine
p = 0.108
N = 2
N = 15
Source
Hermes et al 2019
Müller et al 2019 IOP
Regnery et al 2016a
Teerlink et al 2012
Gabapentin
p = 0.294
N = 16
N = 15
Source
Burke et al 2018
Filter et al 2017
Hellauer et al 2017
Hellauer et al 2019
Hermes et al 2019
Müller et al 2017
Müller et al 2019 - Investigating
Müller et al 2019 EBCT
Onesios et al 2011
Schaper et al. 2018
Schaper et al. 2019
Gabapentin Lactam
p = 0.028
N = 7
N = 7
Source
Burke et al 2018
Hellauer et al 2017
Hermes et al 2019
Müller et al 2019 IOP
Schaper et al. 2019
Gemfibrozil
p = 0.002
N = 35
N = 23
Source
Alidina et al 2014
Amy et al 2007
Hoppe-Jones et al 2010
Hoppe-Jones et al 2012
Laws et al 2011
Maeng et al 2011
Onesios et al 2011
Rattier et al 2014
Rauch-Williams et al 2010
Rauch -Williams et al 2010
Regnery et al 2015
Regnery et al 2016a
Zearley, Summers 2012
Ibuprofen
p = 0.169
N = 31
N = 20
Source
Alidina et al 2014
Amy et al 2007
Hoppe-Jones et al 2010
Hoppe-Jones et al 2012
Laws et al 2011
Maeng et al 2011
Onesios et al 2011
Rattier et al 2014
Rauch-Williams et al 2010
Rauch -Williams et al 2010
Wilt et al 2017
Zearley, Summers 2012

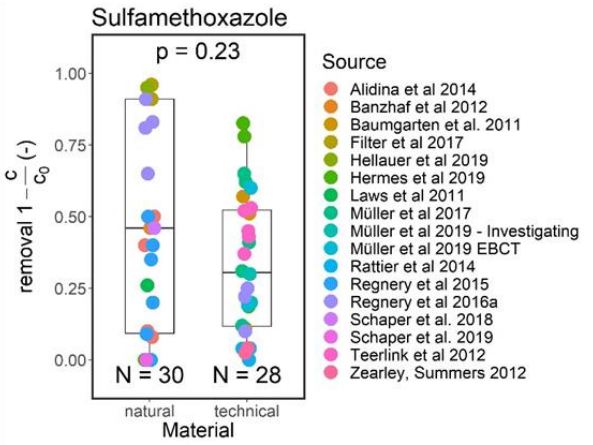

Iopromide
p = 0.051
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 5
N = 12
natural
technical
Material
Source
Hellauer et al 2019
Hermes et al 2019
Laws et al 2011
Müller et al 2019 IOP
Rattier et al 2014
Schaper et al. 2019
Zearley, Summers 2012

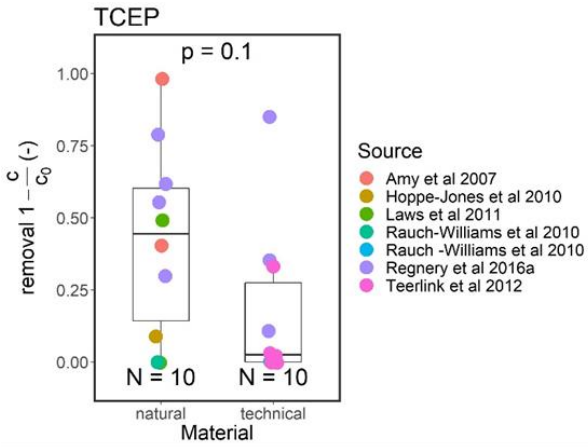

Ketoprofen
p = 0.505
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 14
N = 18
natural
technical
Material
Source
Hoppe-Jones et al 2012
Maeng et al 2011
Onesios et al 2011
Rattier et al 2014
Rauch-Williams et al 2010
Rauch -Williams et al 2010


Meprobamate
p = 0.053
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 6
N = 5
natural
technical
Material
Source
Laws et al 2011
Regnery et al 2016a
Teerlink et al 2012


Metoprolol
p = 0.023
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 14
N = 15
natural
technical
Material
Source
Burke et al 2018
Hellauer et al 2019
Hermes et al 2019
Müller et al 2017
Müller et al 2019 - Investigating
Müller et al 2019 EBCT
Rattier et al 2014
Schaper et al. 2018
Schaper et al. 2019
Wilt et al 2017


Paracetamol
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 8
technical
Material
Source
Maeng et al 2011


Sulfamethoxazole
p = 0.23
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 30
N = 28
natural
technical
Material
Source
Alidina et al 2014
Banzhaf et al 2012
Baumgarten et al. 2011
Filter et al 2017
Hellauer et al 2019
Hermes et al 2019
Laws et al 2011
Müller et al 2017
Müller et al 2019 - Investigating
Müller et al 2019 EBCT
Rattier et al 2014
Regnery et al 2015
Regnery et al 2016a
Schaper et al. 2018
Schaper et al. 2019
Teerlink et al 2012
Zearley, Summers 2012


TCEP
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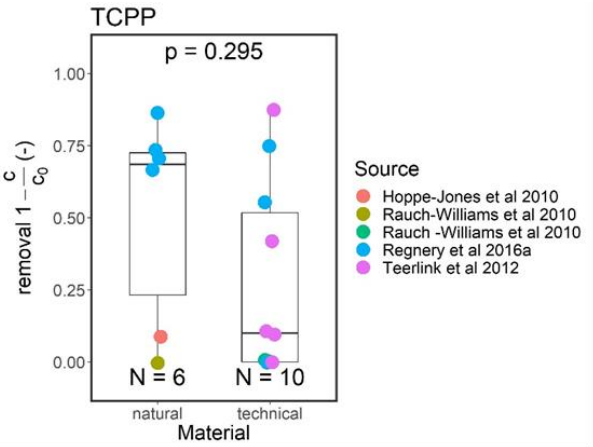
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 10
N = 10
natural
technical
Material
Source
Amy et al 2007
Hoppe-Jones et al 2010
Laws et al 2011
Rauch-Williams et al 2010
Rauch -Williams et al 2010
Regnery et al 2016a
Teerlink et al 2012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removal $1-\frac{c}{c_0}$ (-)
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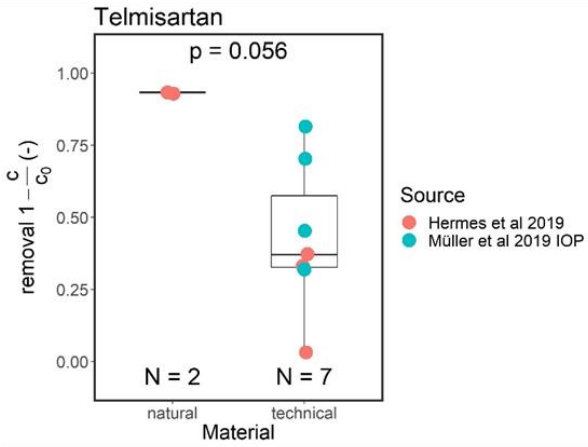
0.50
0.25
0.00
N = 6
N = 10
natural
technical
Material
Source
Hoppe-Jones et al 2010
Rauch-Williams et al 2010
Rauch -Williams et al 2010
Regnery et al 2016a
Teerlink et al 2012


Telmisartan
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removal $1-\frac{c}{c_0}$ (-)
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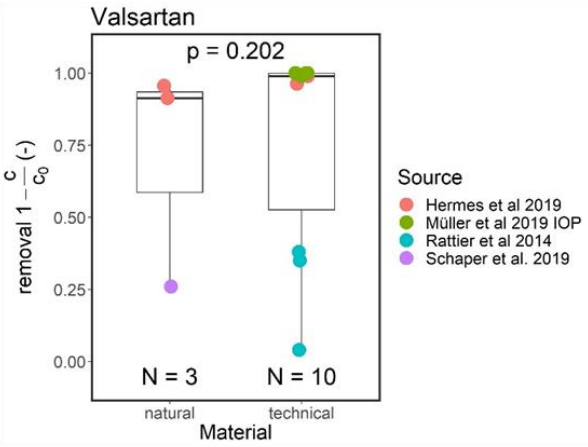
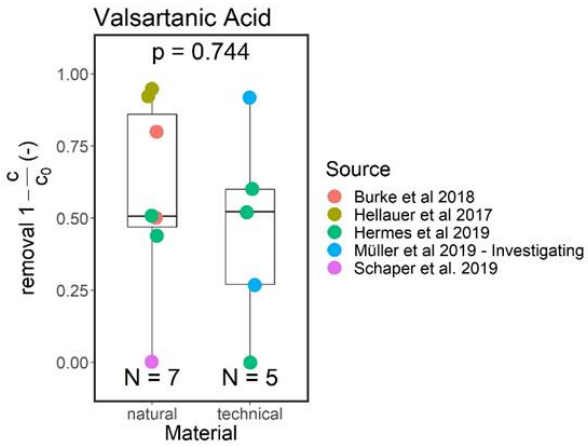
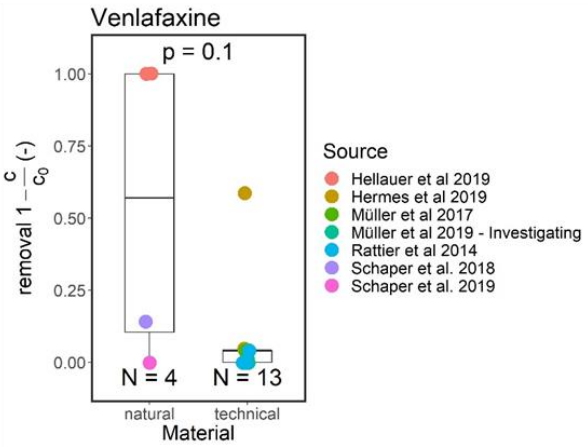
0.75
0.50
0.25
0.00
N = 2
N = 7
natural
technical
Material
Source
Hermes et al 2019
Müller et al 2019 IOP


Valsartan
p = 0.202
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 3
N = 10
natural
technical
Material
Source
Hermes et al 2019
Müller et al 2019 IOP
Rattier et al 2014
Schaper et al. 2019


Valsartanic Acid
p = 0.744
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 7
N = 5
natural
technical
Material
Source
Burke et al 2018
Hellauer et al 2017
Hermes et al 2019
Müller et al 2019 - Investigating
Schaper et al. 2019


Venlafaxine
p = 0.1
removal $1-\frac{c}{c_0}$ (-)
1.00
0.75
0.50
0.25
0.00
N = 4
N = 13
natural
technical
Material
Source
Hellauer et al 2019
Hermes et al 2019
Müller et al 2017
Müller et al 2019 - Investigating
Rattier et al 2014
Schaper et al. 2018
Schaper et al. 2019

11.5.1 References used in the meta-analysis

Achten, C., Kolb, A., Püttmann, W., 2002. Occurrence of methyl tert-butyl ether (MTBE) in riverbank fiftered water and drnking water produced by riverbank filtration. 2. Environ. Sci. Technol. 36 (17), 3662–3670. doi:10.1021/es011493q.

Alidina, M., Li, D., Drewes, J.E., 2014. Investigating the role for adaptation of the microbial community to transform trace organic chemicals during managed aquifer recharge. Water Res. 56, 172–180. https://doi.org/10.1016/j.watres.2014.02.046

Amy, G., Drewes, J., 2007. Soil Aquifer Treatment (SAT) as a Natural and Sustainable Wastewater Reclamation / Reuse Technology : Fate of Wastewater Effluent Organic Matter (EfOM) and Trace Organic Compounds. Environ. Monit. Assess. 129, 19–26. https://doi.org/10.1007/s10661-006-9421-4

Baumgarten, B., Jährig, J., Reemtsma, T., Jekel, M., 2011. Long term laboratory column experiments to simulate bank filtration: Factors controlling removal of sulfamethoxazole. Water Res. 45, 211–220. https://doi.org/10.1016/j.watres.2010.08.034

Banzhaf, S., Nödler, K., Licha, T., Krein, A., Scheytt, T., 2012. Redox-sensitivity and mobility of selected pharmaceutical compounds in a low flow column experiment. The Science of the total environment 438, 113–121. doi:10.1016/j.scitotenv.2012.08.041.

Burke, V., Schneider, L., Greskowiak, J., Baar, P., Sperlich, A., Dünnbier, U., Massmann, G., 2018. Trace Organic Removal during River Bank Filtration for Two Types of Sediment. Water 10 (12), 1736. doi:10.3390/w10121736.

de Wilt, A., He, Y., Sutton, N., Langenhoff, A., Rijnaarts, H., 2018. Sorption and biodegradation of six pharmaceutically active compounds under four different redox conditions. Chemosphere 193, 811–819. https://doi.org/10.1016/j.chemosphere.2017.11.084

Filter, J., Jekel, M., Ruhl, A.S., 2017. Impacts of Accumulated Particulate Organic Matter on Oxygen Consumption and Organic Soil Aquifer Treatment. Water 9. https://doi.org/10.3390/w9050349

Greskowiak, J., Prommer, H., Massmann, G., Nützmann, G., 2006. Modeling seasonal redox dynamics and the corresponding fate of the pharmaceutical residue phenazone during artificial recharge of groundwater. Environ. Sci. Technol. 40 (21), 6615–6621. doi:10.1021/es052506t.

Gruenheid, S., Huebner, U., Jekel, M., 2008. Impact of temperature on biodegradation of bulk and trace organics during soil passage in an indirect reuse system. Water science and Technology : a journal of the International Association on Water Pollution Research 57 (7), 987–994. doi:10.2166/wst.2008.207.

Grünheid, S., Amy, G., Jekel, M., 2005. Removal of bulk dissolved organic carbon (DOC) and trace organic compounds by bank filtration and artificial recharge. Water research 39 (14), 3219–3228. doi:10.1016/j.watres.2005.05.030.

Hass, U., Duennbier, U., Massmann, G., 2012. Occurrence and distribution of psychoactive compounds and their metabolites in the urban water cycle of Berlin (Germany). Water research 46 (18), 6013–6022. doi:10.1016/j.watres.2012.08.025.

Heberer, T., Massmann, G., Fanck, B., Taute, T., Dünnbier, U., 2008. Behaviour and redox sensitivity of antimicrobial residues during bank filtration. Chemosphere 73 (4), 451–460. doi:10.1016/j.chemosphere.2008.06.056.

Heberer, T., Mechlinski, A., Fanck, B., Knappe, A., Massmann, G., Pekdeger, A., Fritz, B., 2004. Field Studies on the Fate and Transport of Pharmaceutical Residues in Bank Filtration. Groundwater Monitoring & Remediation 24 (2), 70–77. doi:10.1111/j.1745-6592.2004.tb00714.x.

Hellauer, K., Martínez Mayerlen, S., Drewes, J.E., Hübner, U., 2019. Biotransformation of trace organic chemicals in the presence of highly refractory dissolved organic carbon. Chemosphere 215, 33–39. https://doi.org/10.1016/j.chemosphere.2018.09.166

Hellauer, K., Mergel, D., Ruhl, A.S., Filter, J., Hübner, U., Jekel, M., Drewes, J.E., 2017. Advancing Sequential Managed Aquifer Recharge Technology (SMART) Using Different Intermediate Oxidation Processes. Water 1–14. https://doi.org/10.3390/w9030221

Henzler, A.F., Greskowiak, J., Massmann, G., 2014. Modeling the fate of organic micropollutants during river bank filtration (Berlin, Germany). J. Contam. Hydrol. 156, 78–92. https://doi.org/10.1016/j.jconhyd.2013.10.005

Hermes, N., Jewell, K.S., Schulz, M., Müller, J., Hübner, U., Wick, A., Drewes, J.E., Ternes, T.A., 2019. Elucidation of removal processes in sequential biofiltration (SBF) and soil aquifer treatment (SAT) by analysis of a broad range of trace organic chemicals (TOrCs) and their transformation products (TPs). Water Res. 163, 114857. https://doi.org/10.1016/j.watres.2019.114857

Hoppe-Jones, C., Dickenson, E.R. V, Drewes, J.E., 2012. The role of microbial adaptation and biodegradable dissolved organic carbon on the attenuation of trace organic chemicals during groundwater recharge. Sci. Total Environ. 437, 137–144. https://doi.org/10.1016/j.scitotenv.2012.08.009

Hoppe-Jones, C., Oldham, G., Drewes, J.E., 2010. Attenuation of total organic carbon and unregulated trace organic chemicals in U.S. riverbank filtration systems. Water Res. 44, 4643–4659. https://doi.org/10.1016/j.watres.2010.06.022

Laws, B. V., Dickenson, E.R. V, Johnson, T. a., Snyder, S. a., Drewes, J.E., 2011. Attenuation of contaminants of emerging concern during surface-spreading aquifer recharge. Sci. Total Environ. 409, 1087–1094. https://doi.org/10.1016/j.scitotenv.2010.11.021

Li, D., Alidina, M., Drewes, J.E., 2014. Role of primary substrate composition on microbial community structure and function and trace organic chemical attenuation in managed aquifer recharge systems. Appl. Microbiol. Biotechnol. 98, 5747–5756. https://doi.org/10.1007/s00253-014-5677-8

Maeng, S.K., Ameda, E., Sharma, S.K., Grützmacher, G., Amy, G.L., 2010. Organic micropollutant removal from wastewater effluent-impacted drinking water sources during bank filtration and artificial recharge. Water Res. 44, 4003–4014. https://doi.org/10.1016/j.watres.2010.03.035

Maeng, S.K., Sharma, S.K., Abel, C.D.T., Magic-Knezev, A., Amy, G.L., 2011. Role of biodegradation in the removal of pharmaceutically active compounds with different bulk organic matter characteristics through managed aquifer recharge: Batch and column studies. Water Res. 45, 4722–4736. https://doi.org/10.1016/j.watres.2011.05.043

Müller, J., Drewes, J.E., Hübner, U., 2019a. Investigating synergies in sequential biofiltration-based hybrid systems for the enhanced removal of trace organic chemicals from wastewater treatment plant effluents. Environ. Sci. Technol. Water Res. Technol. 5, 1423–1435. https://doi.org/10.1039/c9ew00181f

Müller, J., Drewes, J.E., Hübner, U., 2017. Sequential biofiltration – A novel approach for enhanced biological removal of trace organic chemicals from wastewater treatment plant effluent. Water Res. 127, 127–138. https://doi.org/10.1016/j.watres.2017.10.009

Müller, J., Jewell, K.S., Schulz, M., Hermes, N., Ternes, T.A., Drewes, J.E., Hübner, U., 2019b. Capturing the oxic transformation of iopromide - A useful tool for an improved characterization of predominant redox conditions and the removal of trace organic compounds in biofiltration systems? Water Res. 152, 274–284. https://doi.org/10.1016/j.watres.2018.12.055

Müller, J., Levai, S., Titzschkau, L., Popovic, N., Carevic, D., Drewes, J.E., Hübner, U., 2019c. Role of reduced empty bed contact times and pre-treatment by coagulation with Fe (III) salts on the removal of trace organic compounds during sequential biofiltration. Sci. Total Enviroment 685, 220–228. https://doi.org/10.1016/j.scitotenv.2019.05.361

Onesios, K.M., Bouwer, E.J., 2012. Biological removal of pharmaceuticals and personal care products during laboratory soil aquifer treatment simulation with different primary substrate concentrations. Water Res. 46, 2365–2375. https://doi.org/10.1016/j.watres.2012.02.001

Rattier, M., Reungoat, J., Keller, J., Gernjak, W., 2014. Removal of micropollutants during tertiary wastewater treatment by biofiltration: Role of nitrifiers and removal mechanisms. Water Res. 54, 89–99. https://doi.org/10.1016/j.watres.2014.01.030

Rauch-Williams, T., Hoppe-Jones, C., Drewes, J.E., 2010. The role of organic matter in the removal of emerging trace organic chemicals during managed aquifer recharge. Water Res. 44, 449–460. https://doi.org/10.1016/j.watres.2009.08.027

Regnery, J., Barringer, J., Wing, A.D., Hoppe-Jones, C., Teerlink, J., Drewes, J.E., 2015. Start-up performance of a full-scale riverbank filtration site regarding removal of DOC, nutrients, and trace organic chemicals. Chemosphere 127, 136–142. https://doi.org/10.1016/j.chemosphere.2014.12.076

Regnery, J., Wing, A.D., Kautz, J., Drewes, J.E., 2016. Introducing sequential managed aquifer recharge technology (SMART) - From laboratory to full-scale application. Chemosphere 154, 8–16. https://doi.org/10.1016/j.chemosphere.2016.03.097

Schaper, J.L., Seher, W., Nützmann, G., Putschew, A., Jekel, M., Lewandowski, J., 2018. The fate of polar trace organic compounds in the hyporheic zone. Water research 140, 158–166. doi:10.1016/j.watres.2018.04.040.

Schaper, J.L., Posselt, M., Bouchez, C., Jaeger, A., Nuetzmann, G., Putschew, A., Singer, G., Lewandowski, J., 2019. Fate of Trace Organic Compounds in the Hyporheic Zone: In fl uence of Retardation, the Benthic Biolayer, and Organic Carbon. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.8b06231

Teerlink, J., Martinez-Hernandez, V., Higgins, C.P., Drewes, J.E., 2012. Removal of trace organic chemicals in onsite wastewater soil treatment units: A laboratory experiment. Water Res. 46, 5174–5184. https://doi.org/10.1016/j.watres.2012.06.024

Zearley, T.L., Summers, R.S., 2012. Removal of trace organic micropollutants by drinking water biological filters. Environ. Sci. Technol. 46, 9412–9419. https://doi.org/10.1021/es301428e

11.6 Supplementary information for Chapter 9

Removal of trace organic chemicals during long-term biofilter operation

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11.6.1 Investigated TOrCs

Table 11-12: List of influent TOrC concentrations over the duration of the long-term column experiment.

Occurrence in column influent								
Compound	LOQ	Desired concentration in influent of columns	BAC (July 2017-September 2019)			Sand (July 2017-September 2019)		
	ng/L	ng/L	Conc. ng/L	Std. Dev. ng/L	n	Conc. ng/L	Std. Dev. ng/L	n
Atenolol	10	500	426	312	31	457	384	31
Antipyrine	10	500	499	360	31	516	410	31
Benzotriazole	50	not spiked	4,647	1,765	29	4,644	1,867	29
Caffeine	10	2000	610	1,340	29	528	1309	31
Carbamazepine	5	not spiked	426	65	31	415	91	31
Citalopram	5	500	530	331	31	538	329	31
Climbazole	5	100	159	77	31	163	82	31
Diclofenac	5	500	1,629	500	31	1,634	614	31
Gabapentin	2.5	500	2,008	1,232	31	1,972	1,273	31
Iopromide	50	2000	1,654	1,122	31	1,752	1,346	31
Metoprolol	2.5	500	441	150	31	445	158	31
Phenytoin	5	100	72	51	30	75	50	30
Primidone	25	500	401	265	31	430	305	30
Sotalol	5	500	344	260	31	382	349	31
Sulfamethoxazole	5	500	421	194	31	427	204	31
Trimethoprim	5	500	447	303	31	461	357	31
Tramadol	5	500	686	346	31	710	430	31
Valsartan acid	5	not spiked	1,166	1,026	7	1,168	1,027	7
Venlafaxine	2.5	500	857	466	27	762	549	31

11.6.2 Operational disturbances

Table 11-13: Timeline of mechanical and chemical disturbances during column operation.

BVTs	Disturbance	Details
50,447 – 51,688	Mechanical	Pump failure due to high back pressure, feed pumps changed
56,637 – 58,410	Mechanical	High back pressure, led to installation of prefilter
59,498– 59,829	Mechanical	Glass bead leaching from prefilter clogged feed tubes
67,593– 70,201	Chemical	High ammonium in influent leading to recirculation
76,162 – 79,645	Chemical	High $FeCl_3$ dosing into RSF led to precipitates clogging the filters
81,916 - 83,996	Chemical	High ammonium in influent leading to recirculation

11.6.3 Long-term column results

11.6.3.1 DOC and UVA_{254} breakthrough

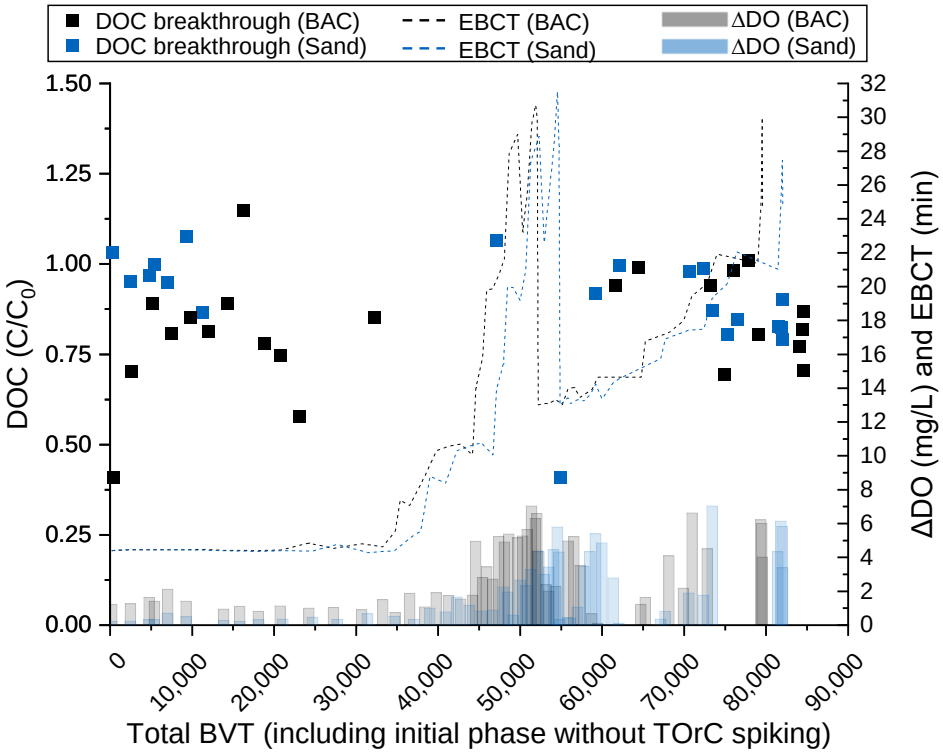

Figure 11-6: DOC breakthrough for sand and BAC filters. Gaps in DOC measurements between 30,000-60,000 BVT were due to the TOC analyzer undergoing repair.

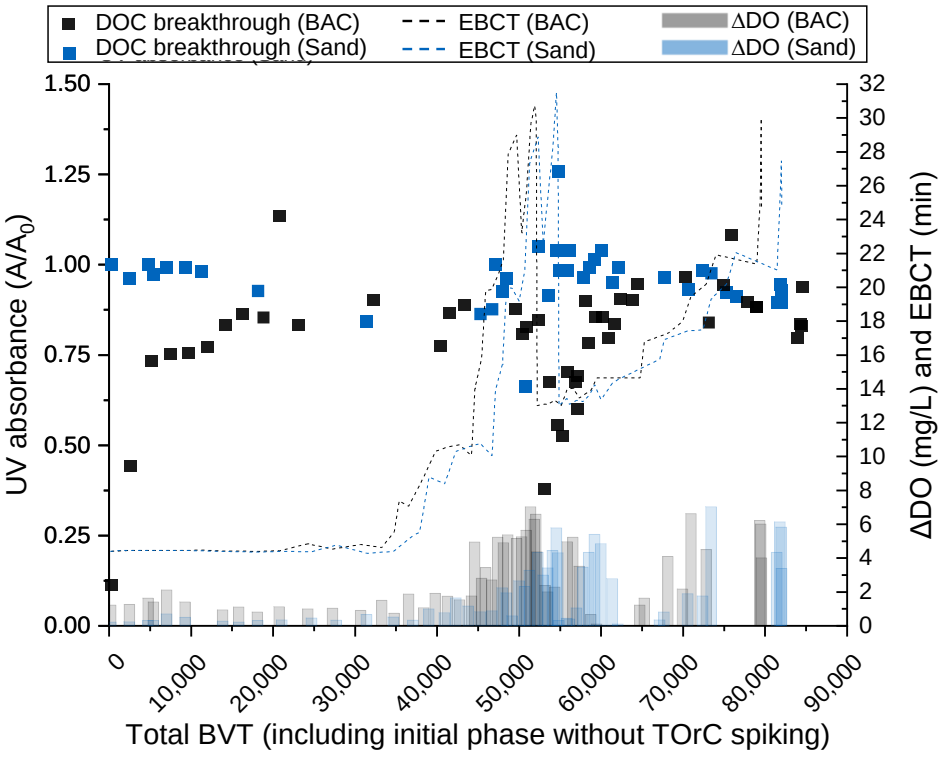

Figure 11-7: UVA_{254} breakthrough for both sand and BAC filters.

11.6.3.2 TOrCs well removed at 80,000 BVT in at least one media (BT<30%)

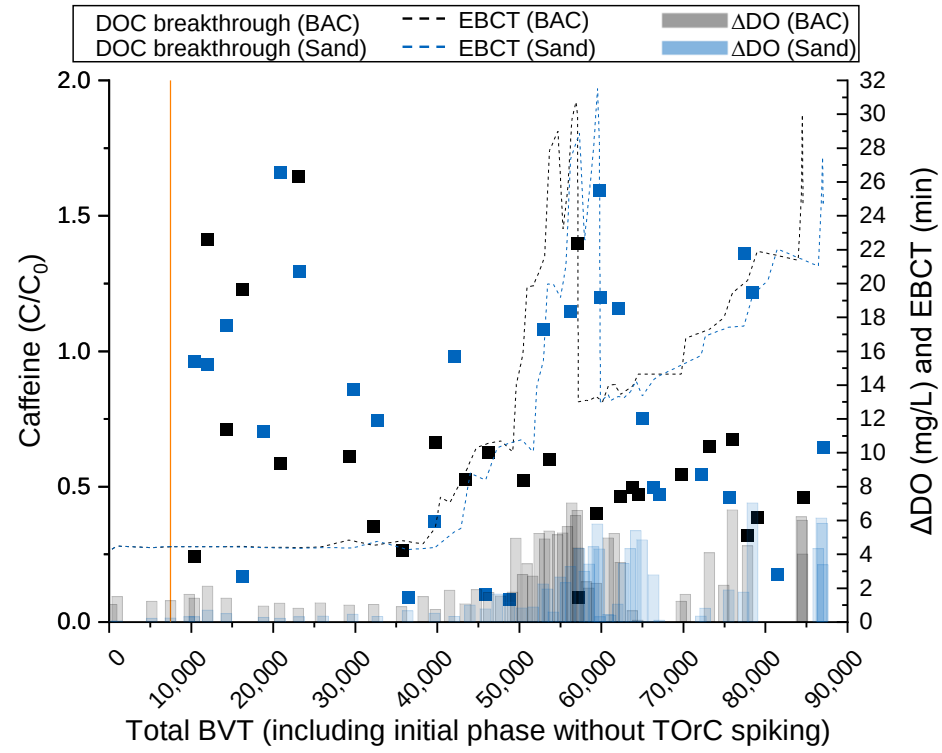

Figure 11-8: Caffeine breakthrough for both sand and BAC filters.

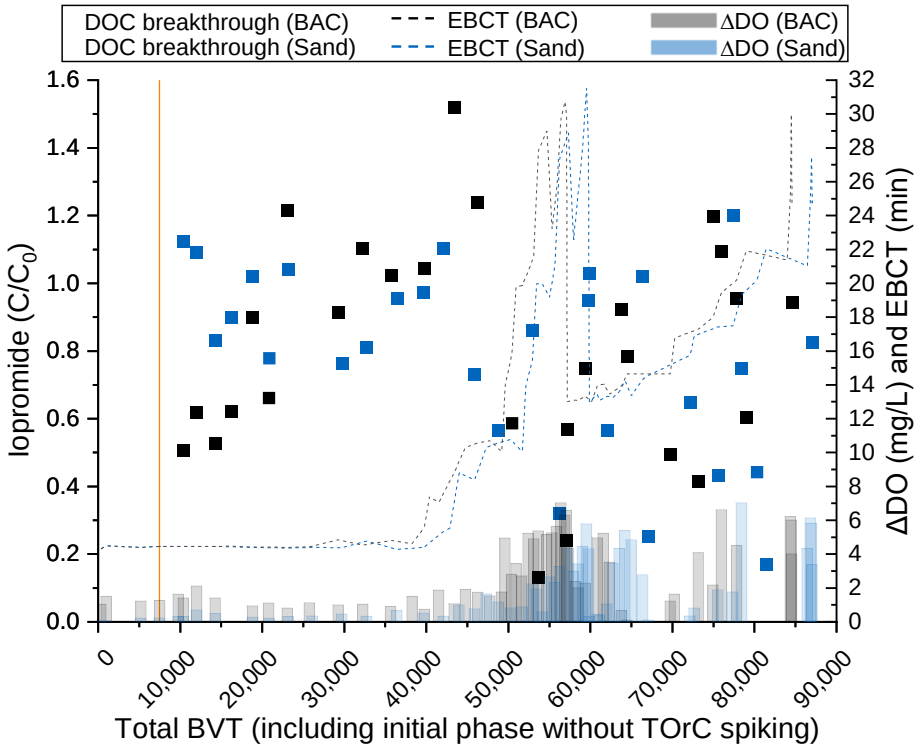

Figure 11-9: Iopromide breakthrough for both sand and BAC filters.

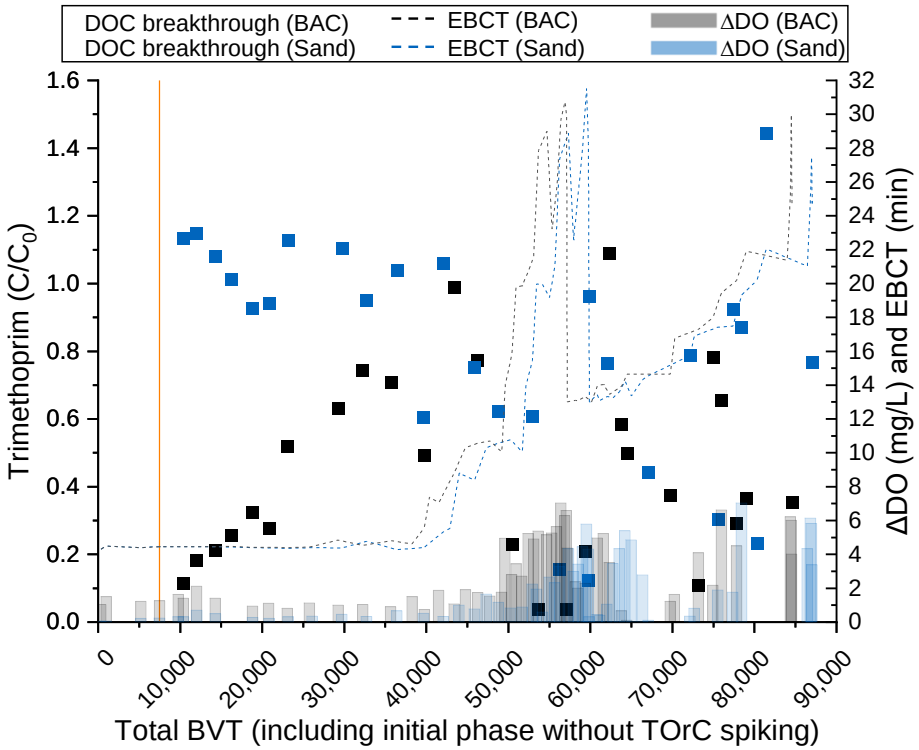

Figure 11-10: Trimethoprim breakthrough for both sand and BAC filters.

11.6.3.3 TOrCs moderately removed at 80,000 BVT in at least one media (30%>BT>70%)

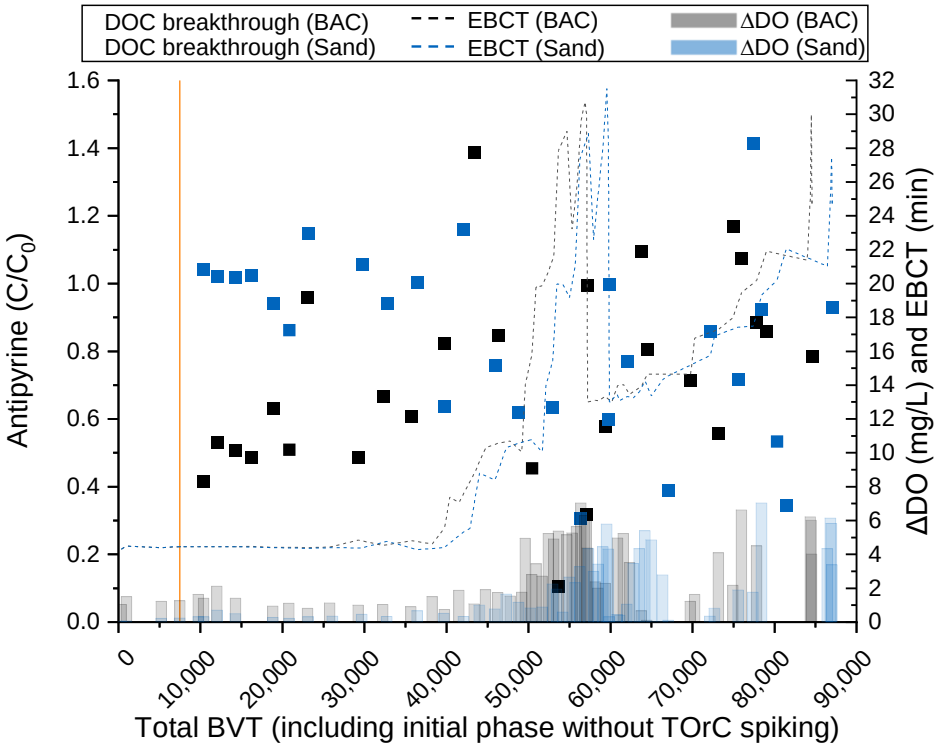

Figure 11-11: Antipyrine breakthrough for both sand and BAC filters.

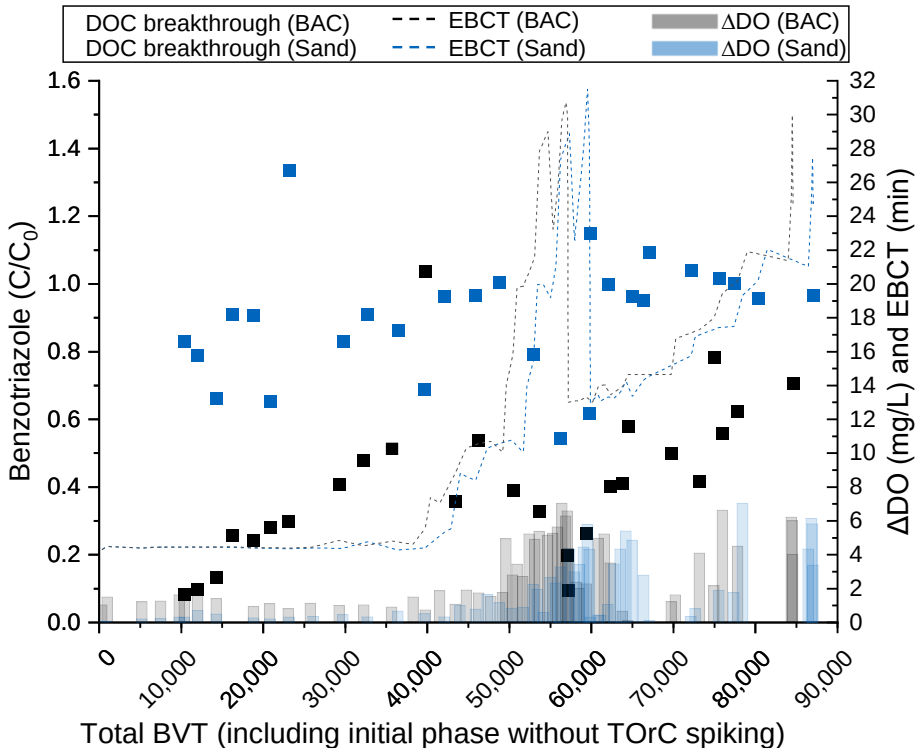

Figure 11-12: Benzotriazole breakthrough for both sand and BAC filters.

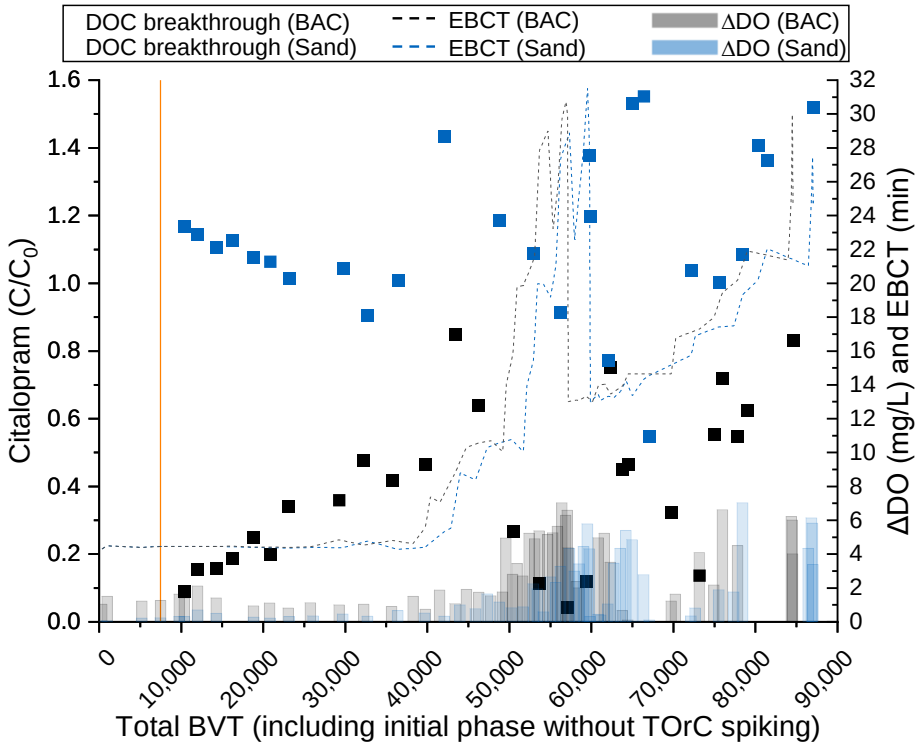

Figure 11-13: Citalopram breakthrough for both sand and BAC filters.

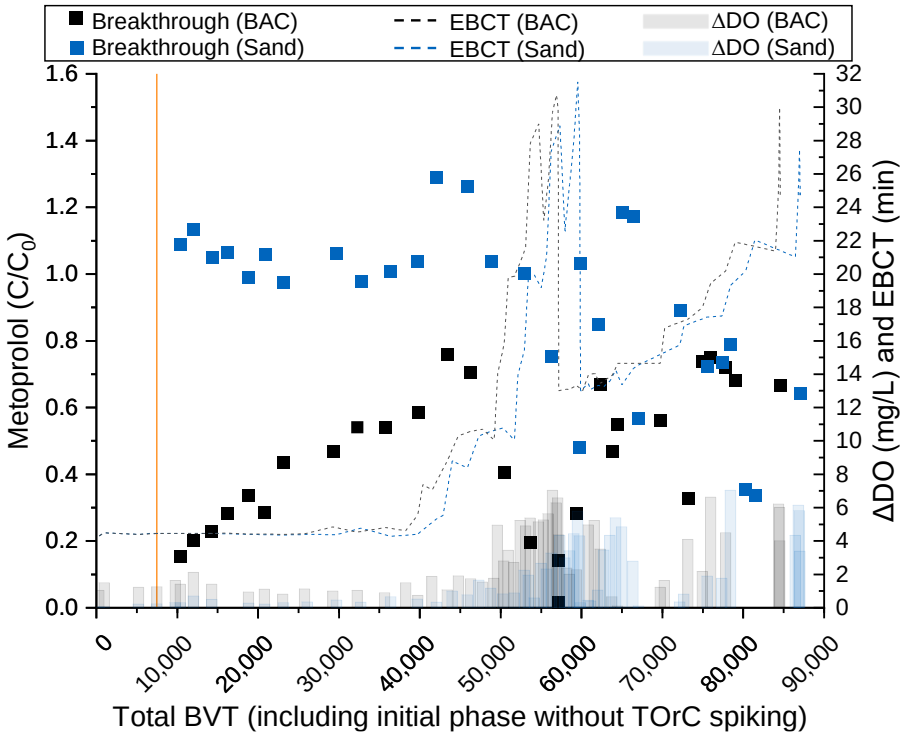

Figure 11-14: Metoprolol breakthrough for both sand and BAC filters.

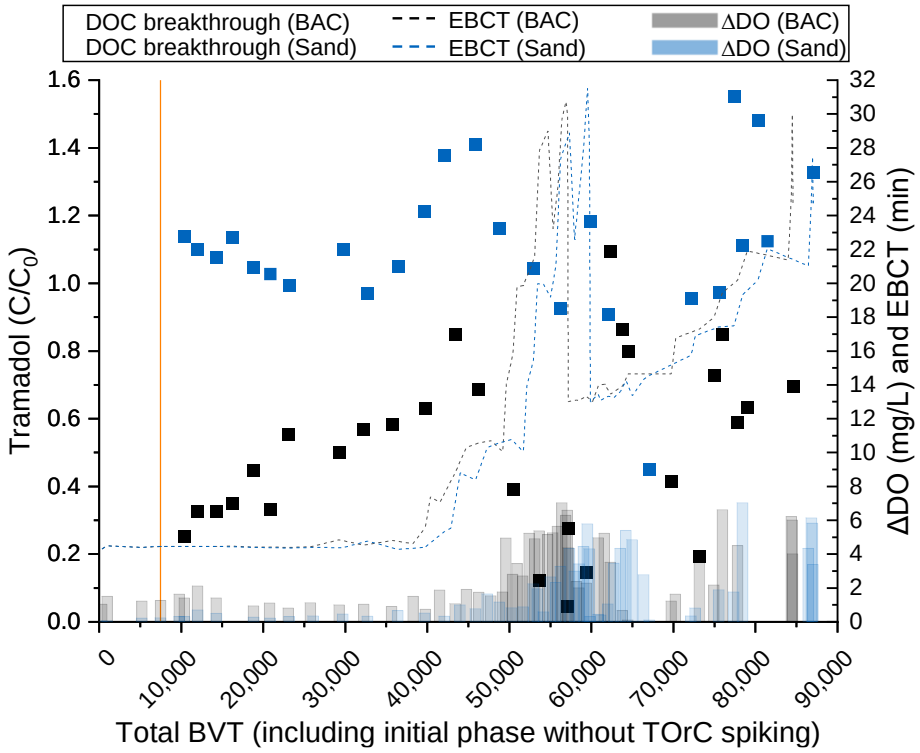

Figure 11-15: Tramadol breakthrough for both sand and BAC filters.

11.6.3.4 TOrCs poorly removed (BT>70%)

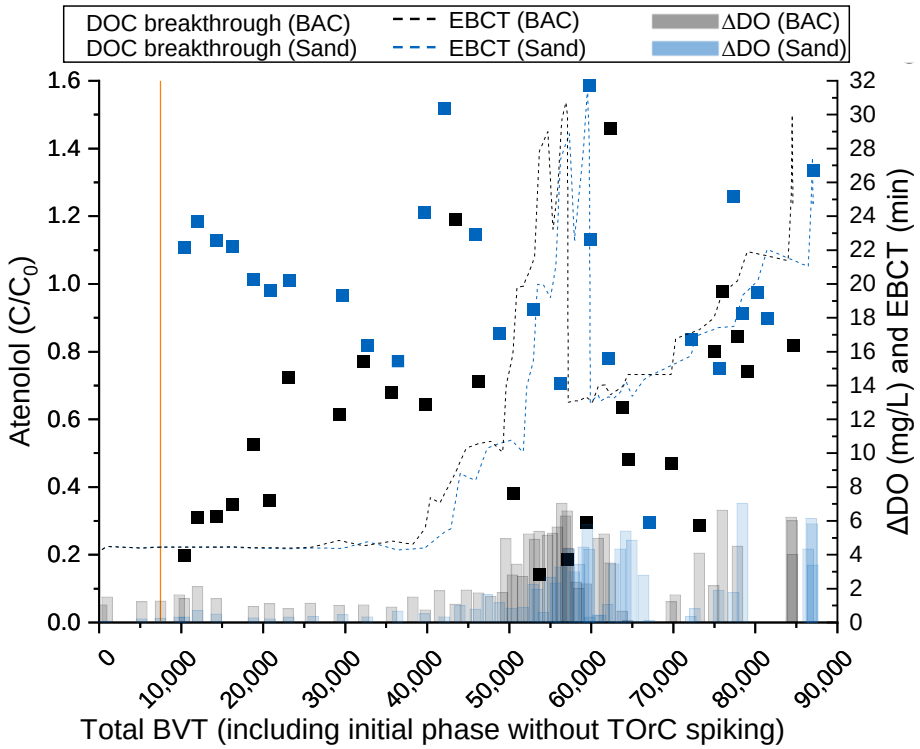

Figure 11-16: Atenolol breakthrough for both sand and BAC filters.

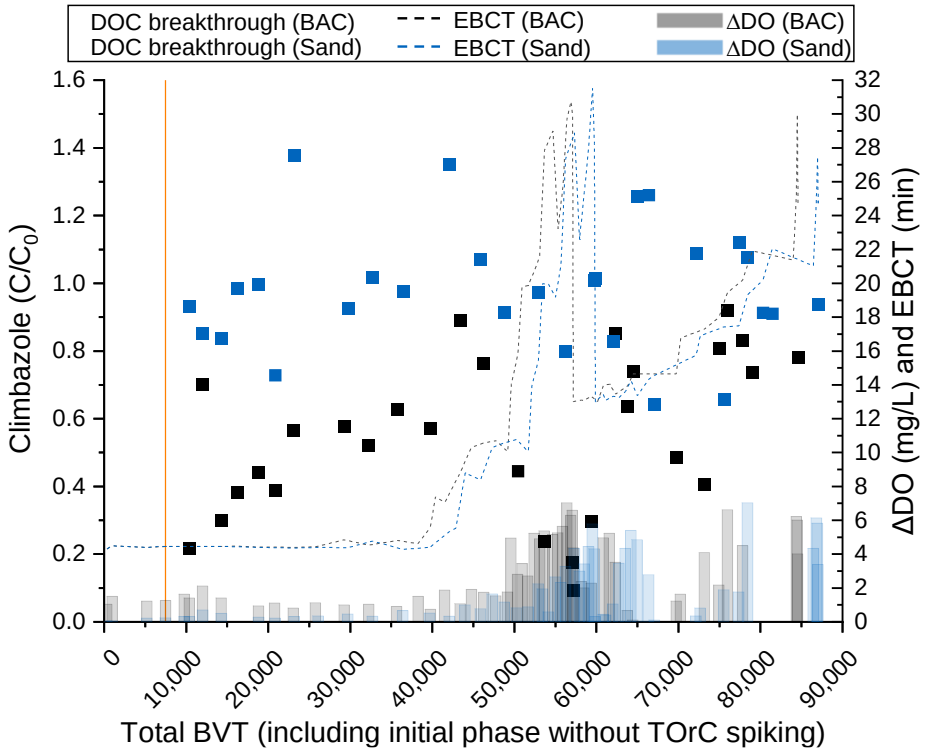

Figure 11-17: Climbazole breakthrough for both sand and BAC filters.

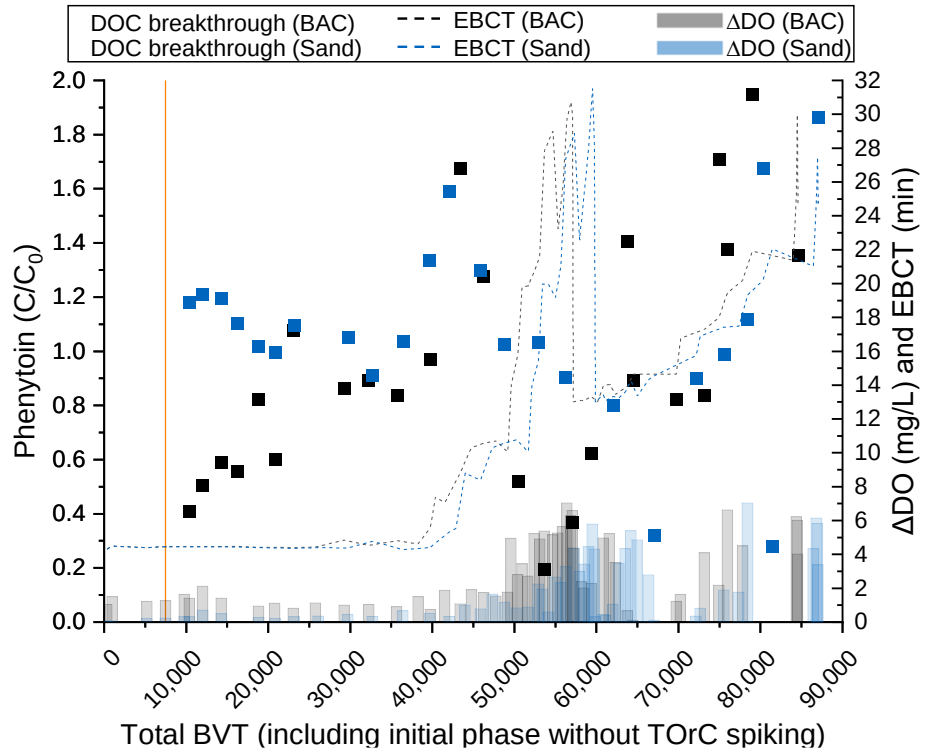

Figure 11-18: Phenytoin breakthrough for both sand and BAC filters.

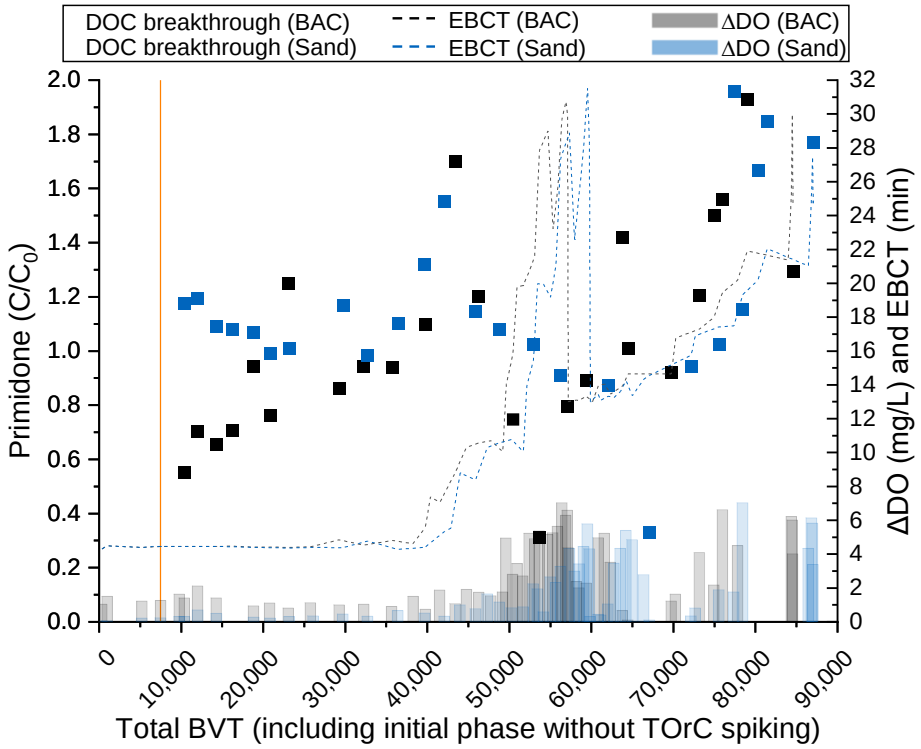

Figure 11-19: Primidone breakthrough for both sand and BAC filters.

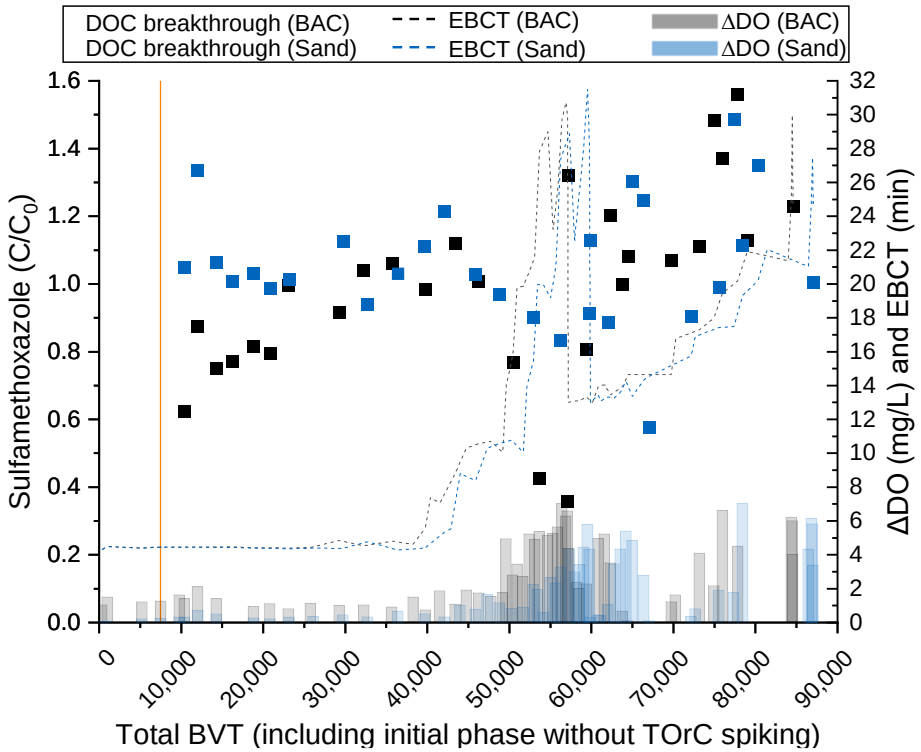

Figure 11-20: Sulfamethoxazole breakthrough for both sand and BAC filters.

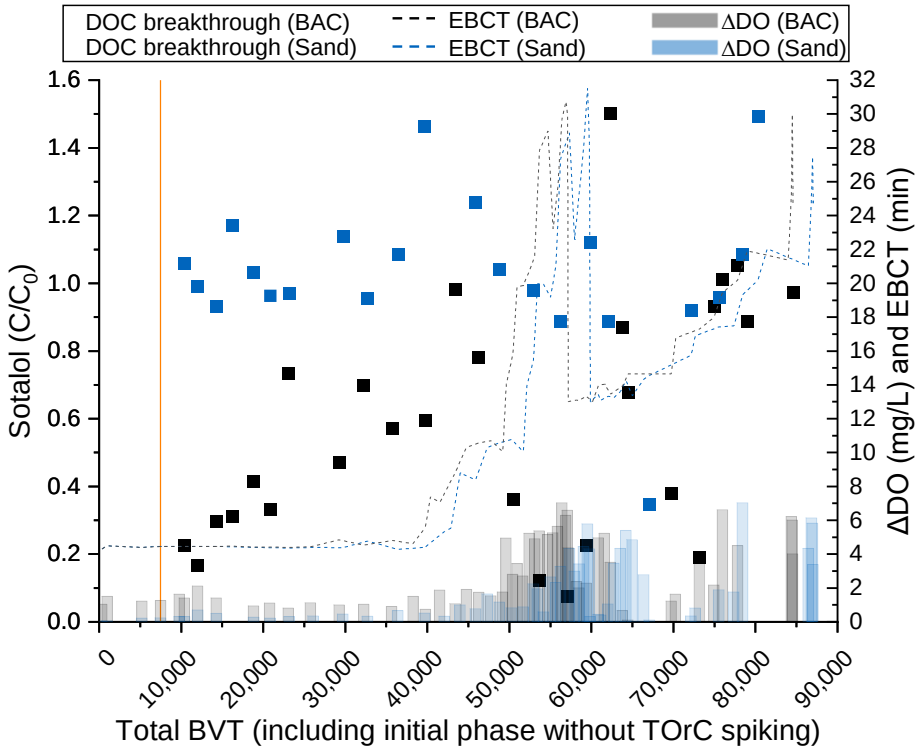

Figure 11-21: Sotalol breakthrough for both sand and BAC filters.

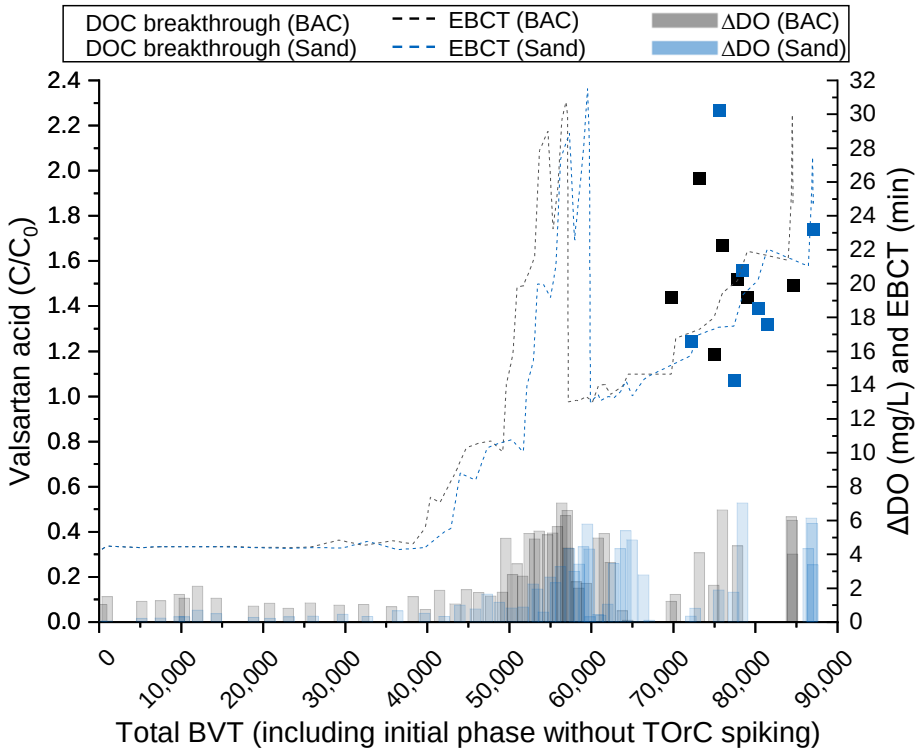

Figure 11-22: Valsartan acid breakthrough for both sand and BAC filters.

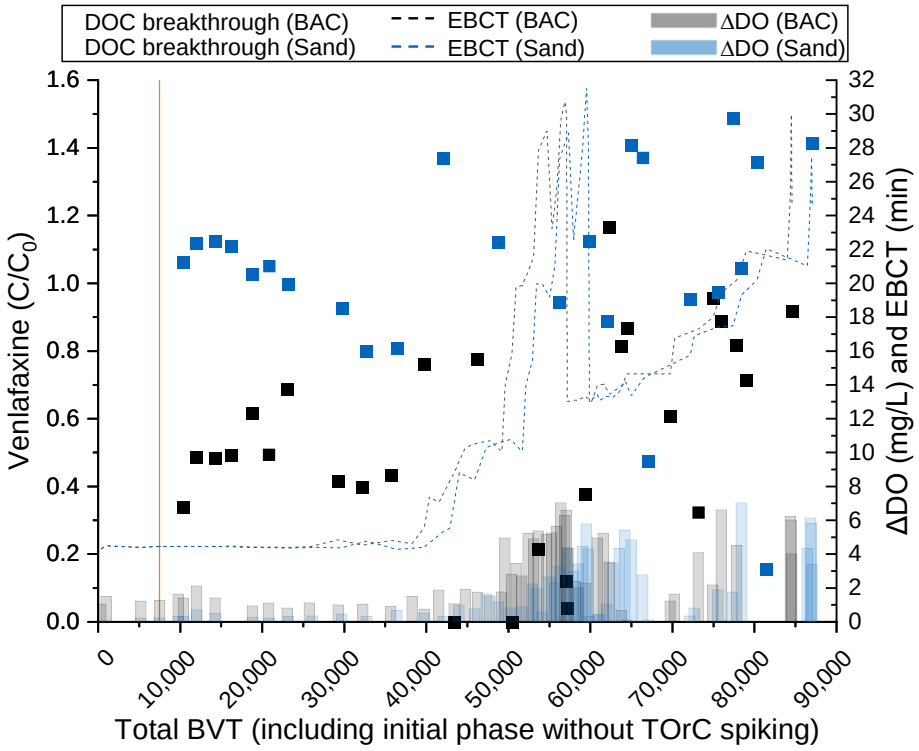

Figure 11-23: Venlafaxine breakthrough for both sand and BAC filters.

11.6.4 Batch biodegradation test results

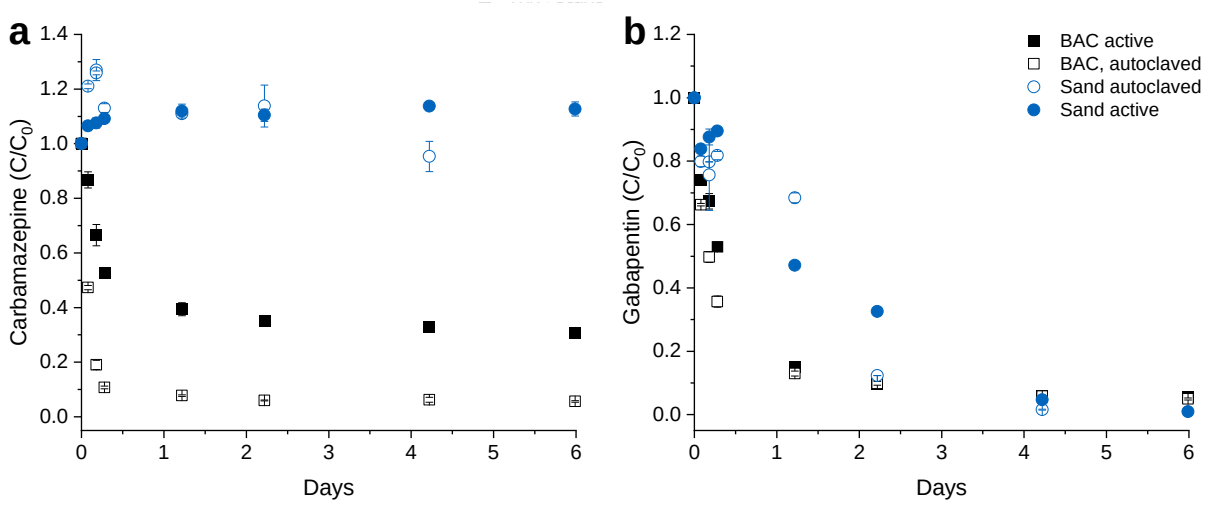

Figure 11-24: Comparison of autoclaved (empty squares) versus active (filled squares) breakthrough for carbamazepine (a) and gabapentin (b) in batch experiments with sand (blue) and BAC (black) filter material.

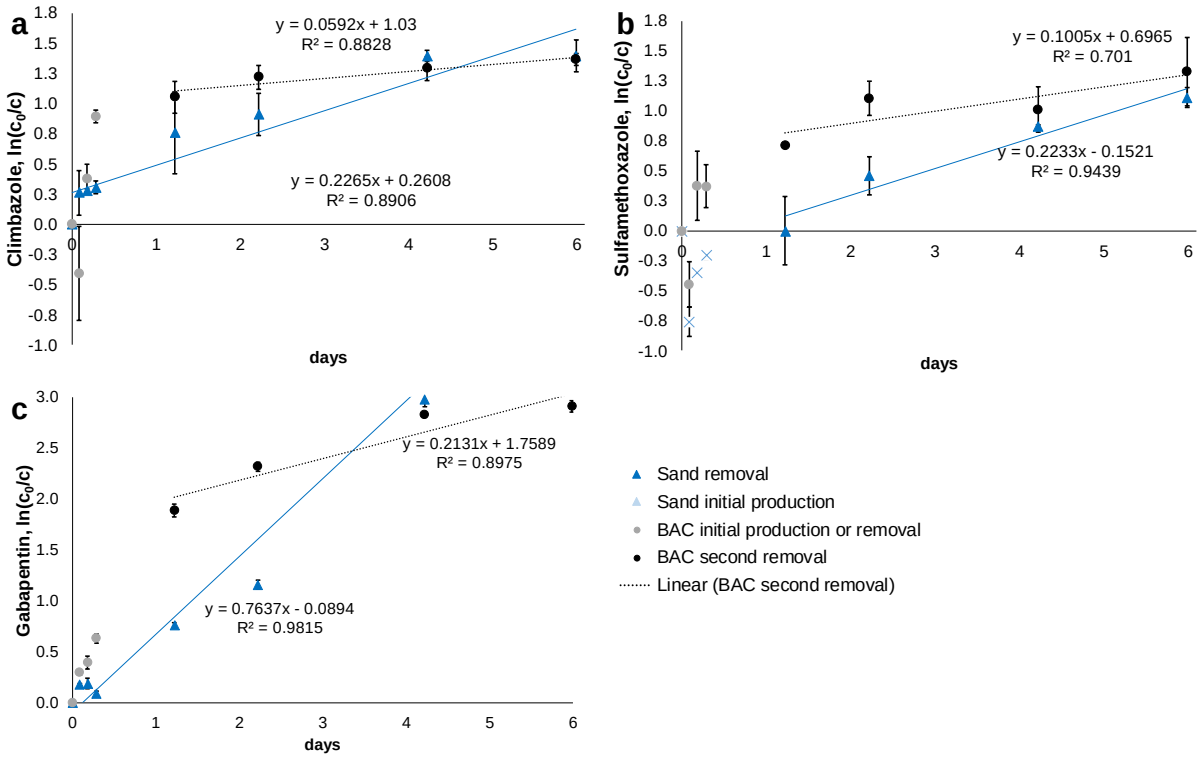

Figure 11-25: Exemplary removal calculations for climbazole (a), sulfamethoxazole (b) and gabapentin (c). The breakthrough of the compounds at the end of 29 hours in BAC was calculated by taking the inverse of e raised to the y intercept value.

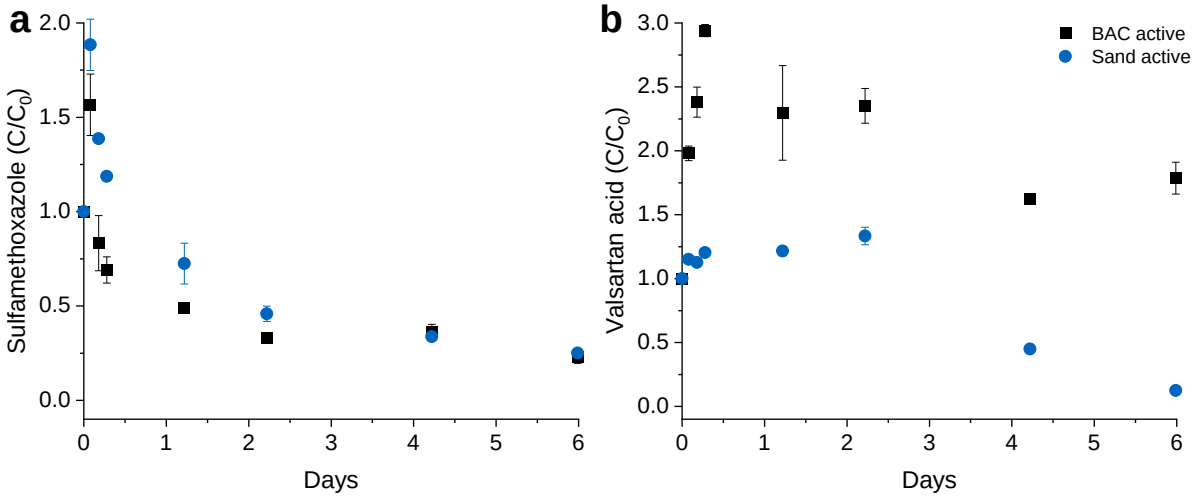

Figure 11-26: Normalized sulfamethoxazole (a) and valsartan acid (b) breakthrough during the batch experiment.

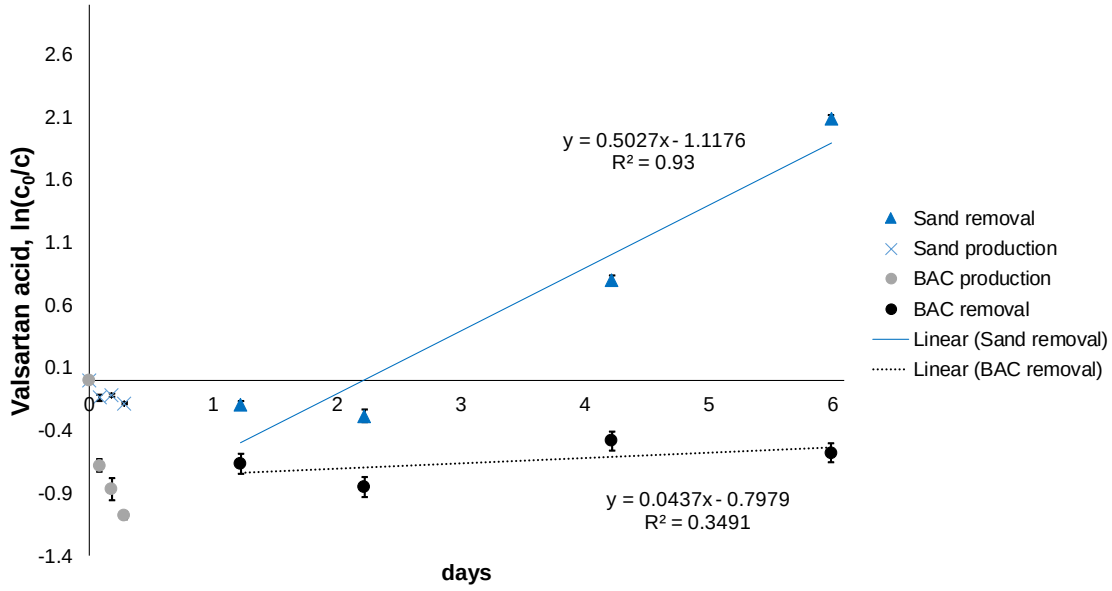

Figure 11-27: Valsartan acid removal rate calculation.

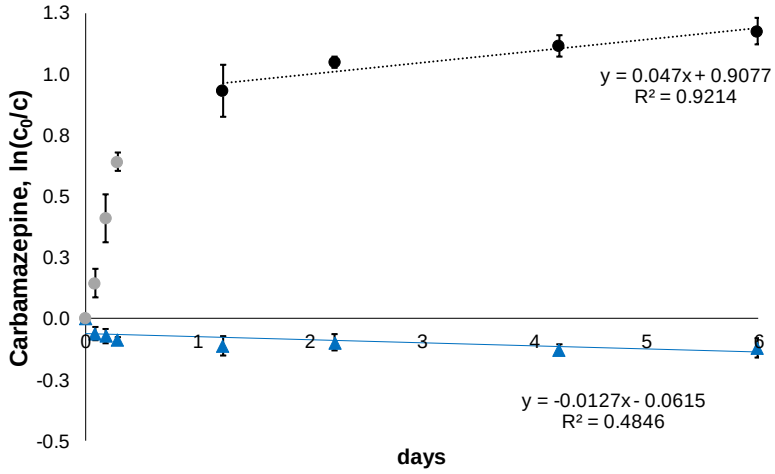

Figure 11-28: Carbamazepine removal rate calculation

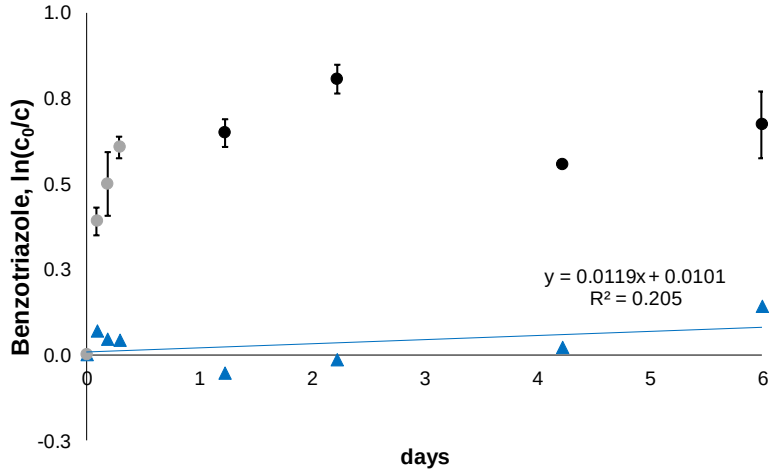

Figure 11-29: Benzotriazole removal rate calculation

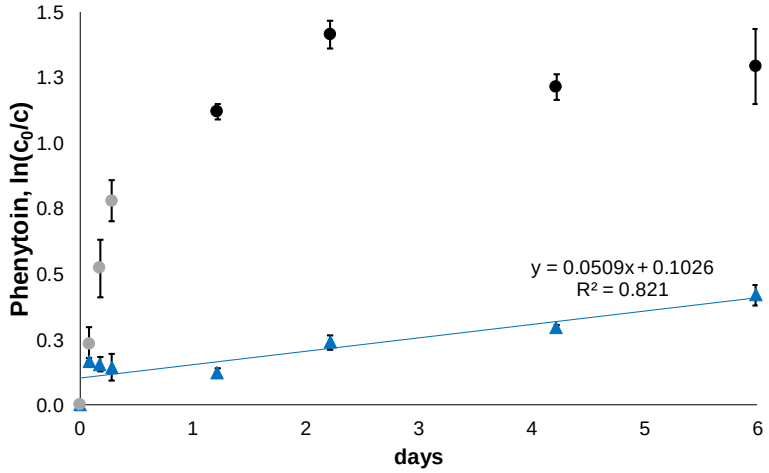

Figure 11-30: Phenytoin removal rate calculation

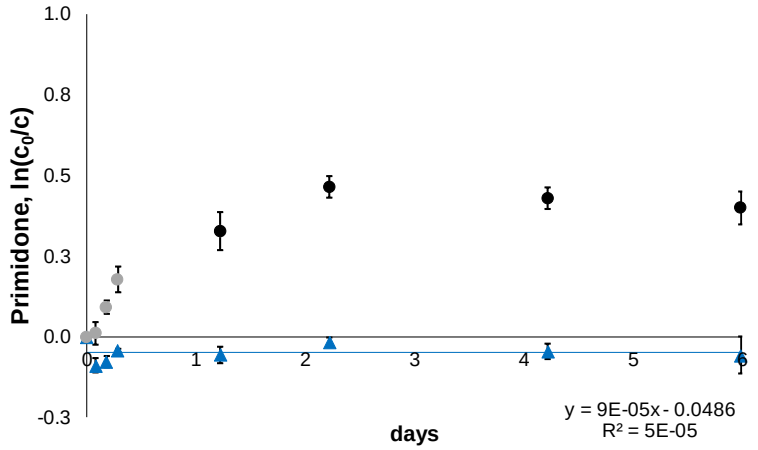

Figure 11-31: Primidone removal rate calculation

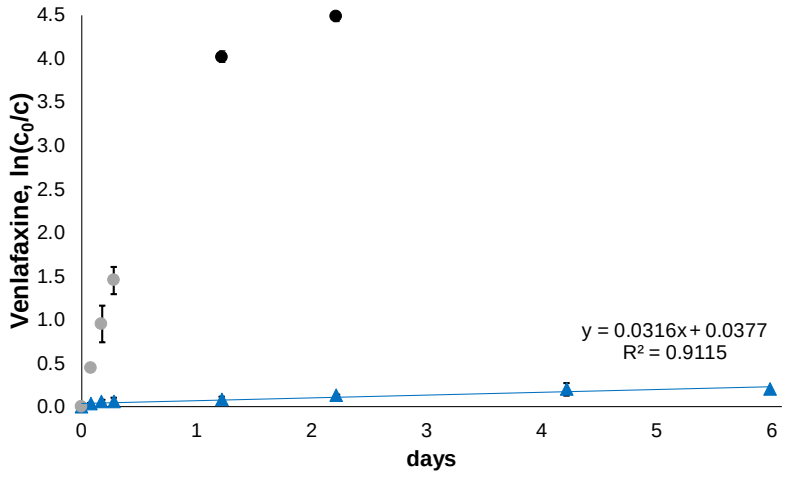

Figure 11-32: Venlafaxine removal rate calculation

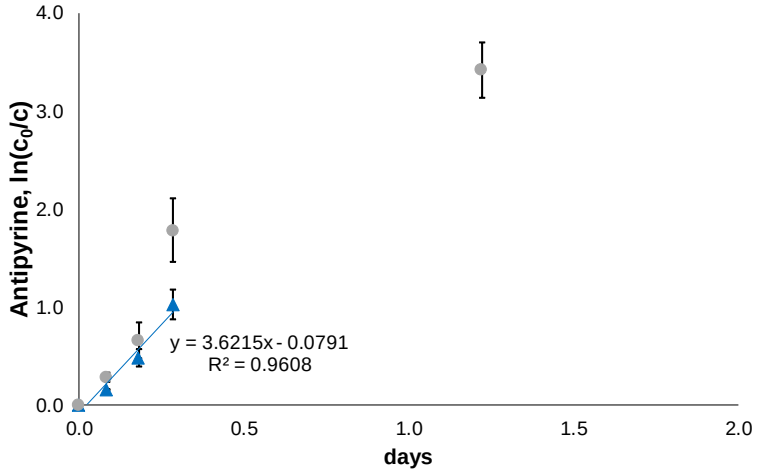

Figure 11-33: Antipyrine removal rate calculation

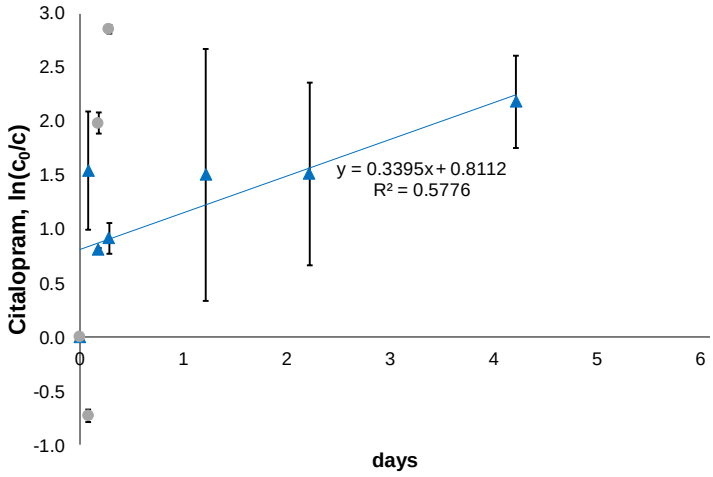

Figure 11-34: Citalopram removal rate calculation

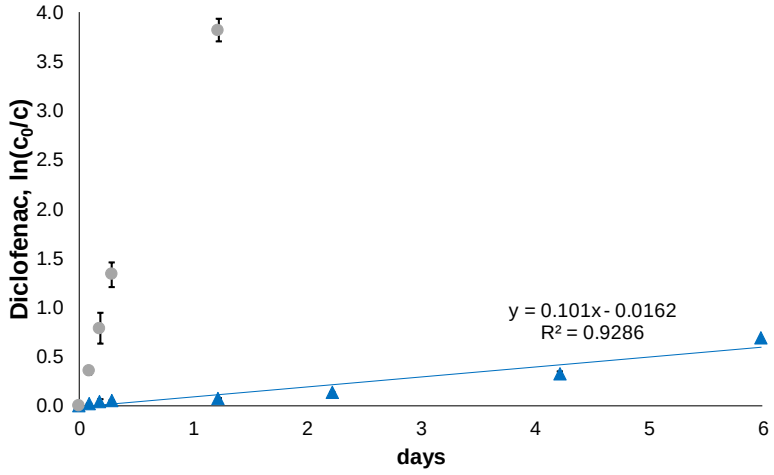

Figure 11-35: Diclofenac removal rate calculation

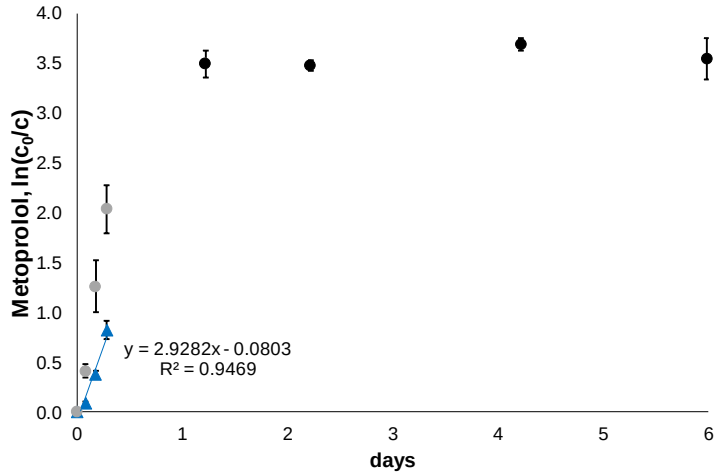

Figure 11-36: Metoprolol removal rate calculation

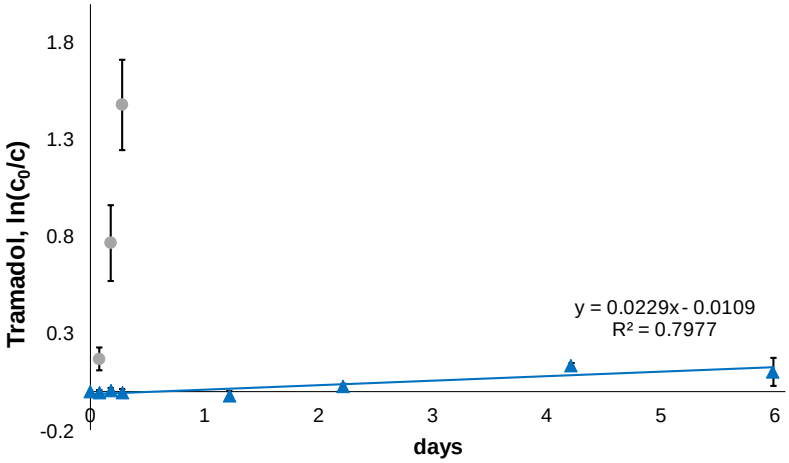

Figure 11-37: Tramadol removal rate calculation

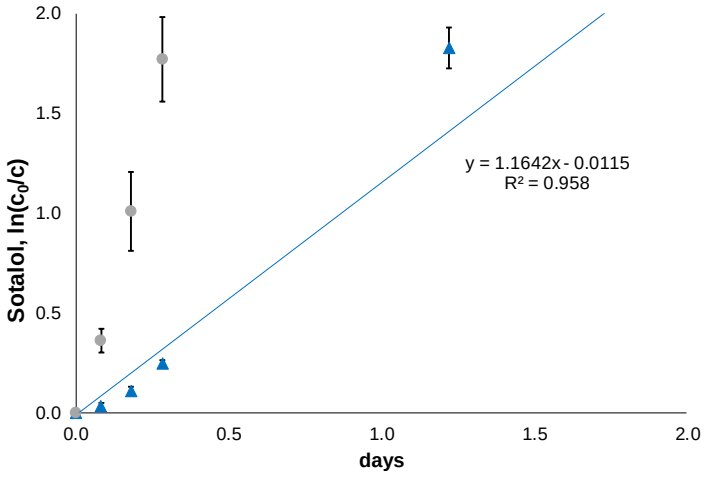

Figure 11-38: Sotalol removal rate calculation

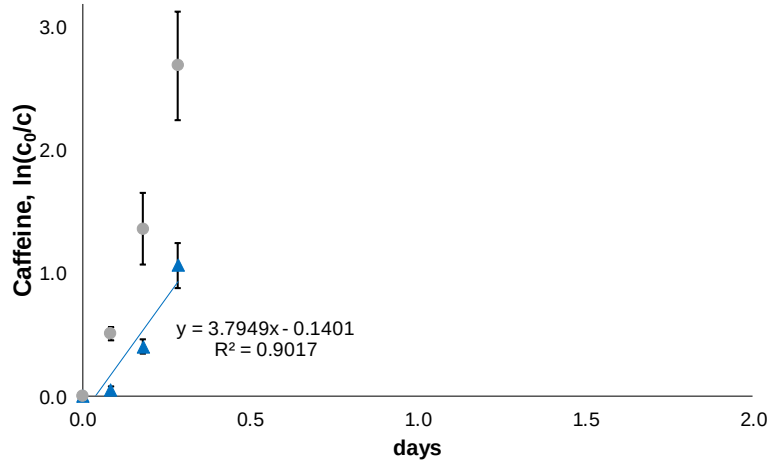

Figure 11-39: Caffeine removal rate calculation

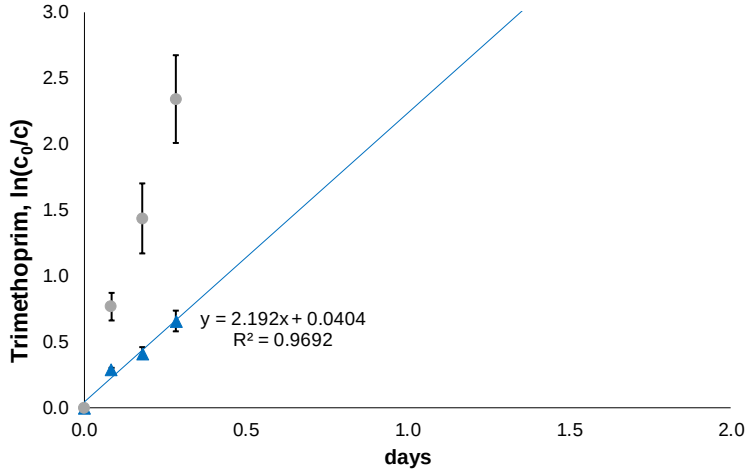

Figure 11-40: Trimethoprim removal rate calculation

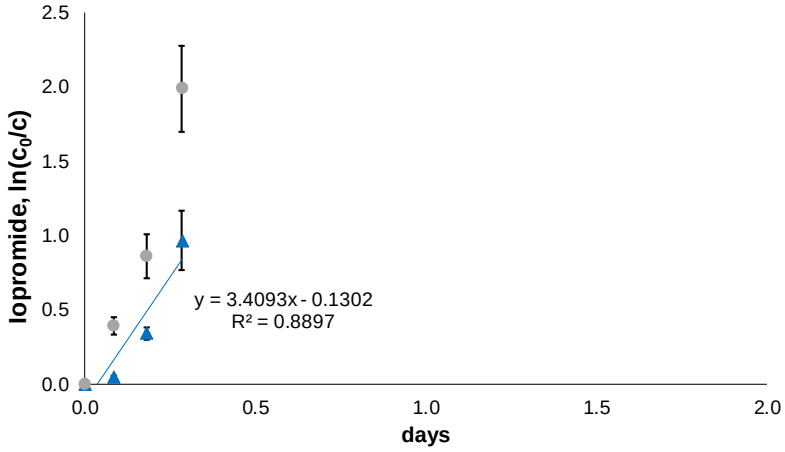

Figure 11-41: Iopromide removal rate calculation

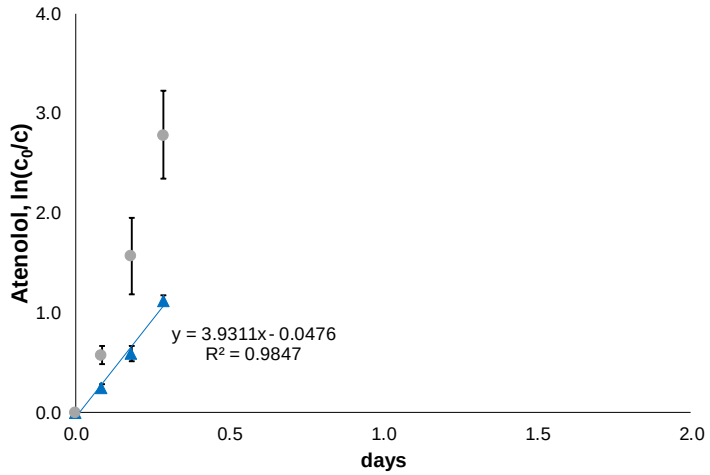

Figure 11-42: Atenolol removal rate calculation

11.7 Supplementary information for Chapter 10

In order to analyze ATP without separating biomass from the media, both the BAC and technical sand samples were prepared according to the methods described in Velten et al. (2007), with some alterations discussed in the following section. To construct a calibration curve, 100 mg wet weight of autoclaved BAC and sand media were placed into 2 mL Eppendorf tubes. Samples were washed once with 1 mL of phosphate buffer solution (PBS) to remove floating biomass from the liquid. 100 µL of an ATP solution was added to each prepared sample, ranging in concentration from 0.0065 µM to 1 µM, as well as 300 µL of Bac-Titer Glo (BTG) reagent. BTG is proprietary cell lysis buffer with luciferase and luciferin reagents which facilitates a luminescence measurement, measured in relative light units (RLU) which can be converted to ATP amounts (Promega Corporation, 2008). Last, 200 µL of the supernatant BTG solution were added to an opaque-walled 96-well plate and measured on the plate reader. The resulting calibration curve, when the 1 µM measurement was omitted, fit well for both sand and BAC (both r^2 = 0.99).

The preparation of samples was conducted differently than in Velten et al. (2007). First, 200 mg wet weight of each thawed sample were weighed into sterile 2 mL Eppendorf tubes, and washed once with 100 µL of phosphate buffer solution (PBS) to remove floating particles which could impact the luminescence measurement. Next, 300 µL of the BacTiter-Glo reagent were added to each Eppendorf tube, which was shaken to ensure optimal contact between the media and the reagent, which. Last, 200 µL of supernatant were transferred to the opaque-walled 96-well plate and measured on the luminometer.

Although reaction time and incubation temperature are the most critical parameters for luminescence measurements (Velten et al., 2007; Hammes et al., 2010), each sample was prepared individually and pipetted individually, therefore the reaction time could not be maintained for each sample. However, the temperature could be maintained, as the plate reader would shake the plates for 10 s at 500 rpm, and then incubate the plate at 27°C. All measurements were conducted with biological duplicates, due to limited media availability from the columns. Blank samples were prepared with the same media, which had been autoclaved to inactivate biological activity, except MilliQ water was added instead of PBS, as there was no biological material on the blank samples.

When preparing a standard curve for media with attached biomass, inactivating the biomass in a water bath as was done in Velten et al. (2007), or via an alternate method, instead of autoclaving, is recommended. Since autoclaving enhanced the residual adsorption capability of BAC as described in section 9.3.3, this could have resulted in adsorption of reagent onto the BAC and consequently a false ATP reading for BAC. Conducting analysis in triplicate is highly recommended. As ATP analysis preparation for liquid samples is relatively straightforward, a similar SOP should be drawn up for quantification of biomass attached to non-adsorptive and adsorptive media.

12.Literature

Achermann, S., Bianco, V., Mansfeldt, C.B., Vogler, B., Kolvenbach, B.A., Corvini, P.F.X., Fenner, K., 2018. Biotransformation of Sulfonamide Antibiotics in Activated Sludge: The Formation of Pterin-Conjugates Leads to Sustained Risk. Environ. Sci. Technol. 52. https://doi.org/10.1021/acs.est.7b06716

Agerstrand, M., Berg, C., Björlenius, B., Breitholtz, M., Brunström, B., Fick, J., Gunnarsson, L., Larsson, D.J., Sumpter, J.P., Tysklind, M., Ruden, C., 2015. Improving Environmental Risk Assessment of Human Pharmaceuticals. Environ. Sci. Policy. https://doi.org/10.1021/acs.est.5b00302

Agulló-Barceló, M., Casas-Mangas, R., Lucena, F., 2012. Direct and indirect QMRA of infectious cryptosporidium oocysts in reclaimed water. J. Water Health 10, 539–548. https://doi.org/10.2166/wh.2012.082

Aktas, O., Cecen, F., 2007. Bioregeneration of activated carbon : A review. Int. Biodeterior. Biodegradation. https://doi.org/10.1016/j.ibiod.2007.01.003

Alidina, M., Li, D., Drewes, J.E., 2014a. Investigating the role for adaptation of the microbial community to transform trace organic chemicals during managed aquifer recharge. Water Res. 56, 172–180. https://doi.org/10.1016/j.watres.2014.02.046

Alidina, M., Li, D., Ouf, M., Drewes, J.E., 2014b. Role of primary substrate composition and concentration on attenuation of trace organic chemicals in managed aquifer recharge systems. J. Environ. Manage. 144, 58–66. https://doi.org/10.1016/j.jenvman.2014.04.032

Alidina, M., Shewchuk, J., Drewes, J.E., 2015. Effect of temperature on removal of trace organic chemicals in managed aquifer recharge systems. Chemosphere 122, 23–31. https://doi.org/10.1016/j.chemosphere.2014.10.064

Altmann, J., Rehfeld, D., Träder, K., Sperlich, A., Jekel, M., Altmann, J., Rehfeld, D., Tr, K., 2016. Combination of granular activated carbon adsorption and deep-bed filtration as a single advanced wastewater treatment step for organic micropollutant and phosphorus removal. Water Res. 92, 131–139. https://doi.org/10.1016/j.watres.2016.01.051

Altmann, J., Zietzschmann, F., Geiling, E.-L., Ruhl, A.S., Sperlich, A., Jekel, M., 2015. Impacts of coagulation on the adsorption of organic micropollutants onto powdered activated carbon in treated domestic wastewater. Chemosphere 125. https://doi.org/10.1016/j.chemosphere.2014.12.061

Alvarino, T., Lema, J., Omil, F., Suárez, S., 2018. Trends in organic micropollutants removal in secondary treatment of sewage. Rev. Environ. Sci. Biotechnol. 17, 447–469. https://doi.org/10.1007/s11157-018-9472-3

Alygizakis, N.A., Urík, J., Beretsou, V.G., Kampouris, I., Galani, A., Oswaldova, M., Berendonk, T., Oswald, P., Thomaidis, N., Slobodnik, J., Vrana, B., Fatta-Kassinos, D., 2020. Evaluation of chemical and biological contaminants of emerging concern in treated wastewater intended for agricultural reuse. Environ. Int. 138. https://doi.org/10.1016/j.envint.2020.105597

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Gerrity, D., 2019a. Equivalency of Indirect and Direct Potable Reuse Paradigms based on a Quantitative Microbial Risk Assessment Framework. Microb. Risk Anal. https://doi.org/10.1016/j.mran.2019.06.003

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Gerrity, D., 2019b. A dynamic quantitative microbial risk assessment for norovirus in potable reuse systems. Microb. Risk Anal. https://doi.org/10.1016/j.mran.2019.100088

Amoueyan, E., Ahmad, S., Eisenberg, J.N.S., Pecson, B., Gerrity, D., 2017. Quantifying pathogen risks associated with potable reuse: A risk assessment case study for Cryptosporidium. Water Res. 119, 252–266. https://doi.org/10.1016/j.watres.2017.04.048

Ander, H., Forss, M., 2011. Microbiological Risk Assessment of the Water Reclamation Plant in Windhoek, Namibia. Chalmers University of Technology.

Anumol, T., Sgroi, M., Park, M., Roccaro, P., Snyder, S.A., 2015. Predicting trace organic compound breakthrough in granular activated carbon using fluorescence and UV absorbance as surrogates. Water Res. 76, 76–87. https://doi.org/10.1016/j.watres.2015.02.019

AquaNES, 2016a. AquaNES QMRA Tool [WWW Document]. URL http://dss.aquanes.eu/Default.aspx?t=1743&ToolID=23 (accessed 6.9.20).

AquaNES, 2016b. QCRA Tool [WWW Document]. URL http://dss.aquanes.eu/Default.aspx?t=1743&ToolID=21 (accessed 6.22.20).

Aschermann, G., Zietzschmann, F., Jekel, M., 2018. Influence of dissolved organic matter and activated carbon pore characteristics on organic micropollutant desorption. Water Res. 133, 123–131. https://doi.org/10.1016/j.watres.2018.01.015

Åström, J., Petterson, S., Bergstedt, O., Pettersson, T.J.R., Stenström, T.A., 2007. Evaluation of the microbial risk reduction due to selective closure of the raw water intake before drinking water treatment closure of the raw water intake before drinking water. J. Water Health. https://doi.org/10.2166/wh.2007.139

aus der Beek, T., Weber, F.-A., Bergmann, A., Grüttner, G., Carius, A., 2016. Pharmaceuticals in the environment: Global occurrence and potential cooperative action under the Strategic Approach to International Chemicals Management (SAICM).

Aymerich, I., Acuña, V., Barceló, D., García, M.J., Petrovic, M., Poch, M., Sabater, S., Rodriguez-Mozaz, S., Rodriguez-Roda, I., von Schiller, D., Corominas, L., 2016. Attenuation of pharmaceuticals and their transformation products in a wastewater treatment plant and its receiving river ecosystem. Water Res. https://doi.org/10.1016/j.watres.2016.04.022

Ayuso-Gabella, N., Page, D., Masciopinto, C., Aharoni, A., Salgot, M., Wintgens, T., 2011. Quantifying the effect of Managed Aquifer Recharge on the microbiological human health risks of irrigating crops with recycled water. Agric. Water Manag. 99, 93–102. https://doi.org/10.1016/j.agwat.2011.07.014

Baken, K.A., Sjerps, R.M.A., Schriks, M., Wezel, A.P. Van, 2018. Toxicological risk assessment and prioritization of drinking water relevant contaminants of emerging concern. Environ. Int. 118, 293–303. https://doi.org/10.1016/j.envint.2018.05.006

Baker, S., Herrman, T., 2002. Evaluating Particle Size, Kansas State University.

Barker-Reid, F., Harper, G.A., Hamilton, A.J., 2010. Affluent effluent: growing vegetables with wastewater in Melbourne , Australia — a wealthy but bone-dry city. Irrig. Drain. Syst. 79–94. https://doi.org/10.1007/s10795-009-9082-x

Barker, S.F., 2013. Risk of norovirus gastroenteritis from consumption of vegetables irrigated with highly treated municipal wastewater-evaluation of methods to estimate sewage quality. Risk Anal. 34, 803–817. https://doi.org/10.1111/risa.12138

Barker, S.F., Amoah, P., Drechsel, P., 2014. A probabilistic model of gastroenteritis risks associated with consumption of street food salads in Kumasi, Ghana: Evaluation of methods to estimate pathogen

dose from water , produce or food quality. Sci. Total Environ. 487, 130–142. https://doi.org/10.1016/j.scitotenv.2014.03.108

Barker, S.F., Packer, M., Scales, P.J., Gray, S., Snape, I., Hamilton, A.J., 2013. Pathogen reduction requirements for direct potable reuse in Antarctica : Evaluating human health risks in small communities. Sci. Total Environ. 461–462, 723–733. https://doi.org/10.1016/j.scitotenv.2013.05.059

Bartak, R., Page, D., Sandhu, C., Grischek, T., Saini, B., Mehrotra, I., Jain, C.K., Ghosh, N.C., 2015. Application of risk-based assessment and management to riverbank filtration sites in India. J. Water Health 13, 174–189. https://doi.org/10.2166/wh.2014.075

Bartam, J., Corrales, L., Davison, A., Deere, D., Drury, D., Gordon, B., Howard, G., Rinehold, A., Stevens, M., 2009. Water safety plan manual: step-by-step risk management for drinking-water suppliers. Geneva.

Baumgarten, B., Jährig, J., Reemtsma, T., Jekel, M., 2011. Long term laboratory column experiments to simulate bank filtration: Factors controlling removal of sulfamethoxazole. Water Res. 45, 211–220. https://doi.org/10.1016/j.watres.2010.08.034

Bayrisches Landesamt für Umwelt, 2020. STOFF-IDENT [WWW Document]. URL https://www.lfu.bayern.de/stoffident/#!home (accessed 6.11.20).

Beaudequin, D., Harden, F., Roiko, A., Mengersen, K., 2017. Potential of Bayesian networks for adaptive management in water recycling. Environ. Model. Softw. 91, 251–270. https://doi.org/10.1016/j.envsoft.2017.01.016

Beaudequin, D., Harden, F., Roiko, A., Mengersen, K., 2016. Utility of Bayesian networks in QMRA-based evaluation of risk reduction options for recycled water. Sci. Total Environ. 541, 1393–1409. https://doi.org/10.1016/j.scitotenv.2015.10.030

Beaudequin, D., Harden, F., Roiko, A., Stratton, H., Lemckert, C., Mengersen, K., 2015a. Beyond QMRA: Modelling microbial health risk as a complex system using Bayesian networks. Environ. Int. 80, 8–18. https://doi.org/10.1016/j.envint.2015.03.013

Beaudequin, D., Harden, F., Roiko, A., Stratton, H., Lemckert, C., Mengersen, K., 2015b. Modelling microbial health risk of wastewater reuse: A systems perspective. Environ. Int. 84, 131–141. https://doi.org/10.1016/j.envint.2015.08.001

Becker, J.G., Seagren, E.A., 2009. Modeling the effects of microbial competition and hydrodynamics on the dissolution and detoxification of dense nonaqueous phase liquid contaminants. Environ. Sci. Technol. 43, 870–877. https://doi.org/10.1021/es801616f

Bekele, E., Page, D., Gonzalez, D., 2018. Water Recycling via Aquifers for Sustainable Urban Water Quality Management: Current Status, Challenges and Opportunities. Water 1–25. https://doi.org/10.3390/w10040457

Benstoem, F., Nahrstedt, A., Boehler, M., Knopp, G., Montag, D., Siegrist, H., Pinnekamp, J., 2017. Performance of granular activated carbon to remove micropollutants from municipal wastewater—A meta-analysis of pilot- and large-scale studies. Chemosphere 185, 105–118. https://doi.org/10.1016/j.chemosphere.2017.06.118

Bergion, V., Lindhe, A., Sokolova, E., Ros, L., 2018. Risk-based cost-benefit analysis for evaluating microbial risk mitigation in a drinking water system. Water Res. 132. https://doi.org/10.1016/j.watres.2017.12.054

Bergion, V., Lindhe, A., Sokolova, E., Rosén, L., 2020. Accounting for Unexpected Risk Events in Drinking Water Systems. Expo. Heal. https://doi.org/10.1007/s12403-020-00359-4

Bertelkamp, C., Reungoat, J., Cornelissen, E.R., Singhal, N., Reynisson, J., Cabo, A.J., van der Hoek, J.P., Verliefde, A.R.D., 2014. Sorption and biodegradation of organic micropollutants during river bank filtration: A laboratory column study. Water Res. 52, 231–241. https://doi.org/10.1016/j.watres.2013.10.068

Biel-Maeso, M., González-González, C., Lara-Martín, P.A., CoradaFfernández, C., 2019. Sorption and degradation of contaminants of emerging concern in soils under aerobic and anaerobic conditions. Sci. Total Environ. 666, 662–671. https://doi.org/10.1016/j.scitotenv.2019.02.279

Blackbeard, J., Lloyd, J., Magyar, M., Mieog, J., Linden, K.G., Lester, Y., 2016. Demonstrating organic contaminant removal in an ozone-based water reuse process at full scale. Environ. Sci. Water Res. Technol. 2. https://doi.org/10.1039/c5ew00186b

Boehm, A.B., Graham, K.E., Jennings, W.C., 2018. Can We Swim Yet? Systematic Review, Meta-Analysis, and Risk Assessment of Aging Sewage in Surface Waters. Environ. Sci. Technol. 52, 9634–9645. https://doi.org/10.1021/acs.est.8b01948

Bourgin, M., Beck, B., Boehler, M., Borowska, E., Fleiner, J., Salhi, E., Teichler, R., Gunten, U. Von, Siegrist, H., McArdell, C.S., 2018. Evaluation of a full-scale wastewater treatment plant upgraded with ozonation and biological post-treatments : Abatement of micropollutants , formation of transformation products and oxidation. Water Res. 129, 486–498. https://doi.org/10.1016/j.watres.2017.10.036

Bradford, S.A., Harvey, R.W., 2017. Future research needs involving pathogens in groundwater. Hydrogeol. J. 931–938. https://doi.org/10.1007/s10040-016-1501-0

Brunner, A.M., Bertelkamp, C., Dingemans, M.M.L., Kolkman, A., Wols, B., Harmsen, D., Siegers, W., Martijn, B.J., Oorthuizen, W.A., ter Laak, Thomas, L., 2020. Integration of target analyses, non-target screening and effect-based monitoring to assess OMP related water quality changes in drinking water treatment. Sci. Total Environ. 705, 135779. https://doi.org/10.1016/j.scitotenv.2019.135779

Brunner, A.M., Dingemans, M.M.L., Baken, K.A., Wezel, A.P. Van, 2019. Prioritizing anthropogenic chemicals in drinking water and sources through combined use of mass spectrometry and ToxCast toxicity data. J. Hazard. Mater. 364, 332–338. https://doi.org/10.1016/j.jhazmat.2018.10.044

Burke, V., Greskowiak, J., Asmuß, T., Bremermann, R., Taute, T., Massmann, G., 2014. Temperature dependent redox zonation and attenuation of wastewater-derived organic micropollutants in the hyporheic zone. Sci. Total Environ. 482–483, 53–61. https://doi.org/10.1016/j.scitotenv.2014.02.098

CAMRA, 2020. QMRA Wiki [WWW Document]. URL http://qmrawiki.org/ (accessed 2.5.20).

Carter, M.C., Weber, W.J., 1994. Modeling Adsorption of TCE by Activated Carbon Preloaded by Background Organic Matter. Environ. Sci. Technol. 614–623. https://doi.org/10.1021/es00053a013

Castronovo, S., Wick, A., Scheurer, M., Nödler, K., Schulz, M., Ternes, T.A., 2017. Biodegradation of the arti fi cial sweetener acesulfame in biological wastewater treatment and sand fi lters. Water Res. 110, 342–353. https://doi.org/10.1016/j.watres.2016.11.041

CDPH, 2014. California Department of Public Health: Regulations Related to Recycled Water.

Çeçen, F., Aktaş, Ö., 2011. Activated Carbon for Water and Wastewater Treatment: Integration of Adsorption and Biological Treatment, First. ed. Wiley-VCH Verland & Co. KGaA, Weinheim.

CEPA, 2019. California Environmental Protection Agency: Water Quality Control Policy for Recycled Water. Sacramento, CA.

Chandrasekaran, S., Jiang, S.C., 2018. A dynamic transport model for quantification of norovirus internalization in lettuce from irrigation water and associated health risk. Sci. Total Environ. 643, 751–761. https://doi.org/10.1016/j.scitotenv.2018.06.158

Chaudhary, D.S., Vigneswaran, S., Ngo, H.-H., 2003. Biofilter in Water and Wastewater Treatment. Korean J. Chem. Eng. 20, 1054–1065.

Chaudhry, R.M., Hamilton, K.A., Haas, C.N., Nelson, K.L., 2017. Drivers of microbial risk for direct potable reuse and de facto reuse treatment schemes: The impacts of source water quality and blending. Int. J. Environ. Res. Public Health 14, 1–20. https://doi.org/10.3390/ijerph14060635

Chefetz, B., Mualem, T., Ben-Ari, J., 2008. Sorption and mobility of pharmaceutical compounds in soil irrigated with reclaimed wastewater. Chemosphere 73, 1335–1343. https://doi.org/10.1016/j.chemosphere.2008.06.070

Chhipi-Shrestha, G., Hewage, K., Sadiq, R., 2017. Microbial quality of reclaimed water for urban reuses: Probabilistic risk-based investigation and recommendations. Sci. Total Environ. 576, 738–751. https://doi.org/10.1016/j.scitotenv.2016.10.105

Chique, C., Hynds, P.D., Andrade, L., Burke, L., Morris, D., Ryan, M.P., Dwyer, J.O., 2020. Cryptosporidium spp . in groundwater supplies intended for human consumption - A descriptive review of global prevalence, risk factors and knowledge gaps. Water Res. 176, 115726. https://doi.org/10.1016/j.watres.2020.115726

Chowdhury, Z.K., Summers, R.S., Westerhoff, G.P., Leto, B.J., Nowack, K.O., Corwin, C.J., 2013. Activated Carbon: Solutions for Improving Water Quality, Activated Carbon: Solutions for Improving Water Quality. American Water Works Association. https://doi.org/10.1021/ed023p98

Christensen, F.M., 1998. Pharmaceuticals in the Environment — A Human Risk ? Regul. Toxicol. Pharmacol. 221, 212–221.

Collins, S.N., James, R.S., Ray, P., Chen, K., 2019. Climate change and freshwater ecosystems: Impacts on water quality and ecological status, HYDRO-CH2018 Project. Bern, Switzerland. https://doi.org/10.5772/49933

Compagni, R.D., Gabrielli, M., Polesel, F., Turolla, A., Vezzaro, L., Antonelli, M., 2019. Risk assessment of contaminants of emerging concern in the context of wastewater reuse for irrigation: An integrated modelling approach. ECSN 125185. https://doi.org/10.1016/j.chemosphere.2019.125185

Corwin, C.J., Summers, R.S., 2011. Adsorption and desorption of trace organic contaminants from granular activated carbon adsorbers after intermittent loading and throughout backwash cycles. Water Res. 45, 417–426. https://doi.org/10.1016/j.watres.2010.08.039

Corwin, C.J., Summers, R.S., 2010. Scaling trace organic contaminant adsorption capacity by granular activated carbon. Environ. Sci. Technol. 44, 5403–8. https://doi.org/10.1021/es9037462

Crittenden, J.C., Reddy, P.S., Arora, H., Trynoski, J., Hand, D.W., Perram, D.L., Summers, R.S., 1991. Predicting GAC Performance with Rapid Small-Scale Column Tests. J. Am. Water Works Assoc. 83. https://doi.org/https://doi.org/10.1002/j.1551-8833.1991.tb07088.x

Crittenden, J.C., Trussell, R.R., Hand, D.W., Howe, K. j., Tchobanoglous, G., 2012. MWH's Water Treatment Principles and Design, Third. ed. John Wiley & Sons, Inc., Hoboken, New Jersey.

Cunningham, V.L., Binks, S.P., Olson, M.J., 2009. Human health risk assessment from the presence of human pharmaceuticals in the aquatic environment. Regul. Toxicol. Pharmacol. 53, 39–45. https://doi.org/10.1016/j.yrtph.2008.10.006

de Vera, G.A., Lauderdale, C., Alito, C.L., Hooper, J., Wert, E.C., 2019. Using upstream oxidants to minimize surface biofouling and improve hydraulic performance in GAC bio fi lters. Water Res. 148, 526–534. https://doi.org/10.1016/j.watres.2018.10.085

de Vera, G.A., Wert, E.C., 2019. Using discrete and online ATP measurements to evaluate regrowth potential following ozonation and (non) biological drinking water treatment. Water Res. 154, 377–386. https://doi.org/10.1016/j.watres.2019.02.006

Delgado, N., Capparelli, A., Navarro, A., Marino, D., 2019. Pharmaceutical emerging pollutants removal from water using powdered activated carbon: Study of kinetics and adsorption equilibrium. J. Environ. Manage. 236, 301–308. https://doi.org/10.1016/j.jenvman.2019.01.116

Dewettinck, T., Van Houtte, E., Geenens, D., Van Hege, K., Verstraete, W., 2001. HACCP (Hazard Analysis and Critical Control Points) to guarantee safe water reuse and drinking water production - A case study. Water Sci. Technol. 43, 31–38. https://doi.org/10.2166/wst.2001.0708

Dias, E.H.O., 2016. Bacteriophages as surrogates of viral pathogens in wastewater treatment processes. University of Brighton.

Dillon, P., Stuyfzand, P., Grischek, T., Lluria, M., Pyne, R.D.G., Jain, R.C., Bear, J., Schwarz, J., Wang, W., 2019. Sixty years of global progress in managed aquifer recharge. Hydrogeol. J. 27, 1–30. https://doi.org/10.1007/s10040-018-1841-z

Dingemans, M.M.L., Smeets, P.W.M.H., Medema, G., Frijns, J., 2020. Responsible Water Reuse Needs an Interdisciplinary Approach to Balance Risks and Benefits 1–13. https://doi.org/10.3390/w12051264

Donn, M., Reed, D., Vanderzalm, J., Page, D., 2020. Assessment of E. coli Attenuation during Infiltration of Treated Wastewater: A Pathway to Future Managed Aquifer Recharge. Water 1–17. https://doi.org/10.3390/w12010173

dos Santos, P.R., Daniel, L.A., 2019. A review: organic matter and ammonia removal by biological activated carbon filtration for water and wastewater treatment. Int. J. Environ. Sci. Technol. https://doi.org/10.1007/s13762-019-02567-1

Drakvik, E., Altenburger, R., Aoki, Y., Backhaus, T., Bahadori, T., Barouki, R., Brack, W., Cronin, M.T.D., Demeneix, B., Bennekou, S.H., Klaveren, J. van, Kneuer, C., Kolossa-Gehring, M., Lebret, E., Posthuma, L., Reiber, L., Rider, C., Rüegg, J., Testa, G., Burg, B. van der, Voet, H. van der, Warhurst, A.M., Water, B. van de, Yamazaki, K., Öberg, M., Bergman, Åke, 2020. Statement on advancing the assessment of chemical mixtures and their risks for human health and the environment. Environ. Int. 134. https://doi.org/10.1016/j.envint.2019.105267

Drewes, J.E., Anderson, P., Denslow, N., Jakubowski, W., Olivieri, A., Schlenk, D., Snyder, S., 2018. Monitoring Strategies for Constituents of Emerging Concern (CECs) in Recycled Water. Recommendations of a science advisory panel. SCCWRP Technical Report 1032.

Drewes, J.E., Anderson, P., Denslow, N., Olivieri, A., Schlenk, D., Snyder, S.A., Maruya, K.A., 2013. Designing monitoring programs for chemicals of emerging concern in potable reuse - What to include and what not to include? Water Sci. Technol. 67, 433–439. https://doi.org/10.2166/wst.2012.520

Drewes, J.E., Regnery, J., Dickenson, E., Gerba, C.P., Snyder, S.A., Missimer, T., 2015. Role of Retention Time in the Environmental Buffer of Indirect Potable Reuse Projects: An Investigation on Managed Aquifer Recharge.

Drewes, J.E., Reinhard, M., Fox, P., 2003. Comparing microfiltration-reverse osmosis and soil-aquifer treatment for indirect potable reuse of water. Water Res. 37, 3612–3621. https://doi.org/10.1016/S0043-1354(03)00230-6

EASAC, 2019. The imperative of climate action to protect human health in Europe.

Eawag, 2017. EAWAG-BBD/PPS [WWW Document]. URL http://eawag-bbd.ethz.ch/predict/ (accessed 6.11.20).

Eggen, R.I.L., Hollender, J., Joss, A., Schärer, M., Stamm, C., 2014. Reducing the Discharge of Micropollutants in the Aquatic Environment: The Benefits of Upgrading Wastewater Treatment Plants. Environ. Sci. Technol. 48, 7683–7689. https://doi.org/dx.doi.org/10.1021/es500907n

Elliott, J.G., Taylor-Edmonds, L., Andrews, R.C., 2019. Quantitative microbial risk assessments for drinking water facilities: evaluation of a range of treatment strategies. Environ. Sci. Water Res. Technol. https://doi.org/10.1039/C9EW00348G

Emelko, M.B., Huck, P.M., Coffey, B.M., Smith, E.F., 2006. Effects of media, backwash, and temperature on full-scale biological filtration. J. Am. Water Works Assoc. 61–73. https://doi.org/10.1002/j.1551-8833.2006.tb07824.x

Emelko, M.B., Schmidt, P.J., Borchardt, M.A., 2019. Confirming the need for virus disinfection in municipal subsurface drinking water supplies. Water Res. 157, 356–364. https://doi.org/10.1016/j.watres.2019.03.057

EU Commission, 2003. Technical Guidance Document on Risk Assessment TGD Part II in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances Directive 98/8/EC of th.

EU Parliament, 2020. Regulation (EU) 2020/741 of the European Parliament and of the Council of 25 May 2020 on minimum requirements for water reuse. EU Parliament.

European Commission, 2019. European Union Strategic Approach to Pharmaceuticals in the Environment.

European Medicines Agency, 2006. Guideline on the environmental risk assessment of medicinal products for human use.

Falas, P., Baillon-Dhumez, A., Andersen, H.R., Ledin, A., Jansen, J., 2012. Suspended biofilm carrier and activated sludge removal of acidic pharmaceuticals. Water Res. 6. https://doi.org/10.1016/j.watres.2011.12.003

Fan, L.-S., Zhu, C., 1998. Principles of Gas-Solid Flows. Cambridge University Press.

Ferrer, A., Nguyen-viet, H., Zinsstag, J., 2012. Quantification of Diarrhea Risk Related to Wastewater Contact in Thailand Quantification of Diarrhea Risk Related to Wastewater Contact in Thailand. Ecohealth. https://doi.org/10.1007/s10393-012-0746-x

Fischer, A., Bronders, J., Desmet, N., Christoffels, E., Wezel, A. Van, Peter, J., Hoek, V. Der, 2017. Decision support for water quality management of contaminants of emerging concern. J. Environ. Manage. 193, 360–372. https://doi.org/10.1016/j.jenvman.2017.02.002

Fischer, A., Wezel, A.P. Van, Hollender, J., Cornelissen, E., Hofman, R., Peter, J., Hoek, V. Der, 2019. Development and application of relevance and reliability criteria for water treatment removal efficiencies of chemicals of emerging concern. Water Res. 161, 274–287. https://doi.org/10.1016/j.watres.2019.05.088

Fonseca, A.C., Summers, R.S., Hernandez, M.T., 2001. Comparative Measurements of Microbial Activity in Drinking Water Biofilters. Water Res. 35, 3817–3824.

Fuzawa, M., Smith, R.L., Ku, K., Shisler, J.L., Feng, H., Juvik, J.A., Nguyen, T.H., 2019. Roles of Vegetable Surface Properties and Sanitizer Type on Annual Disease Burden of Rotavirus Illness by Consumption of Rotavirus-Contaminated Fresh Vegetables : A Quantitative Microbial Risk Assessment. Risk Anal. 1. https://doi.org/10.1111/risa.13426

Gagliano, E.; Sgroi, M.; Falciglia, P. P.; Vagliasindi, F. G. A.; Roccaro, P., Removal of poly- and perfluoroalkyl substances (PFAS) from water by adsorption: Role of PFAS chain length, effect of organic matter and challenges in adsorbent regeneration. Water Res 2020, 171, 115381.

Gauthier, H., Yargeau, V., Cooper, D.G., 2010. Biodegradation of pharmaceuticals by Rhodococcus rhodochrous and Aspergillus niger by co-metabolism. Sci. Total Environ. 408, 1701–1706. https://doi.org/10.1016/j.scitotenv.2009.12.012

Gerba, C.P., Betancourt, W.Q., 2019. Assessing the Occurrence of Waterborne Viruses in Reuse Systems: Analytical Limits and Needs. Pathogens 7, 1–12. https://doi.org/doi:10.3390/pathogens8030107

Gerba, C.P., Betancourt, W.Q., Kitajima, M., 2017. How much reduction of virus is needed for recycled water: A continuous changing need for assessment? Water Res. 108, 25–31. https://doi.org/10.1016/j.watres.2016.11.020

Gerba, C.P., Betancourt, W.Q., Kitajima, M., Rock, C.M., 2018. Reducing uncertainty in estimating virus reduction by advanced water treatment processes. Water Res. 133, 282–288. https://doi.org/10.1016/j.watres.2018.01.044

Gerrity, D., Arnold, M., Dickenson, E., Moser, D., Sackett, J.D., Wert, E.C., 2018. Microbial community characterization of ozone-biofiltration systems in drinking water and potable reuse applications. Water Res. 135, 207–219. https://doi.org/10.1016/j.watres.2018.02.023

Gerrity, D., Gamage, S., Holady, J.C., Mawhinney, D.B., Quiñones, O., Trenholm, R.A., Snyder, S.A., 2011. Pilot-scale evaluation of ozone and biological activated carbon for trace organic contaminant mitigation and disinfection. Water Res. 45, 2155–2165. https://doi.org/10.1016/j.watres.2010.12.031

Global Water Research Coalition, 2020. COVID-19 Virus.

Gnielinksi, V., 1978. Gleichungen zur Berechnung des Wärme- und Stoffaustausches in durschströmten Kugelschütungen bei mittleren und großen Peclet-Zahlen [Equations for estimating the heat and mass transfer in packed beds of spherical particles at medium and high Peclet number. Verfahrenstechnik 12, 363–366.

Golovko, O., Lundqvist, J., Örn, S., Ahrens, L., 2020. Assessing the cumulative pressure of micropollutants in Swedish wastewater effluents and recipient water systems using integrated toxicological and chemical methods.

Gonzales-Gustavson, E., Rusinol, M., Medema, G., Calvo, M., Girones, R., 2019. Quantitative risk assessment of norovirus and adenovirus for the use of reclaimed water to irrigate lettuce in Catalonia. Water Res. 153, 91–99. https://doi.org/10.1016/j.watres.2018.12.070

Government of the Netherlands, 2018. Reducing pharmaceutical residues in water: a chain approach.

Graham, M.R., Summers, R.S., Simpson, M.R., Macleod, B.W., 2000. Modeling equilibrium adsorption of 2-methylisoborneol and geosmin in natural waters. Water Res. 34. https://doi.org/https://doi.org/10.1016/S0043-1354(99)00390-5

Greenstein, K.E., Lew, J., Dickenson, E.R.V., Wert, E.C., 2018. Investigation of biotransformation, sorption, and desorption of multiple chemical contaminants in pilot-scale drinking water biofilters. Chemosphere 200, 248–256. https://doi.org/10.1016/j.chemosphere.2018.02.107

Greiner, M., Smid, J., Havelaar, A.H., Müller-graf, C., 2013. Graphical models and Bayesian domains in risk modelling: Application in microbiological risk assessment. Prev. Vet. Med. 110, 4–11. https://doi.org/10.1016/j.prevetmed.2013.02.008

Greskowiak, J., Hamann, E., Burke, V., Massmann, G., 2017. The uncertainty of biodegradation rate constants of emerging organic compounds in soil and groundwater – A compilation of literature values for 82 substances. Water Res. 126, 122–133. https://doi.org/10.1016/j.watres.2017.09.017

Grevatt, P., Gerrity, D., Pletl, J., Williamson, K., 2020. Environmental Surveillance of the Genetic Footprint of COVID-19 in Sewersheds. May 21, 2020.

Grundwasserverordnung, 2010.

Guillossou, R., Le Roux, J., Mailler, R., Vulliet, E., Morlay, C., Nauleau, F., Gasperi, J., Rocher, V., 2019. Organic micropollutants in a large wastewater treatment plant: What are the benefits of an advanced treatment by activated carbon adsorption in comparison to conventional treatment? Chemosphere 218, 1050–1060. https://doi.org/10.1016/j.chemosphere.2018.11.182

Guillossou, R., Roux, J. Le, Mailler, R., Pereira-Derome, C.S., Varrault, G., Bressy, A., Vulliet, E., Morlay, C., Nauleau, F., Rocher, V., Gasperi, J., 2020. Influence of dissolved organic matter on the removal of 12 organic micropollutants from wastewater effluent by powdered activated carbon adsorption. Water Res. https://doi.org/10.1016/j.watres.2020.115487

Haas, C.N., 1983. Estimation of Risk due to Low Doses of Microorganisms: A Comparison of Alternative Methodologies. Am. J. Epidemiol. 118, 573–582. https://doi.org/https://doi.org/10.1093/oxfordjournals.aje.a113662

Haas, C.N., Crockett, C.S., Rose, J.B., Gerba, C.P., Fazil, A.M., 1996. Assessing the risk posed by oocysts in drinking water. J. Am. Water Works Assoc. 88, 131–136.

Haas, C.N., Rose, J.B., Gerba, C.P., 2014. Quantitative Microbial Risk Assessment, Second. ed. John Wiley & Sons, Inc.

Haas, C.N., Trussell, R.R., 1998. Frameworks for Assessing Reliability of Multiple, Independent Barriers in Potable Water Reuse. Water Sci. Technol.

Hallé, C., Huck, P.M., Peldszus, S., 2015. Emerging Contaminant Removal by Biofiltration: Temperature, Concentration, and EBCT Impacts. J. Am. Water Works Assoc. https://doi.org/10.5942/jawwa.2015.107.0086

Hammes, F., Berney, M., Wang, Y., Vital, M., Köster, O., Egli, T., 2008. Flow-cytometric total bacterial cell counts as a descriptive microbiological parameter for drinking water treatment processes. Water Res. 42, 269–277. https://doi.org/10.1016/j.watres.2007.07.009

Hammes, F., Goldschmidt, F., Vital, M., Wang, Y., Egli, T., 2010. Measurement and interpretation of microbial adenosine tri-phosphate (ATP) in aquatic environments. Water Res. 44, 3915–3923. https://doi.org/10.1016/j.watres.2010.04.015

Harada, B.K., 2014. Comparative Evaluation of Six Different Activated Carbon for TCP Removal Using Rapid Small Scale Column Test. University of Hawai'i at Manoa.

Havelaar, A.H., 1994. Application of HACCP to drinking water supply. Food Control 5, 145–152. https://doi.org/10.1016/0956-7135(94)90074-4

Hayduk, W., Laudie, H., 1974. Prediction of diffusion coefficients for nonelectrolyte in dilute aqueous solutions. AIchE J. 20, 611–615. https://doi.org/https://doi.org/10.1002/aic.690200329

Heberer, T., 2002. Tracking persistent pharmaceutical residues from municipal sewage to drinking water. J. Hydrol. 266, 175–189. https://doi.org/10.1016/S0022-1694(02)00165-8

Hellauer, K., Karakurt, S., Sperlich, A., Burke, V., Massmann, G., Hübner, U., Drewes, J.E., 2018a. Establishing sequential managed aquifer recharge technology (SMART) for enhanced removal of trace organic chemicals: Experiences from field studies in Berlin, Germany. J. Hydrol. 563, 1161–1168. https://doi.org/10.1016/j.jhydrol.2017.09.044

Hellauer, K., Martínez Mayerlen, S., Drewes, J.E., Hübner, U., 2019. Biotransformation of trace organic chemicals in the presence of highly refractory dissolved organic carbon. Chemosphere 215, 33–39. https://doi.org/10.1016/j.chemosphere.2018.09.166

Hellauer, K., Mergel, D., Ruhl, A.S., Filter, J., Hübner, U., Jekel, M., Drewes, J.E., 2017. Advancing Sequential Managed Aquifer Recharge Technology (SMART) Using Different Intermediate Oxidation Processes. Water 1–14. https://doi.org/10.3390/w9030221

Hellauer, K., Uhl, J., Lucio, M., Schmitt-kopplin, P., Wibberg, D., Hu, U., Drewes, J.E., 2018b. Microbiome-Triggered Transformations of Trace Organic Chemicals in the Presence of Effluent Organic Matter in Managed Aquifer Recharge (MAR) Systems. Environ. Sci. Technol. 52. https://doi.org/10.1021/acs.est.8b04559

Hellmér, M., Paxéus, N., Magnius, L., Enache, L., Arnholm, B., Johansson, A., Bergström, T., 2014. Detection of Pathogenic Viruses in Sewage Provided Early Warnings of Hepatitis A Virus and Norovirus Outbreaks 80, 6771–6781. https://doi.org/10.1128/AEM.01981-14

Henning, N., Kunkel, U., Wick, A., Ternes, T.A., 2018. Biotransformation of gabapentin in surface water matrices under different redox conditions and the occurrence of one major TP in the aquatic environment. Water Res. https://doi.org/10.1016/j.watres.2018.01.027

Henzler, A.F., Greskowiak, J., Massmann, G., 2014. Modeling the fate of organic micropollutants during river bank. J. Contam. Hydrol. 156, 78–92. https://doi.org/10.1016/j.jconhyd.2013.10.005

Hermes, N., Jewell, K.S., Schulz, M., Müller, J., Hübner, U., Wick, A., Drewes, J.E., Ternes, T.A., 2019. Elucidation of removal processes in sequential biofiltration (SBF) and soil aquifer treatment (SAT) by analysis of a broad range of trace organic chemicals (TOrCs) and their transformation products (TPs). Water Res. 163, 114857. https://doi.org/10.1016/j.watres.2019.114857

Hochstrat, R., Peter, M., Wintgens, T., Kraus, F., Seis, W., Miehe, U., 2013. D 3.4: Water Reuse Safety Plans - a manual for practitioners.

Hockanson, D.R., Hand, D.W., Crittenden, J.C., 1999. Adsorption Design Software™ (AdDesignS™).

Hoppe-Jones, C., Dickenson, E.R. V, Drewes, J.E., 2012. The role of microbial adaptation and biodegradable dissolved organic carbon on the attenuation of trace organic chemicals during groundwater recharge. Sci. Total Environ. 437, 137–144. https://doi.org/10.1016/j.scitotenv.2012.08.009

Hu, J., Shang, R., Heijman, B., Rietveld, L., 2016. Influence of activated carbon preloading by EfOM fractions from treated wastewater on adsorption of pharmaceutically active compounds. Chemosphere 150, 49–56. https://doi.org/10.1016/j.chemosphere.2016.01.121

Hübner, U., Miehe, U., Jekel, M., 2012. Optimized removal of dissolved organic carbon and trace organic contaminants during combined ozonation and artificial groundwater recharge. Water Res. 46, 6059–6068. https://doi.org/http://dx.doi.org/10.1016/j.watres.2012.09.001

Hübner, U., Seiwert, B., Reemtsma, T., Jekel, M., 2014. Ozonation products of carbamazepine and their removal from secondary effluents by soil aquifer treatment – Indications from column experiments. Water Res. 49, 34–43. https://doi.org/http://dx.doi.org/10.1016/j.watres.2013.11.016

Hunt, R.J., Johnson, W.P., 2017. Pathogen transport in groundwater systems : contrasts with traditional solute transport. Hydrogeol. J. 25, 921–930. https://doi.org/10.1007/s10040-016-1502-z

Hynds, P.D., Thomas, M.K., Pintar, K.M.D., 2014. Contamination of Groundwater Systems in the US and Canada by Enteric Pathogens, 1990 – 2013: A Review and Pooled-Analysis. PLoS One 9. https://doi.org/10.1371/journal.pone.0093301

Imran, U., Khan, M., Jamal, R., Sahulka, S.Q., Goel, R., Mahar, R., Weidhaas, J., 2020. Probabilistic risk assessment of water distribution system in Hyderabad, Pakistan reveals unacceptable health hazards and areas for rehabilitation. Ecotoxicol. Environ. Saf. 191, 110233. https://doi.org/10.1016/j.ecoenv.2020.110233

ISO, 2018. ISO 20426: Guidelines for health risk assessment and management for non-potable water reuse.

Ito, T., Kitajima, M., Kato, T., Ishii, S., Segawa, T., Okabe, S., Sano, D., 2017. Target virus log10 reduction values determined for two reclaimed wastewater irrigation scenarios in Japan based on tolerable annual disease burden. Water Res. 125, 438–448. https://doi.org/10.1016/j.watres.2017.08.057

Jachner, S., Petzoldt, T., 2007. Statistical Methods for the Qualitative Assessment of Dynamic Models with Time Delay (R Package qualV). J. Stat. Softw. 22.

Jarvie, M.E.J., Hand, D.W., Bhuvendralingam, S., Crittenden, J.C., Hokanson, D.R., 2005. Simulating the performance of fixed-bed granular activated carbon adsorbers: Removal of synthetic organic chemicals in the presence of background organic matter. Water Res. https://doi.org/10.1016/j.watres.2005.04.023

Jeirani, Z., Niu, C.H., Soltan, J., 2017. Adsorption of emerging pollutants on activated carbon. Rev. Chem. Eng. 33, 491–522. https://doi.org/10.1515/revce-2016-0027

Jekel, M., Dott, W., Bergmann, A., Dünnbier, U., Gnirß, R., Haist-Gulde, B., Hamscher, G., Letzel, M., Licha, T., Lyko, S., Miehe, U., Sacher, F., Scheurer, M., Schmidt, C.K., Reemtsma, T., Sebastian, A., Ruhl, A.S., 2015. Selection of organic process and source indicator substances for the anthropogenically influenced water cycle. Chemosphere 125, 155–167. https://doi.org/10.1016/j.chemosphere.2014.12.025

Jekel, M., Ruhl, A.S., Meinel, F., Zietzschmann, F., Lima, S.P., Baur, N., Wenzel, M., Gnirß, R., Sperlich, A., Dünnbier, U., Böckelmann, U., Hummelt, D., Van Baar, P., Wode, F., Petersohn, D.,

Grummt, T., Eckhardt, A., Schulz, W., Heermann, A., Reemtsma, T., Seiwert, B., Schlittenbauer, L., Lesjean, B., Miehe, U., Remy, C., Stapf, M., Mutz, D., 2013. Anthropogenic organic micro-pollutants and pathogens in the urban water cycle: assessment, barriers and risk communication (ASKURIS). Environ. Sci. Eur. 25, 1–8. https://doi.org/10.1186/2190-4715-25-20

Jewell, K.S., Castronovo, S., Wick, A., Falås, P., Joss, A., Ternes, T.A., 2016a. New insights into the transformation of trimethoprim during biological wastewater treatment. Water Res. 88, 550–557. https://doi.org/10.1016/j.watres.2015.10.026

Jewell, K.S., Falås, P., Wick, A., Joss, A., Ternes, T.A., 2016b. Transformation of diclofenac in hybrid bio fi lm e activated sludge processes. Water Res. 105, 559–567. https://doi.org/10.1016/j.watres.2016.08.002

Johnson, A.C., Dumont, E., Williams, R.J., Oldenkamp, R., Cisowska, I., Sumpter, J.P., 2013. Do concentrations of ethinylestradiol , estradiol and diclofenac in European rivers exceed proposed EU environmental quality standards ? Environ. Sci. Technol.

Jones, O.A.H., Voulvoulis, N., Lester, J.N., 2004. Potential Ecological and Human Health Risks Associated With the Presence of Pharmaceutically Active Compounds in the Aquatic Environment ASSESSMENT OF DRUGS IN. Crit. Rev. Toxicol. 34, 335–350. https://doi.org/10.1080/10408440490464697

Karakurt-Fischer, S., Bein, E., Drewes, J.E., Hübner, U., 2020a. Characterizing a novel in-situ oxygen delivery device for establishing controlled redox zonation within a high infiltration rate sequential biofilter. Water Res. 182, 1–11. https://doi.org/10.1016/j.watres.2020.116039

Karakurt-Fischer, S., Sanz-Prat, A., Greskowiak, J., Ergh, M., Gerdes, H., Massmann, G., Ederer, J., Regnery, J., Hübner, U., Drewes, J.E., 2020b. Developing a novel biofiltration treatment system by coupling high-rate infiltration trench technology with a plug- flow porous-media bioreactor. Sci. Total Environ. 722, 137890. https://doi.org/10.1016/j.scitotenv.2020.137890

Karakurt-Fischer, S., Rien, C., Sanz-Prat, A., Szewzyk, R., Drewes, J.E., Hübner, U., Selinka, H.C., 2021. Fate and Transport of Viruses within a High Infiltration Rate Plug Flow Biofilter Designed for Non-Membrane Based Potable Reuse Applications. Re-submitted to ACS ES&T Water.

Karakurt, S., Schmid, L., Hübner, U., Drewes, J.E., 2019. Dynamics of Wastewater Effluent Contributions in Streams and Impacts on Drinking Water Supply via Riverbank Filtration in Germany - A National Reconnaissance. Environ. Sci. Technol. 53, 6154–6161. https://doi.org/10.1021/acs.est.8b07216

Karges, U., Ott, D., Boer, S. De, Püttmann, W., 2019. 1,4-Dioxane Contamination Of German Drinking Water Obtained By Managed Aquifer Recharge Systems: Distribution And Main Influencing Factors. Sci. Total Environ. 134783. https://doi.org/10.1016/j.scitotenv.2019.134783

Kennedy, A.M., Reinert, A.M., Knappe, D.R.U., Ferrer, I., Summers, R.S., 2015. Full- and pilot-scale GAC adsorption of organic micropollutants. Water Res. 68, 238–248. https://doi.org/10.1016/j.watres.2014.10.010

Kennedy, A.M., Reinert, A.M., Knappe, D.R.U., Summers, R.S., 2017. Prediction of Full-Scale GAC Adsorption of Organic Micropollutants. Environ. Eng. Sci. 00. https://doi.org/10.1089/ees.2016.0525

Khan, S.J., 2013. Drinking Water Through Recyling: The Benefits and Costs of Supplying Direct to the Distribution System. https://doi.org/10.1080/00139157.1973.9930695

Khan, S.J., 2010. Quantitative chemical exposure assessment for water recycling schemes, Waterlines report. Canberra, Australia. https://doi.org/978-1-921107-94-8

Khan, S.J., Fisher, R., Roser, D.J., 2018. Potable reuse: What chemicals to be concerned about. Curr. Opin. Environ. Sci. Heal. https://doi.org/10.1016/j.coesh.2018.12.002

Kjaerulff, U., Gaag, L.C. van der, 2000. Making Sensitivity Analysis Computationally Efficient, in: 16th Conference on Uncertainty in Artificial Intelligence Proceedings. San Francisco, California, pp. 317–325.

Knappe, D.R.U., Matsui, Y., Snoeyink, V.L., Roche, P., Prados, M.J., Bourbigot, M.-M., 1998. Predicting the Capacity of Powdered Activated Carbon for Trace Organic Compounds in Natural Waters. Environ. Sci. Technol. 32, 1694–1698. https://doi.org/https://doi.org/10.1021/es970833y

Lee, C.O., Howe, K.J., Thomson, B.M., 2012. Ozone and biofiltration as an alternative to reverse osmosis for removing PPCPs and micropollutants from treated wastewater. Water Res. 46, 1005–1014. https://doi.org/10.1016/j.watres.2011.11.069

Lee, Y., von Gunten, U., 2016. Advances in predicting organic contaminant abatement during ozonation of municipal wastewater effluent: reaction kinetics, transformation products, and changes of biological effects. Environ. Sci. Water Res. Technol. https://doi.org/10.1039/C6EW00025H

Lester, Y., Mamane, H., Zucker, I., Avisar, D., 2013. Treating wastewater from a pharmaceutical formulation facility by biological process and ozone. Water Res. 47, 4349–4356. https://doi.org/10.1016/j.watres.2013.04.059

Letzel, T., Bayer, A., Schulz, W., Heermann, A., Lucke, T., Greco, G., Grosse, S., Schüssler, W., Sengl, M., Letzel, M., 2015. LC–MS screening techniques for wastewater analysis and analytical data handling strategies : Sartans and their transformation products as an example. Chemosphere 137, 198–206. https://doi.org/10.1016/j.chemosphere.2015.06.083

Li, D., Alidina, M., Drewes, J.E., 2014. Role of primary substrate composition on microbial community structure and function and trace organic chemical attenuation in managed aquifer recharge systems. Appl. Microbiol. Biotechnol. 98, 5747–5756. https://doi.org/10.1007/s00253-014-5677-8

Li, D., Alidina, M., Ouf, M., Sharp, J.O., Saikaly, P., Drewes, J.E., 2013. Microbial community evolution during simulated managed aquifer recharge in response to different biodegradable dissolved organic carbon (BDOC) concentrations. Water Res. 47, 2421–2430. https://doi.org/10.1016/j.watres.2013.02.012

Li, D., Sharp, J.O., Saikaly, P.E., Ali, S., Alidina, M., Alarawi, M.S., Keller, S., Hoppe-Jones, C., Drewes, J.E., 2012. Dissolved organic carbon influences microbial community composition and diversity in managed aquifer recharge systems. Appl. Environ. Microbiol. 78, 6819–6828. https://doi.org/10.1128/AEM.01223-12

Li, Z., Dvorak, B., Li, X., 2012. Removing 17ß-estradiol from drinking water in a biologically active carbon (BAC) reactor modified from a granular activated carbon (GAC) reactor. Water Res. 46, 2828–2836. https://doi.org/10.1016/j.watres.2012.03.033

Lim, K.-Y., Wu, Y., Jiang, S.C., 2017. Assessment of Cryptosporidium and norovirus risk associated with de facto wastewater reuse in Trinity River, Texas. Microb. Risk Anal. 5, 15–24. https://doi.org/10.1016/j.mran.2016.11.002

Loos, R., Carvalho, R., Antonio, D.C., Comero, S., Locoro, G., Tavazzi, S., Paracchini, B., Ghiani, M., Lettieri, T., Blaha, L., Jarosova, B., Voorspoels, S., Servaes, K., Haglund, P., Fick, J., Lindberg, R.H.,

Schwesig, D., Gawlik, B.M., 2013. EU-wide monitoring survey on emerging polar organic contaminants in wastewater treatment plant effluents. Water Res. 7. https://doi.org/10.1016/j.watres.2013.08.024

Loos, R., Gawlik, B.M., Locoro, G., Rimaviciute, E., Contini, S., Bidoglio, G., 2015. EU-wide survey of polar organic persistent pollutants in European river waters. Environ. Pollut. 157, 561–568. https://doi.org/10.1016/j.envpol.2008.09.020

Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., Hai, F.I., Zhang, J., Liang, S., Wang, X.C., 2014. A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. Sci. Total Environ. 473–474, 619–641. https://doi.org/10.1016/j.scitotenv.2013.12.065

Ma, B., Arnold, W.A., Hozalski, R.M., 2018. The relative roles of sorption and biodegradation in the removal of contaminants of emerging concern (CECs) in GAC-sand biofilters. Water Res. https://doi.org/https://doi.org/10.1016/j.watres.2018.09.023

Ma, X.Y., Li, Q., Wang, X.C., Wang, Y., Wang, D., 2018. Micropollutants removal and health risk reduction in a water reclamation and ecological reuse system. Water Res. 138, 272–281. https://doi.org/10.1016/j.watres.2018.03.059

MacKenzie, W.R., Hoxie, N.J., Proctor, M.E., Gradus, M.S., Blair, K.A., Peterson, D.E., Kazmierczak, J.J., Addiss, D.G., Fox, K.R., Rose, J.B., Davis, J.P., 1994. A Massive Outbreak in Milwaukee of Cryptosporidium Infection Transmitted through the Public Water Supply. N. Engl. J. Med. 331. https://doi.org/10.1056/NEJM199407213310304

Maeng, S.K., Sharma, S.K., Abel, C.D.T., Magic-Knezev, A., Amy, G.L., 2011. Role of biodegradation in the removal of pharmaceutically active compounds with different bulk organic matter characteristics through managed aquifer recharge: Batch and column studies. Water Res. 45, 4722–4736. https://doi.org/10.1016/j.watres.2011.05.043

Mara, D., 2011. Water- and wastewater-related disease and infection risks: What is an appropriate value for the maximum tolerable additional burden of disease? J. Water Health 9, 217–224. https://doi.org/10.2166/wh.2010.109

Mara, D.D., Sleigh, P.A., Blumenthal, U.J., Carr, R., 2007. Health risks in wastewater irrigation: Comparing estimates from quantitative microbial risk analyses and epidemiological studies. J. Water Health 5, 39–50. https://doi.org/10.2166/wh.2006.055

Martínez-Hernández, V., Meffe, R., Herrera López, S., de Bustamante, I., 2016. The role of sorption and biodegradation in the removal of acetaminophen, carbamazepine, caffeine, naproxen and sulfamethoxazole during soil contact: A kinetics study. Sci. Total Environ. 559, 232–241. https://doi.org/10.1016/j.scitotenv.2016.03.131

Massmann, G., Du, U., 2008. Behaviour and redox sensitivity of pharmaceutical residues during bank filtration – Investigation of residues of phenazone-type analgesics 71, 1476–1485. https://doi.org/10.1016/j.chemosphere.2007.12.017

Medema, G., Heijnen, L., Elsinga, G., Italiaander, R., Brouwer, A., 2020. Presence of SARS-Coronavirus-2 RNA in sewage and correlation with reported COVID-19 prevalence in the early stage of the epidemic in the Netherlands. Environ. Sci. Technol. Lett. https://doi.org/10.1021/acs.estlett.0c00357

Medema, G.J., Teunis, P.F.M., Havelaar, A.H., Haas, C.N., 1996. Assessment of the dose-response relationship of Campylobacter jejuni. Int. J. Food Microbiol. 30, 101–111.

Messner, M.J., Berger, P., 2016. Cryptosporidium Infection Risk: Results of New Dose-Response Modeling. Risk Anal. 000. https://doi.org/10.1111/risa.12541

Messner, M.J., Berger, P., Nappier, S.P., 2014. Fractional Poisson — A Simple Dose-Response Model for Human Norovirus. Risk Anal. 34, 1820–1829. https://doi.org/10.1111/risa.12207

Miklos, D.B., Remy, C., Jekel, M., Linden, K.G., Drewes, J.E., Hübner, U., 2018. Evaluation of advanced oxidation processes for water and wastewater treatment – A critical review. Water Res. 139, 118–131. https://doi.org/10.1016/j.watres.2018.03.042

Miklos, D.B., Wang, W.-L., Linden, K.G., Drewes, J.E., Hübner, U., 2019a. Comparison of UV-AOPs (UV/H2O2, UV/PDS and UV/Chlorine) for TOrC removal from municipal wastewater effluent and optical surrogate model evaluation. Chem. Eng. J. 362, 537–547. https://doi.org/10.1016/j.cej.2019.01.041

Miklos, D.B., Wang, W., Linden, K.G., Drewes, J.E., Hübner, U., 2019b. Comparison of UV-AOPs (UV/H2O2 , UV/PDS and UV/Chlorine) for TOrC removal from municipal wastewater effluent and optical surrogate model evaluation. Chem. Eng. J. 362, 537–547. https://doi.org/10.1016/j.cej.2019.01.041

Moazeni, M., Nikaeen, M., Hadi, M., Moghim, S., Mouhebat, L., Hatamzadeh, M., Hassanzadeh, A., 2017. Estimation of health risks caused by exposure to enteroviruses from agricultural application of wastewater effluents. Water Res. https://doi.org/10.1016/j.watres.2017.08.028

Mohamed, M., Hatfield, K., 2011. Dimensionless parameters to summarize the influence of microbial growth and inhibition on the bioremediation of groundwater contaminants. Biodegradation 22, 877–896. https://doi.org/10.1007/s10532-010-9445-x

Mok, H.-F., Hamilton, A.J., 2014. Exposure Factors for Wastewater-Irrigated Asian Vegetables and a Probabilistic Rotavirus Disease Burden Model for Their Consumption. Risk Anal. 34, 602–613. https://doi.org/10.1111/risa.12178

Mok, H.F., Barker, S.F., Hamilton, A.J., 2014. A probabilistic quantitative microbial risk assessment model of norovirus disease burden from wastewater irrigation of vegetables in Shepparton, Australia. Water Res. 54, 347–362. https://doi.org/10.1016/j.watres.2014.01.060

Momba, M., Ebdon, J., Kamika, I., Verbyla, M., 2019. Using indicators to assess microbial treatment and disinfection efficacy, in: Rose, J., Jimenez-Cisneros, B., Farnleitner, A., Blanch, A. (Eds.), Global Water Pathogen Project. Michigan State University, E. Lansing, MI, UNESCO. https://doi.org/https://doi.org/10.14321/waterpathogens.9 Acknowledgements:

Müller, J., Drewes, J.E., Hübner, U., 2019a. Investigating synergies in sequential biofiltration-based hybrid systems for the enhanced removal of trace organic chemicals from wastewater treatment plant effluents. Environ. Sci. Technol. Water Res. Technol. 5, 1423–1435. https://doi.org/10.1039/c9ew00181f

Müller, J., Drewes, J.E., Hübner, U., 2019b. Investigating synergies in sequential biofiltration- trace organic chemicals from wastewater. Environ. Sci. Water Res. Technol. https://doi.org/10.1039/c9ew00181f

Müller, J., Drewes, J.E., Hübner, U., 2017. Sequential biofiltration – A novel approach for enhanced biological removal of trace organic chemicals from wastewater treatment plant effluent. Water Res. 127, 127–138. https://doi.org/10.1016/j.watres.2017.10.009

Müller, J., Jewell, K.S., Schulz, M., Hermes, N., Ternes, T.A., Drewes, J.E., Hübner, U., 2019c. Capturing the oxic transformation of iopromide - A useful tool for an improved characterization of predominant redox conditions and the removal of trace organic compounds in biofiltration systems? Water Res. 152, 274–284. https://doi.org/10.1016/j.watres.2018.12.055

Müller, J., Levai, S., Titzschkau, L., Popovic, N., Carevic, D., Drewes, J.E., Hübner, U., 2019d. Role of reduced empty bed contact times and pre-treatment by coagulation with Fe (III) salts on the removal of trace organic compounds during sequential biofiltration. Sci. Total Enviroment 685, 220–228. https://doi.org/10.1016/j.scitotenv.2019.05.361

Mun, J., 2008. Appendix C: Understanding and Choosing the Right Probability Distributions, in: Advanced Analytical Models: Over 800 Models and 300 Applications from the Basel II Accord to Wall Street and Beyond. pp. 899–917.

Munro, I.C., Renwick, A.G., Danielewska-Nikiel, B., 2008. The Threshold of Toxicological Concern (TTC) in risk assessment. Toxicol. Lett. 180, 151–156. https://doi.org/10.1016/j.toxlet.2008.05.006

Murphy, H.M., Prioleau, M.D., Borchardt, M.A., Hynds, P.D., 2017. Review: Epidemiological evidence of groundwater contribution to global enteric disease, 1948 – 2015. Hydrogeol. J. 981–1001. https://doi.org/10.1007/s10040-017-1543-y

Murphy, H.M., Thomas, M.K., Schmidt, P.J., Medeiros, D.T., McFadyen, S., Pintar, K.D.M., 2016. Estimating the burden of acute gastrointestinal illness due to Giardia , Cryptosporidium , Campylobacter , E . coli O157 and norovirus associated with private wells and small water systems in Canada. Epidemilogical Infect. 1355–1370. https://doi.org/10.1017/S0950268815002071

MZmine Development, 2011. MZmine 2.3 manual.

Nam, S., Choi, D., Kim, S., Her, N., Zoh, K., 2014. Adsorption characteristics of selected hydrophilic and hydrophobic micropollutants in water using activated carbon. J. Hazard. Mater. 270, 144–152. https://doi.org/10.1016/j.jhazmat.2014.01.037

Nappier, S.P., Soller, J.A., Eftim, S.E., 2018. Potable Water Reuse : What Are the Microbiological Risks ? 283–292. https://doi.org/10.1007/s40572-018-0195-y

National Research Council, 2012. Water Reuse: Potential for Expanding the Nation's Water Supply Through Reuse of Municipal Wastewater. The National Academies Press, Washington, DC. https://doi.org/10.17226/13303

National Water Research Institute, 2013. Examining the Criteria for Direct Potable Reuse.

NHMRC-NRMMC-NHMR, 2011. Australian Drinking Water Guidelines Paper 6 National Water Quality Management Strategy. Commonwealth of Australia, Canberra. https://doi.org/1864965118

NHMRC-NRMMC, 2019. Australian Drinking Water Guidelines 6.

Nihemaiti, M., Miklos, D.B., Hübner, U., Linden, K.G., Drewes, J.E., Croué, J.-P., 2018. Removal of trace organic chemicals in wastewater effluent by UV/H2O2 and UV/PDS. Water Res. https://doi.org/10.1016/j.watres.2018.08.052

Nödler, K., Hillebrand, O., Idzik, K., Strathmann, M., Schiperski, F., Zirlewagen, J., Licha, T., 2013. Occurrence and fate of the angiotensin II receptor antagonist transformation product valsartan acid in the water cycle - A comparative study with selected b -blockers and the persistent anthropogenic wastewater indicators carbamazepine and acesulfame. Water Res. 47. https://doi.org/10.1016/j.watres.2013.08.034

Noh, J.H., Yoo, S.H., Son, H., Fish, K.E., Douterelo, I., Maeng, S.K., 2019. Effects of phosphate and hydrogen peroxide on the performance of a biological activated carbon filter for enhanced biofiltration. J. Hazard. Mater. https://doi.org/10.1016/j.jhazmat.2019.121778

NRMMC-EPHC-NHMR, 2008. Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 2) Augmentation of Drinking Water Supplies.

NRMMC-EPHC–NHMRC, 2009. Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 2). Managed Aquifer Recharge.

NRMMC–EPHC–AHMC, 2006. Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 1) National Water Quality Management Strategy. Canberra, Australia.

NSW Office of Water, 2015. Indicators, Reference Pathogens & Log10 Reductions: What does it all mean?, NSW Office of Water.

Oberoi, A.S., Jia, Y., Zhang, H., Khanal, S.K., Lu, H., 2019. Insights into the Fate and Removal of Antibiotics in Engineered Biological Treatment Systems: A Critical Review. Environ. Sci. Technol. 53, 7234–7264. https://doi.org/10.1021/acs.est.9b01131

Ødegaard, H., Østerhus, S., Melin, E., 2009. Optimal disinfection practice phase 2. Hamar.

OECD, 2019. Pharmaceutical Residues in Freshwater, Hazards and Policy Responses in Freshwater.

Oh, W. Da, Lim, P.E., Seng, C.E., Sujari, A.N.A., 2012. Kinetic modeling of bioregeneration of chlorophenol-loaded granular activated carbon in simultaneous adsorption and biodegradation processes. Bioresour. Technol. 114, 179–187. https://doi.org/10.1016/j.biortech.2012.03.065

Oldenkamp, R., 2016. Uncertainty and variability in environmental risk assessment of human pharmaceuticals. Radboud University Nijmegen.

Olivieri, A.W., Crook, J., Anderson, M.A., Bull, R.J., Drewes, J.E., Haas, C., E., 2016. Expert panel final report: Investigation on the Feasibility of Developing Uniform Water Recycling Criteria for Direct Potable Reuse.

Olivieri, A., Eisenberg, D., Soller, J., Eisenberg, J., Cooper, R., Tchobanoglous, G., Trussell, R., Gagliardo, P., 1999. Estimation of Pathogen removal in an Advanced Water Treatment Facility using Monte Carlo Simulation. Water Sci. Technol. 40, 223–233. https://doi.org/10.1016/S0273-1223(99)00504-1

Olivieri, A.W., Seto, E., Cooper, R.C., Cahn, M.D., Colford, J., Crook, J., Debroux, J., Mandrell, R., Suslow, T., 2014. Risk-Based Review of California's Water-Recycling Criteria for Agricultural Irrigation. J. Environ. Eng. https://doi.org/10.1061/(ASCE)EE.1943-7870.0000833

Onesios, K.M., Bouwer, E.J., 2012. Biological removal of pharmaceuticals and personal care products during laboratory soil aquifer treatment simulation with different primary substrate concentrations. Water Res. 46, 2365–2375. https://doi.org/10.1016/j.watres.2012.02.001

Owens, C.E.L., Angles, M.L., Cox, P.T., Byleveld, P.M., Nicholas, J., Rahman, B., 2020. Implementation of quantitative microbial risk assessment (QMRA) for public drinking water supplies: Systematic review. Water Res. 115614. https://doi.org/10.1016/j.watres.2020.115614

Owusu-Ansah, E. de G.J., Sampson, A., Amponsah, S.K., Abaidoo, R.C., Dalsgaard, A., Hald, T., 2017. Probabilistic quantitative microbial risk assessment model of norovirus from wastewater irrigated

vegetables in Ghana using genome copies and fecal indicator ratio conversion for estimating exposure dose. Sci. Total Environ. 601–602, 1712–1719. https://doi.org/10.1016/j.scitotenv.2017.05.168

Page, D., Dillon, P., Toze, S., Bixio, D., Genthe, B., Jiménez Cisneros, B.E., Wintgens, T., 2010. Valuing the subsurface pathogen treatment barrier in water recycling via aquifers for drinking supplies. Water Res. 44, 1841–1852. https://doi.org/10.1016/j.watres.2009.12.008

Paredes, L., Fernandez-Fontaina, E., Lema, J.M., Omil, F., Carballa, M., 2016. Understanding the fate of organic micropollutants in sand and granular activated carbon biofiltration systems. Sci. Total Environ. 551–552, 640–648. https://doi.org/10.1016/j.scitotenv.2016.02.008

Particle Analysis Using ImageJ [WWW Document], n.d. URL http://www.nuance.northwestern.edu/docs/epic-pdf/Particle Analysis Using ImageJ.pdf

Paruch, L., Paruch, A.M., Sørheim, R., 2020. DNA-based faecal source tracking of contaminated drinking water causing a large Campylobacter outbreak in Norway 2019. Int. J. Hyg. Environ. Health 224, 113420. https://doi.org/10.1016/j.ijheh.2019.113420

Pavione, D.M.., Bastos, R.K.X., Bevilacqua, P.D., 2013. Quantitative microbial risk assessment applied to irrigation of salad crops with waste stabilization pond effluents. Water Sci. Technol. https://doi.org/10.2166/wst.2013.674

Pecson, B., Gerrity, D., Bibby, K., Drewes, J.E., Gerba, C., Gersberg, R., Gonzalez, R., Haas, C.N., Hamilton, K.A., Nelson, K.L., Olivieri, A., Rock, C., Rose, J., Sobsey, M., 2020. Editorial Perspectives: will SARS-CoV-2 reset public health requirements in the water industry? Integrating lessons of the past and emerging research. Environ. Sci. Water Res. Technol. 6–9. https://doi.org/10.1039/d0ew90031a

Pecson, B.M., Triolo, S.C., Olivieri, S., Chen, E.C., Pisarenko, A.N., Yang, C., Olivieri, A., Haas, C.N., Trussell, R.S., Trussell, R.R., 2017. Reliability of pathogen control in direct potable reuse : Performance evaluation and QMRA of a full-scale 1 MGD advanced treatment train. Water Res. 122, 258–268. https://doi.org/10.1016/j.watres.2017.06.014

Petterson, S.R., Ashbolt, N.J., Sharma, A., 2001. Microbial Risks from Wastewater Irrigation of Salad Crops: a Screening-Level Risk Assessment. Water Environ. Res. 72. https://doi.org/10.2175/106143002X140161

Pharand, L., Van Dyke, M.I., Anderson, W.B., Huck, P.M., 2014. Assessment of Biomass in Drinking Water Biofilters by Adenosine Triphosphate. J. Am. Water Works Assoc. 106, E433–E444. https://doi.org/10.5942/jawwa.2014.106.0107

Piai, L., Blokland, M., Wal, A. Van Der, Langenhoff, A., 2020. Biodegradation and adsorption of micropollutants by biological activated carbon from a drinking water production plant. J. Hazard. Mater. https://doi.org/10.1016/j.jhazmat.2020.122028

Poma, H.R., Kundu, A., Wuertz, S., Rajal, V.B., 2019. Data fitting approach more critical than exposure scenarios and treatment of censored data for quantitative microbial risk assessment. Water Res. https://doi.org/10.1016/j.watres.2019.01.041

Prest, E.I., Hammes, F., Kötzsch, S., van Loosdrecht, M.C.M., Vrouwenvelder, J.S., 2013. Monitoring microbiological changes in drinking water systems using a fast and reproducible flow cytometric method. Water Res. 47, 7131–7142. https://doi.org/10.1016/j.watres.2013.07.051

Promega Corporation, 2008. Application of the BacTiter-Glo ™ Assay for Rapid Enumeration and Screening of Antimicrobial Compounds for Mycobacterium avium Complex Bacteria.

R Core Team, 2019. R: A Language and Environment for Statistical Computing.

Rattier, M., Reungoat, J., Gernjak, W., Joss, A., Keller, J., 2012a. Investigating the role of adsorption and biodegradation in the removal of organic micropollutants during biological activated carbon filtration of treated wastewater. J. Water Reuse Desalin. 2, 127–139. https://doi.org/10.2166/wrd.2012.012

Rattier, M., Reungoat, J., Gernjak, W., Keller, J., 2012b. Organic Micropollutant Removal by Biological Activated Carbon Filtration : A Review Urban Water Security Research Alliance Technical Report No . 53, Urban Water Security Research Alliance Technical Report No. 53.

Rattier, M., Reungoat, J., Keller, J., Gernjak, W., 2014. Removal of micropollutants during tertiary wastewater treatment by biofiltration: Role of nitrifiers and removal mechanisms. Water Res. 54, 89–99. https://doi.org/10.1016/j.watres.2014.01.030

Rauch-Williams, T., Hoppe-Jones, C., Drewes, J.E., 2010. The role of organic matter in the removal of emerging trace organic chemicals during managed aquifer recharge. Water Res. 44, 449–460. https://doi.org/10.1016/j.watres.2009.08.027

Rauch, T., Drewes, J.E., 2005. Quantifying Biological Organic Carbon Removal in Groundwater Recharge Systems. J. Environ. Eng. 131.

Reaume, M.J., Seth, R., Mcphedran, K.N., Fidalgo, E., Porter, L.A., 2015. Effect of Media on Biofilter Performance Following Ozonation of Secondary Treated Municipal Wastewater Effluent: Sand vs . GAC. Ozone Sci. Eng. 37, 143–153. https://doi.org/10.1080/01919512.2014.939741

Reemtsma, T., Berger, U., Arp, H.P.H., Gallard, H., Knepper, T.P., Neumann, M., Quintana, J.B., de Voogt, P., 2016. Mind the Gap: Persistent and Mobile Organic Compounds - Water Contaminants That Slip Through. Environ. Sci. Technol. 50. https://doi.org/10.1021/acs.est.6b03338

Regnery, J., Gerba, C.P., Dickenson, E.R. V, Drewes, J.E., 2017a. The importance of key attenuation factors for microbial and chemical contaminants during managed aquifer recharge: A review. Crit. Rev. Environ. Sci. Technol. 47, 1409–1452. https://doi.org/10.1080/10643389.2017.1369234

Regnery, J., Gerba, C.P., Dickenson, E.R. V, Drewes, J.E., 2017b. The importance of key attenuation factors for microbial and chemical contaminants during managed aquifer recharge: A review. Crit. Rev. Environ. Sci. Technol. 47, 1409–1452. https://doi.org/10.1080/10643389.2017.1369234

Regnery, J., Lee, J., Drumheller, Z.W., Drewes, J.E., Illangasekare, T.H., Kitanidis, P.K., McCray, J.E., Smits, K.M., 2017c. Trace organic chemical attenuation during managed aquifer recharge: Insights from a variably saturated 2D tank experiment. J. Hydrol. 548, 641–651. https://doi.org/10.1016/j.jhydrol.2017.03.038

Regnery, J., Wing, A.D., Alidina, M., Drewes, J.E., 2015. Biotransformation of trace organic chemicals during groundwater recharge: How useful are first-order rate constants? J. Contam. Hydrol. 179, 65–75. https://doi.org/10.1016/j.jconhyd.2015.05.008

Regnery, J., Wing, A.D., Kautz, J., Drewes, J.E., 2016. Introducing sequential managed aquifer recharge technology (SMART) – From laboratory to full-scale application. Chemosphere 154, 8–16. https://doi.org/10.1016/j.chemosphere.2016.03.097

Reinert, A.M., 2013. Granular Activated Carbon Adsorption of Micropollutants from Surface Water: Field- Scale Adsorber Performance and Scale-Up of Bench-Scale Data. North Carolina State University.

Reungoat, J., Escher, B.I., Macova, M., Argaud, F.X., Gernjak, W., Keller, J., 2012. Ozonation and biological activated carbon filtration of wastewater treatment plant effluents. Water Res. 46, 863–872. https://doi.org/10.1016/j.watres.2011.11.064

Reungoat, J., Escher, B.I., Macova, M., Keller, J., 2011. Biofiltration of wastewater treatment plant effluent: Effective removal of pharmaceuticals and personal care products and reduction of toxicity. Water Res. 45, 2751–2762. https://doi.org/10.1016/j.watres.2011.02.013

Rice, J., Westerhoff, P., 2015. Spatial and Temporal Variation in De Facto Wastewater Reuse in Drinking Water Systems across the U.S.A. Environ. Sci. Technol. 982–989. https://doi.org/10.1021/es5048057

RIVM, 2016. QMRAspot [WWW Document]. URL https://www.rivm.nl/en/who-collaborating-centre-risk-assessment-of-pathogens-in-food-and-water/tools/qmraspot (accessed 6.9.20).

Rose, J.B., 1997. Environmental Ecology of Cryptosporidium and Public Health Implications. Annu. Rev. Public Health. https://doi.org/10.1146/annurev.publhealth.18.1.135

Rose, J.B., Farrah, S.R., Harwood, V.J., Levine, A.D., Lukasik, J., Menendez, P., Scott, T.M., 2005. Reduction of Pathogens, Indicator Bacteria, and Alternative Indicators by Wastewater Treatment and Reclamation Processes, Water Environment Research Foundation.

Rose, J.B., Gurian, P.L., Haas, C.N., Weir, M.H., Eisenberg, J., 2013. Theory and Practice of Quantitative Microbial Risk Assessment: An Introduction, Camra.

Rossner, A., Snyder, S.A., Knappe, D.R.U., 2009. Removal of emerging contaminants of concern by alternative adsorbents. Water Res. 43, 3787–3796. https://doi.org/10.1016/j.watres.2009.06.009

Rücker, C., Kümmerer, K., 2012. Modeling and predicting aquatic aerobic biodegradation – a review from a user' s perspective. Green Chem. 875–887. https://doi.org/10.1039/c2gc16267a

Sales-Ortells, H., Fernandez-Cassi, X., Timoneda, N., Dürig, W., Girones, R., Medema, G., 2015. Health risks derived from consumption of lettuces irrigated with tertiary effluent containing norovirus. Food Res. Int. 68, 70–77. https://doi.org/10.1016/j.foodres.2014.08.018

Salveson, A., Dickenson, E., Soller, J., Angelotti, B., Parker, A., 2018. Pathogen Risk Evaluation of Treatment and Monitoring System Performance for Potable Reuse.

Sampson, A., Owusu-Ansah, E.J., Mills-Robertson, F.C., Ayi, I., Abaidoo, R.C., Hald, T., Permin, A., 2017. Probabilistic quantitative microbial risk assessment model of farmer exposure to Cryptosporidium spp . in irrigation water within Kumasi. Microb. Risk Anal. 6, 1–8. https://doi.org/10.1016/j.mran.2017.06.001

Sato, M.I.Z., Galvani, A.T., Padula, J.A., Nardocci, A.C., Lauretto, M. de S., Razzolini, M.T.P., Hachich, E.M., 2013. Assessing the infection risk of Giardia and Cryptosporidium in public drinking water delivered by surface water systems in Sao Paulo State, Brazil. Sci. Total Environ. 442, 389–396. https://doi.org/10.1016/j.scitotenv.2012.09.077

Sbardella, L., Comas, J., Fenu, A., Rodriguez-Roda, I., Weemaes, M., 2018. Advanced biological activated carbon filter for removing pharmaceutically active compounds from treated wastewater. Sci. Total Environ. 636, 519–529. https://doi.org/https://doi.org/10.1016/j.scitotenv.2018.04.214

Schaper, J.L., Posselt, M., Bouchez, C., Jaeger, A., Nuetzmann, G., Putschew, A., Singer, G., Lewandowski, J., 2019. Fate of Trace Organic Compounds in the Hyporheic Zone: In fl uence of

Retardation, the Benthic Biolayer, and Organic Carbon. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.8b06231

Schijven, J., Derx, J., de Roda Husman, A.M., Blaschke, A.P., Farnleitner, A.H., 2015. QMRAcatch: Microbial Quality Simulation of Water Resources including Infection Risk Assessment. J. Environ. Qual. 44, 1491–1502. https://doi.org/10.2134/jeq2015.01.0048.QMRAcatch

Schijven, J.F., Teunis, P.F.M., Rutjes, S.A., Bouwknegt, M., de Roda Husman, A.M., 2011. QMRAspot: A tool for Quantitative Microbial Risk Assessment from surface water to potable water. Water Res. 45, 5564–5576. https://doi.org/10.1016/j.watres.2011.08.024

Schmidt, P.J., Anderson, W.B., Emelko, M.B., 2020. Describing water treatment process performance: Why average log-reduction can be a misleading statistic. Water Res. 115702. https://doi.org/10.1016/j.watres.2020.115702

Schmidt, S.K., Simkins, S., Alexander, M., 1985. Models for the Kinetics of Biodegradation of Organic Compounds Not Supporting Growth. Appl. Environ. Microbiol. 50, 323–331. https://doi.org/10.1128/AEM.50.2.323-331.1985

Schoen, M.E., Jahne, M.A., Garland, J., 2020. A risk-based evaluation of onsite, non-potable reuse systems developed in compliance with conventional water quality measures. J. Water Health 1–14. https://doi.org/10.2166/wh.2020.221

Schollee, J.E., Schymanski, E.L., Avak, S.E., Loos, M., Hollender, J., 2015. Prioritizing Unknown Transformation Products from Biologically- Treated Wastewater Using High-Resolution Mass Spectrometry, Multivariate Statistics, and Metabolic Logic. Anal. Chem. https://doi.org/10.1021/acs.analchem.5b02905

Schriks, M., Heringa, M.B., Kooi, M.M.E. Van Der, Voogt, P. De, Wezel, A.P. Van, 2010. Toxicological relevance of emerging contaminants for drinking water quality. Water Res. 44, 461–476. https://doi.org/10.1016/j.watres.2009.08.023

Schulz, M., Löffler, D., Wagner, M., Ternes, T.A., 2008. Transformation of the X-ray Contrast Medium Iopromide In Soil and Biological Wastewater Treatment. Environ. Sci. Technol. 42, 7207–7217. https://doi.org/10.1021/es800789r

Schwab, B.W., Hayes, E.P., Fiori, J.M., Mastrocco, F.J., Roden, N.M., Cragin, D., Meyerhoff, R.D., D'Aco, V.J., Anderson, P.D., 2005. Human pharmaceuticals in US surface waters: A human health risk assessment. Regul. Toxicol. Pharmacol. https://doi.org/10.1016/j.yrtph.2005.05.005

Scutari, M., Denis, J.-B., 2015. Bayesian Networks with examples in R. CRC Press, Taylor & Francis Group. https://doi.org/10.1111/j.1467-7687.2007.00584.x

Seidu, R., Heistad, A., Amoah, P., Drechsel, P., Jenssen, P.D., Stenström, T.A., 2008. Quantification of the health risk associated with wastewater reuse in Accra, Ghana: A contribution toward local guidelines. J. Water Health 6, 461–471. https://doi.org/10.2166/wh.2008.118

Semerjian, L., Shanableh, A., Semreen, M.H., 2018. Human health risk assessment of pharmaceuticals in treated wastewater reused for non-potable applications in Sharjah , United Arab Emirates 121, 325–331. https://doi.org/10.1016/j.envint.2018.08.048

Servais, P., Anzil, A., Ventresque, C., 1989. Simple Method for Determination of Biodegradable Dissolved Organic Carbon in Water. Appl. Environ. Microbiol. 55, 2732–2734.

Sharma, B.M., Becanova, J., Scheringer, M., Sharma, A., Bharat, G.K., Whitehead, P.G., Klánová, J., Nizzetto, L., 2019. Health and ecological risk assessment of emerging contaminants (pharmaceuticals , personal care products , and artificial sweeteners) in surface and groundwater (drinking water) in the Ganges River. Sci. Total Environ. 646, 1459–1467. https://doi.org/10.1016/j.scitotenv.2018.07.235

Shimabuku, K.K., Zearley, T.L., Dowdell, K.S., Summers, R.S., 2019. Biodegradation and attenuation of MIB and 2,4-D in drinking water biologically active sand and activated carbon filters. Environ. Sci. Water Res. Technol. https://doi.org/10.1039/c9ew00054b

Simpson, D.R., 2008. Biofilm processes in biologically active carbon water purification. Water Res. 42, 2839–2848. https://doi.org/10.1016/j.watres.2008.02.025

Sinclair, M., O'Toole, J., Gibney, K., Leder, K., 2015. Evolution of regulatory targets for drinking water quality. J. Water Health 413–426. https://doi.org/10.2166/wh.2014.242

Sjerps, R.M.A., Brunner, A.M., Fujita, Y., Bajema, B., de Jonge, M., Bäuerlein, P., de Munk, J., Schriks, M., 2018. Clustering and prioritisation to design a risk based monitoring program in groundwater sources for drinking.

Sjerps, R.M.A., Thomas, L., Zwolsman, G.J.J.G., 2017. Projected impact of climate change and chemical emissions on the water quality of the European rivers Rhine and Meuse: A drinking water perspective. Sci. Total Environ. 601–602, 1682–1694. https://doi.org/10.1016/j.scitotenv.2017.05.250

Slobodnik, J., 2020. NORMAN Ecotoxicology Database [WWW Document]. URL https://www.norman-network.com/nds/ecotox/ (accessed 6.18.20).

Smeets, P., 2008. Stochastic Modelling of Drinking Water Treatment in Quantitative Microbial Risk Assessment. https://doi.org/10.2166/9781780401591

Smeets, P., Medema, G., van Dijk, J.C., 2009. The Dutch secret: how to provide safe drinking water without chlorine in the Netherlands. Drink. Water Eng. Sci. https://doi.org/10.5194/dwes-2-1-2009

Smeets, P., Rietveld, L., Hijnen, W., Medema, G., Stenström, T.A., 2006. Efficacy of water treatment processes.

Smeets, P.W.M.H., Dullemont, Y.J., Van Gelder, P.H.A.J.M., Van Dijk, J.C., Medema, G.J., 2008. Improved methods for modelling drinking water treatment in quantitative microbial risk assessment; a case study of Campylobacter reduction by filtration and ozonation. J. Water Health 6, 301–314. https://doi.org/10.2166/wh.2008.066

Snyder, S.A., Adham, S., Redding, A.M., Cannon, F.S., DeCarolis, J., Oppenheimer, J., Wert, E.C., Yoon, Y., 2007. Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. Desalination 202, 156–181. https://doi.org/10.1016/j.desal.2005.12.052

Soller, J., Eftim, S., Nappier, S., 2019. Comparison of Predicted Microbiological Human Health Risks Associated with de facto, Indirect, and Direct Potable Water Reuse. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.9b02002

Soller, J.A., Eftim, S.E., Nappier, S.P., 2018a. Direct potable reuse microbial risk assessment methodology: Sensitivity analysis and application to State log credit allocations. Water Res. 128, 286–292. https://doi.org/10.1016/j.watres.2017.10.034

Soller, J.A., Eftim, S.E., Warren, I., Nappier, S.P., 2017. Evaluation of microbiological risks associated with direct potable reuse. Microb. Risk Anal. 5, 3–14. https://doi.org/10.1016/j.mran.2016.08.003

Soller, J.A., Eisenberg, J.N.S., 2008. An evaluation of parsimony for microbial risk assessment models. Environmetrics 19, 61–78. https://doi.org/10.1002/env

Soller, J.A., Parker, A.M., Salveson, A., 2018b. Public Health Implications of Short Duration, Off-Specification Conditions at Potable Reuse Water Treatment Facilities. Environ. Sci. Technol. Lett. https://doi.org/10.1021/acs.estlett.8b00470

Song, Z., Zhang, X., Hao, H., Guo, W., Wen, H., Li, C., 2019. Occurrence, fate and health risk assessment of 10 common antibiotics in two drinking water plants with different treatment processes. Sci. Total Environ. 674, 316–326. https://doi.org/10.1016/j.scitotenv.2019.04.093

Sontheimer, H., Crittenden, J.C., Summers, R.S., 1988. Activated carbon for water treatment, 2nd ed. DWGWForschungsstelle.

Sotelo, J.L., Ovejero, G., Rodríguez, A., Álvarez, S., Galán, J., García, J., 2014. Competitive adsorption studies of caffeine and diclofenac aqueous solutions by activated carbon. Chem. Eng. J. 240, 443–453. https://doi.org/10.1016/j.cej.2013.11.094

Sotelo, J.L., Rodríguez, A., Álvarez, S., García, J., 2012. Removal of caffeine and diclofenac on activated carbon in fixed bed column. Chem. Eng. Res. Des. 90, 967–974. https://doi.org/10.1016/j.cherd.2011.10.012

Sperlich, A., Harder, M., Zietzschmann, F., Gnirß, R., 2017. Fate of Trace Organic Compounds in Granular Activated Carbon (GAC) Adsorbers for Drinking Water Treatment. Water 9. https://doi.org/10.3390/w9070479

Sperlich, A., Schimmelpfennig, S., Baumgarten, B., Genz, A., Amy, G., Worch, E., Jekel, M., 2008. Predicting anion breakthrough in granular ferric hydroxide (GFH) adsorption filters. Water Res. 42, 2073–2082. https://doi.org/10.1016/j.watres.2007.12.019

Staatsblad, 2001. Besluit van 9 januari 2001 tot wijziging van het Waterleidingbesluit in verband met de richtlijn betreffende de kwaliteit van voor menselijke consumptie bestemd water (Adaptation of Dutch drinking water legislation).

Stokdyk, J.P., Firnstahl, A.D., Walsh, J.F., Spencer, S.K., Jane, R., Lambert, D., Anderson, A.C., Rezania, L.W., Kieke, B.A., Mark, A., 2020. Viral, bacterial, and protozoan pathogens and fecal markers in wells supplying groundwater to public water systems in Minnesota, USA. Water Res. 115814. https://doi.org/10.1016/j.watres.2020.115814

Stokdyk, J.P., Spencer, S.K., Walsh, J.F., Lambert, J.R. De, Firnstahl, A.D., Anderson, A.C., Rezania, L.W., Borchardt, M.A., 2019. Cryptosporidium Incidence and Surface Water Influence of Groundwater Supplying Public Water Systems in Minnesota, USA. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.8b05446

Storck, F.R., Skark, C., Remmler, F., Brauch, H.-J., 2016. Environmental fate and behavior of acesulfame in laboratory experiments. Water Sci. Technol. 74, 2832–2842. https://doi.org/10.2166/wst.2016.452

Sun, Y., Angelotti, B., Brooks, M., Dowbiggin, B., Evans, P.J., Wang, Z., 2018. A pilot-scale investigation of disinfection by-product precursors and trace organic removal mechanisms in ozone-biologically activated carbon treatment for potable reuse. Chemosphere 210. https://doi.org/10.1016/j.chemosphere.2018.06.162

Sundaram, V., Pagilla, K., 2019. Trace and bulk organics removal during ozone – biofiltration treatment for potable reuse applications. Water Environ. Res. 92, 430–440. https://doi.org/10.1002/wer.1202

Sundaram, V., Pagilla, K., Guarin, T., Li, L., Marfil-Vega, R., Bukhari, Z., 2020. Extended field investigations of ozone-biofiltration advanced water treatment for potable reuse. Water Res. 172. https://doi.org/10.1016/j.watres.2020.115513

Swedish EPA, 2016. Behov av avancerad rening vid avloppsreningsverk -Finns det recipienter som är känsligare än andra?

Swiss Federal Council, 2017. Gewässerschutzverordnung. Switzerland.

Sylvestre, E., Burnet, J.-B., Smeets, P., Medema, G., Prevost, M., Dorner, S., 2020. Can routine monitoring of E . coli fully account for peak event concentrations at drinking water intakes in agricultural and urban. Water Res. 170. https://doi.org/10.1016/j.watres.2019.115369

Symonds, E.M., Verbyla, M.E., Lukasik, J.O., Kafle, R.C., Breitbart, M., Mihelcic, J.R., 2014. A case study of enteric virus removal and insights into the associated risk of water reuse for two wastewater treatment pond systems in Bolivia. Water Res. 65, 257–270. https://doi.org/10.1016/j.watres.2014.07.032

Tadkaew, N., Hai, F.I., McDonald, J. a., Khan, S.J., Nghiem, L.D., 2011. Removal of trace organics by MBR treatment: The role of molecular properties. Water Res. 45, 2439–2451. https://doi.org/10.1016/j.watres.2011.01.023

Teunis, P., van der Brandhof, W., Nauta, M., Wagenaar, J., van den Kerkhof, H., van Pelt, W., 2005. A reconsideration of the Campylobacter dose – response relation. Epidemiol. Infect. 583–592.

Teunis, P.F.M., Havelaar, A.H., 2000. The Beta Poisson Dose-Response Model Is Not a Single-Hit Model. Risk Anal. 20. https://doi.org/10.1111/0272-4332.204048

Teunis, P.F.M., Moe, C.L., Liu, P., Miller, S.E., Lindesmith, L., Baric, R.S., Le Pendu, J., Calderon, R.L., 2008. Norwalk Virus: How Infections is it? J. Med. Virol. 80, 1468–1476. https://doi.org/10.1002/jmv

Teunis, P.F.M., Nagelkerke, N.J.D., Haas, C.N., 1999. Dose Response Models For Infectious Gastroenteritis. Risk Anal. 19.

Texas Water Development Board and Alan Plummer Associates, 2015. Final Report: Direct Potable Reuse Resource Document. Austin, Texas, USA.

Thomaidi, V.S., Tsahouridou, A., Matsoukas, C., Stasinakis, A.S., Petreas, M., Kalantzi, O.I., 2020. Risk assessment of PFASs in drinking water using a probabilistic risk quotient methodology. Sci. Total Environ. 712, 136485. https://doi.org/10.1016/j.scitotenv.2019.136485

Tolouei, S., Dewey, R., Snodgrass, W.J., Edge, T.A., Andrews, R.C., Taghipour, M., Prévost, M., Dorner, S., 2019. Assessing microbial risk through event-based pathogen loading and hydrodynamic modelling. Sci. Total Environ. 693, 133567. https://doi.org/10.1016/j.scitotenv.2019.07.373

Tousova, Z., Oswald, P., Slobodnik, J., Blaha, L., Muz, M., Hu, M., Brack, W., Krauss, M., Di, C., Tarcai, Z., Seiler, T., Hollert, H., Koprivica, S., Ahel, M., Schollée, J.E., Hollender, J., Suter, M.J., Hidasi, A.O., Schirmer, K., Sonavane, M., Ait-aissa, S., Creusot, N., Brion, F., Froment, J., Catarina, A., Thomas, K., Erik, K., Tu, S., Ouyang, X., Leonards, P., Lamoree, M., Osorio, V., Kolkman, A., Schriks, M., Spirhanzlova, P., Tindall, A., Schulze, T., 2017. European demonstration program on the effect-based and chemical identification and monitoring of organic pollutants in European surface waters. Sci. Total Environ. 602, 1849–1868. https://doi.org/10.1016/j.scitotenv.2017.06.032

Toze, S., Bekele, E., Page, D., Sidhu, J., Shackleton, M., 2010. Use of static Quantitative Microbial Risk Assessment to determine pathogen risks in an unconfined carbonate aquifer used for Managed Aquifer Recharge. Water Res. 44, 1038–1049. https://doi.org/10.1016/j.watres.2009.08.028

Tran, N.H., Reinhard, M., Gin, K.Y.H., 2018. Occurrence and fate of emerging contaminants in municipal wastewater treatment plants from different geographical regions-a review. Water Res. 133, 182–207. https://doi.org/10.1016/j.watres.2017.12.029

Tran, N.H., Reinhard, M., Khan, E., Chen, H., Nguyen, V.T., Li, Y., Goh, S.G., Nguyen, Q.B., Saeidi, N., Gin, K.Y.H., 2019. Emerging contaminants in wastewater, stormwater runoff, and surface water: Application as chemical markers for diffuse sources. Sci. Total Environ. 676, 252–267. https://doi.org/10.1016/j.scitotenv.2019.04.160

Tran, N.H., Urase, T., Ngo, H.H., Hu, J., Ong, S.L., 2013. Insight into metabolic and cometabolic activities of autotrophic and heterotrophic microorganisms in the biodegradation of emerging trace organic contaminants. Bioresour. Technol. 146, 721–731. https://doi.org/10.1016/j.biortech.2013.07.083

Trinkwasserverordnung, 2018.

Tsitsifli, S., Tsoukalas, D.S., 2019. Water Safety Plans and HACCP implementation in water utilities around the world: benefits , drawbacks and critical success factors.

U.S. Environmental Protection Agency, 2015. Review of Coliphages As Possible Indicators of Fecal Contamination for Ambient Water Quality. Washington, D.C.

U.S. Environmental Protection Agency, 2006. Ultraviolet Disinfection Guidance Manual for the Final Long Term 2 Enhanced Surface Water Treatment rule. Washington, D.C.

U.S. Environmental Protection Agency, 1998. National Primary Drinking Water Regulations: Disinfectants and Disinfection Byproducts: 40 CFR 9, 141, 142, Federal Register.

Umweltbundesamt, 2019. Liste der nach GOW bewerteten Stoffe.

Urfer, D., Huck, P.M., Booth, S.D.J., Coffey, B.M., 1997. Biological filtration for BOM and particle removal: a critical review. J. Am. Water Works Assoc. 83–98. https://doi.org/10.1002/j.1551-8833.1997.tb08342.x

US EPA, 2019. National Water Reuse Action Plan Draft.

US EPA, 2017. 2017 Potable Reuse Compendium. Washington, D.C.

US EPA, 2006. National primary drinking water regulations: Long term 2 enhanced surface water treatment rule: Final Rule.

Uusitalo, L., 2007. Advantages and challenges of Bayesian networks in environmental modelling. Ecol. Modell. 3, 312–318. https://doi.org/10.1016/j.ecolmodel.2006.11.033

Van Abel, N., Schoen, M.E., Kissel, J.C., Meschke, J.S., Van Abel, N., Schoen, M.E., Kissel, J.C., Meschke, J.S., 2017. Comparison of Risk Predicted by Multiple Norovirus Dose – Response Models and Implications for Quantitative Microbial Risk Assessment. Risk Anal. 37, 245–264. https://doi.org/10.1111/risa.12616

Varga, M., ELabadsa, M., Tatár, E., Mihuez, V., 2019. Removal of selected pharmaceuticals from aqueous matrices with activated carbon under batch conditions. Microchem. J. 148. https://doi.org/10.1016/j.microc.2019.05.038

Velten, S., Hammes, F., Boller, M., Egli, T., 2007. Rapid and direct estimation of active biomass on granular activated carbon through adenosine tri-phosphate (ATP) determination. Water Res. 41, 1973–1983. https://doi.org/10.1016/j.watres.2007.01.021

Verbyla, M.E., Symonds, E.M., Kafle, R.C., Cairns, M.R., Iriarte, M., Mercado Guzmán, A., Coronado, O., Breitbart, M., Ledo, C., Mihelcic, J.R., 2016. Managing Microbial Risks from Indirect Wastewater Reuse for Irrigation in Urbanizing Watersheds. Environ. Sci. Technol. 50, 6803–6813. https://doi.org/10.1021/acs.est.5b05398

Vignola, M., Werner, D., Hammes, F., King, L.C., Russell, J., 2018a. Flow-cytometric quantification of microbial cells on sand from water biofilters. Water Res. https://doi.org/10.1016/j.watres.2018.05.053

Vignola, M., Werner, D., Wade, M.J., Meynet, P., Davenport, R.J., 2018b. Medium shapes the microbial community of water filters with implications for effluent quality. Water Res. 129, 499–508. https://doi.org/10.1016/j.watres.2017.09.042

Vital, M., Dignum, M., Magic-Knezev, A., Ross, P., Rietveld, L., Hammes, F., 2012. Flow cytometry and adenosine tri-phosphate analysis: Alternative possibilities to evaluate major bacteriological changes in drinking water treatment and distribution systems. Water Res. 46, 4665–4676. https://doi.org/10.1016/j.watres.2012.06.010

Vose, D., 2008. Risk Analysis, A quantitative guide, 3rd ed. John Wiley & Sons, Ltd.

Walck, C., 2007. Hand-book on statistical distributions for experimentalists.

WaterReuse Research Foundation, 2015. Framework for Direct Potable Reuse.

WaterReuse Research Foundation, 2011. Direct Potable Reuse-a path forward. Alexandria, VA.

Watershare, 2016a. QMRA Treatment Calculator [WWW Document]. URL https://www.watershare.eu/tool/qmra-treatment-calculator/ (accessed 6.16.20).

Watershare, 2016b. AbatES [WWW Document]. URL https://www.watershare.eu/tool/abates/ (accessed 6.21.20).

Westrell, T., 2004. Microbial risk assessment and its implications for risk management in urban water systems. Linköping University.

Wicker, J., Lorsbach, T., Gütlein, M., Schmid, E., Latino, D., Kramer, S., Fenner, K., 2020. enviPath - The environmental contaminant biotransformation pathway resource [WWW Document]. Nucleic Acids Res. URL https://envipath.org/ (accessed 6.11.20).

Wiese, B., Massmann, G., Jekel, M., Heberer, T., Dünnbier, U., Orlikowski, D., Grützmacher, G., 2011. Removal kinetics of organic compounds and sum parameters under field conditions for managed aquifer recharge. Water Res. 45, 4939–4950. https://doi.org/10.1016/j.watres.2011.06.040

Worch, E., 2012. Adsorption Technology in Water Treatment: Fundamentals, Processes, and Modeling. De Gruyter. https://doi.org/10.1515/9783110240238

World Health Organization, 2019. Strengthening Drinking Water Surveillance Using Risk-Based Approaches.

World Health Organization, 2017a. Potable reuse: Guidance for producing safe drinking-water. Geneva.

World Health Organization, 2017b. Guidelines for Drinking-Water Quality: Fourth edition incorporating the first addendum, WHO Library Cataloguing-in-Publication Data. https://doi.org/10.1016/S1462-0758(00)00006-6

World Health Organization, 2016. Quantitative Microbial Risk Assessment: Application for Water Safety Management. https://doi.org/10.1002/9781118910030

World Health Organization, 2011. Guidelines for Drinking-water Quality. https://doi.org/10.1016/S1462-0758(00)00006-6

World Health Organization, 2006. Safe Use of Wastewater, Excreta and Greywater. https://doi.org/10.1007/s13398-014-0173-7.2

World Health Organization, 2004. Guidelines for Drinking-water Quality.

Xiao, S., Hu, S., Zhang, Y., Zhao, X., Pan, W., 2018. Influence of sewage treatment plant effluent discharge into multipurpose river on its water quality: A quantitative health risk assessment of Cryptosporidium and Giardia. Environ. Pollut. 233, 797–805. https://doi.org/10.1016/j.envpol.2017.11.010

Yang, Y., Sik, Y., Kim, K., Kwon, E.E., Fai, Y., 2017. Occurrences and removal of pharmaceuticals and personal care products (PPCPs) in drinking water and water/sewage treatment plants : A review. Sci. Total Environ. 596–597, 303–320. https://doi.org/dx.doi.org/10.1016/j.scitotenv.2017.04.102

Ye, N., Cimetiere, N., Heim, V., Fauchon, N., Feliers, C., Wolbert, D., 2018. Upscaling fixed bed adsorption behaviors towards emerging micropollutants in treated natural waters with aging activated carbon: model development and validation. Water Res. 148. https://doi.org/10.1016/j.watres.2018.10.029

Yu, J.T., Bouwer, E.J., Coelhan, M., 2006. Occurrence and biodegradability studies of selected pharmaceuticals and personal care products in sewage. Agric. Water Manag. 86, 72–80. https://doi.org/10.1016/j.agwat.2006.06.015

Yu, Z., Peldszus, S., Huck, P.M., 2009. Adsorption of Selected Pharmaceuticals and an Endocrine Disrupting Compound by Granular Activated Carbon . 1 . Adsorption Capacity and Kinetics. Environ. Sci. Technol. 43, 1467–1473. https://doi.org/10.1021/es801961y

Zearley, T.L., Summers, R.S., 2012. Removal of trace organic micropollutants by drinking water biological filters. Environ. Sci. Technol. 46, 9412–9419. https://doi.org/10.1021/es301428e

Zhang, L., Carvalho, P.N., Bollmann, U.E., EI-taliawy, H., Brix, H., Bester, K., 2019. Enhanced removal of pharmaceuticals in a biofilter: Effects of manipulating co-degradation by carbon feeding. Chemosphere 236, 124303. https://doi.org/10.1016/j.chemosphere.2019.07.034

Zhang, S., Gitungo, S.W., Axe, L., Raczko, R.F., Dyksen, J.E., 2017. Biologically active filters – An advanced water treatment process for contaminants of emerging concern. Water Res. 114, 31–41. https://doi.org/http://dx.doi.org/10.1016/j.watres.2017.02.014

Zhiteneva, V., Hübner, U., Medema, G.J., Drewes, J.E. Trends in conducting quantitative microbial risk assessments for water reuse systems: a review. 2020a. Microbial Risk Analysis 16, 100132. https://doi.org/10.1016/j.mran.2020.100132.

Zhiteneva, V., Ziemendorf, É., Sperlich, A., Drewes, J.E., Hübner, U., 2020b. Differentiating between adsorption and biodegradation mechanisms while removing trace organic chemicals (TOrCs) in

biological activated carbon (BAC) filters. Sci. Total Environ. 743, 140567. https://doi.org/10.1016/j.scitotenv.2020.140567

Zhiteneva, V., Carvajal, G., Shehata, O., Hübner, U., Drewes, J.E. Quantitative microbial risk assessment of a non-membrane based indirect potable water reuse system using Bayesian networks. 2021. Science of the Total Environment 780, 146462. https://doi.org/10.1016/j.scitotenv.2021.146462.

Zhou, S., Di, C., Wu, X., Shao, Y., Seiler, T.-B., 2019. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environ. Int. 128, 1–10. https://doi.org/10.1016/j.envint.2019.04.034

Zhu, I.X., Wang, J., Wieland, A., 2015. Ozone-Enhanced Biologically Active Filtration for Wastewater Reuse. J. Am. Water Works Assoc. 107, 685–692. https://doi.org/https ://doi.org/10.5942/jawwa.2015.107.0165

Zietzschmann, F., Aschermann, G., Jekel, M., 2016. Comparing and modeling organic micro-pollutant adsorption onto powdered activated carbon in different drinking waters and WWTP effluents. Water Res. 102, 190–201. https://doi.org/10.1016/j.watres.2016.06.041

Zietzschmann, F., Worch, E., Altmann, J., Ruhl, A.S., Sperlich, A., Meinel, F., Jekel, M., 2014. Impact of EfOM size on competition in activated carbon adsorption of organic micro-pollutants from treated wastewater. Water Res. 65, 297–306. https://doi.org/10.1016/j.watres.2014.07.043

Zucker, I., Lester, Y., Avisar, D., Hübner, U., Jekel, M., Weinberger, Y., Mamane, H., 2015. Influence of Wastewater Particles on Ozone Degradation of Trace Organic Contaminants. Environ. Sci. Technol. 49, 301–308. https://doi.org/10.1021/es504314t

Zucker, I., Mamane, H., Cikurel, H., Jekel, M., Hübner, U., Avisar, D., 2015. A hybrid process of biofiltration of secondary effluent followed by ozonation and short soil aquifer treatment for water reuse. Water Res. 84, 315–322. https://doi.org/10.1016/j.watres.2015.07.034