

# **Analysis, occurrence, and fate of psychoactive compounds in an urban water cycle**

Dissertation

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# Preface

The present thesis was conducted as part of the research project "Bewertung der organischen Zusammensetzung des Grundwassers im Einzugsgebiet der Nordgalerien des Wasserwerks Friedrichshagen, Berlin" – English title: "Evaluation of organic compounds in the groundwater of the catchment area of the waterworks Friedrichshagen (Berlin, Germany)" – and is the result of the cooperation between the Freie Universität Berlin (FUB) and the Berliner Wasserbetriebe (BWB). The work outlined in this dissertation was carried out over a period of three years (March 2009 to February 2012). Financial support was provided by the BWB.

The main chapters of this thesis have been published or submitted for publication, to which I contributed as the first author. I have been in charge of the development and the conducting of the research work described. I have been responsible for the composition of the scientific content and for the preparation of the manuscripts, including literature review, data interpretation, preparation of figures and tables, and manuscript writing. Co-authors have played an advisory and supervisory role.

The thesis contains the following contributions by other scientists, technicians and students:

- Most of the samples (wastewater, groundwater, surface water, drinking water) were collected by the technicians of the pigadi GmbH and the BWB.
- Data on groundwater levels, filter depths, and coordinates of observation and abstraction wells were kindly provided by the BWB.
- Analysis of standard water parameters (Chapter 3 and Chapter 5) was performed by the staff of the BWB.
- Samples for age dating (Chapter 3) were collected with the help of Dipl. Geol. Victoria Burke (PhD student, Carl von Ossietzky Universität Oldenburg). Analysis of  $^3\text{H}$ , He isotopes, and Ne was carried out by Dr. Jürgen Sültenfuß at the University of Bremen.
- Field sampling for the aeration experiment (Chapter 5) was undertaken together with Victoria Burke, Dr. Raffaella Meffe (Madrid Institute for Advanced Studies), and Jan Loth (BWB).

- Sorbent material for sorption experiments (Chapter 5) was provided by the BWB. Determination of the sorbent properties was carried out in collaboration with Janka Schmidt (Bachelor student, Carl von Ossietzky Universität Oldenburg).

## **Declaration of originality**

I hereby certify, as the author of this thesis, and as one of the main authors of the publications arising, that I was the person involved in fieldwork, organization, implementation, analysis, evaluation, and manuscript preparation.

I declare that this thesis and the work reported herein is to the best of my knowledge original, except as acknowledged in the text, and that the work was not submitted previously to any other institution.

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Ulrike Hass

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"Aman Iman" (Water is Life)

*Touareg saying*

## Summary

Groundwater within the catchment area of the drinking water treatment plant Friedrichshagen (DWTP FRI) in Berlin (Germany) was previously found to be heavily polluted with a number of anthropogenic contaminants. Groundwater pollution at this site is a consequence of decades of continuous wastewater irrigation at the nearby sewage farm district Münchehofe. Operation of the sewage farm was terminated in the 1980s in the course of the construction of a wastewater treatment plant (WWTP). However, the soils and the adjacent groundwater are still highly contaminated.

Prior to the present research project, gas chromatography-mass spectrometry (GC-MS) screenings revealed the presence of several psychoactive drugs in the groundwater below and downgradient of the former sewage farm. The substances were identified as primidone, its metabolites phenobarbital and phenylethylmalonamide, meprobamate, and pyrithyldione.

Their detection in groundwater used for drinking water production purposes raised concerns and triggered this study. Extensive field sampling was conducted and laboratory experiments were performed with the aim to investigate the occurrence, behavior, and fate of the selected psychoactive compounds in groundwater as well as in other stages of the aquatic system of Berlin and to estimate potentially resulting risks. In particular, the question arose whether the health-based precautionary values (HPV), which are recommended by the German Federal Environmental Agency (UBA) for only partially or non-assessable substances in drinking water, can be met today and in the future. According to the report by Dieter (2011), a maximum primidone concentration of 3 µg/L in drinking water is tolerable for lifetime consumption. With respect to phenobarbital, a HPV of 0.30 µg/L has been recommended (Dieter, 2011). For the other investigated pharmaceuticals human toxicological relevance has not yet been assessed, and therefore, a HPV of 0.10 µg/L is applicable.

First of all, a reliable technique for the routine determination of these pharmaceutical residues was needed. Hence, an **analytical method** was developed and validated allowing a sensitive and simultaneous quantification of the selected compounds and, additionally, oxazepam and diazepam, two nowadays widely used psychotropic drugs, in environmental



water samples. The method employs solid phase extraction (SPE) and ultrahigh-performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS). Limits of quantification (LOQs) were between 0.02 and 0.03 µg/L for groundwater and between 0.10 and 0.15 µg/L in the case of wastewater. Using surrogate standards analyte recoveries generally exceeded 80 %. Applying the described method, an initial occurrence study confirmed the presence of some of the target analytes in groundwater that had been affected by former sewage irrigation for several decades.

Highest detected concentrations in the groundwater ranged up to 1.35 µg/L (phenobarbital). These results gave rise for further investigations below and downgradient of the decommissioned sewage farm with the objective to comprehensively study the occurrence and distribution of the psychoactive compounds in the mostly anoxic **groundwater** and to evaluate the current and future risk of drinking water contamination. To this end, a large number of observation and production wells was sampled at the field site. Monitoring revealed elevated concentrations of five out of the seven compounds ranging up to 1 µg/L. The results indicate a strong persistence of the detected psychoactive drugs in the environment under anoxic aquifer conditions. The contaminant plumes extend to some production wells and affect the local raw water quality. Moreover, findings suggest that the legacy of sewage irrigation will continue to impair raw water quality in the area for decades. Nevertheless, concentrations in the final drinking water at the DWTP FRI were below the LOQ what is primarily due to dilution effects. To gain better understanding of the present hydrogeological settings, groundwater ages were estimated using the helium-tritium ( $^3\text{He}$ - $^3\text{H}$ ) dating method. Groundwater was found to be up to four decades old at 40 m below ground, while ages of shallow groundwater ranged from years to a decade. Also, results exhibited that concentrations of the compounds increase with groundwater ages.

Owing to the characteristics of the city's aquatic system, particularly polar, poorly degradable pollutants may potentially reach drinking water resources via bank filtration and artificial recharge if present in WWTP effluents and/or surface waters. Hence, another part of this study was focusing on the occurrence and fate of the psychoactive compounds in several compartments of the Berlin **water cycle**. For this purpose, WWTP effluents, surface water, groundwater of a bank filtration site, raw and final drinking water, and groundwater influenced by former wastewater irrigation were analyzed. Primidone and its metabolite phenylethylmalonamide were found to be omnipresent in the aquatic environment of Berlin

with maximum concentrations occurring in treated wastewater (0.87 and 0.42  $\mu\text{g/L}$ , respectively). Both compounds are apparently not removed along the flow path and concentrations are only lowered by dilution. They consequently reach raw water resources and potentially even final drinking water. With the exception of raw and final drinking water, phenobarbital was present at every stage of the Berlin water cycle, whereat highest concentrations were measured in groundwater below decommissioned sewage farms (up to 0.96  $\mu\text{g/L}$ ). Oxazepam was only detected in WWTP effluents and surface waters (up to 0.18  $\mu\text{g/L}$ ), while diazepam was not encountered in any matrix. Meprobamate and pyrithyldione were only found in sewage farm groundwater (up to 0.50 and 0.04  $\mu\text{g/L}$ , respectively) and, in case of meprobamate, also in decade old bank filtrate (0.03  $\mu\text{g/L}$ ). These results underline again a high persistence of some of the investigated compounds in the aquatic system.

Motivated by the collected results, especially the positive findings in groundwater of the catchment area of the DWTP FRI and, in case of primidone and phenylethylmalonamide even in final drinking water of a DWTP, it became crucial to further explore the **environmental behavior** of the pollutants. Therefore, laboratory experiments were carried out in a next step of this thesis. For one thing, aeration experiments with anoxic groundwater were performed to investigate the behavior of the psychoactive compounds under different redox conditions (oxic and anoxic). Oxazepam and diazepam were not included in this portion of the study since they were not present in the anoxic groundwater used for the experiment. Results showed that the studied compounds were not degraded under either oxic or anoxic conditions, indicating persistence irrespective of the predominant redox conditions. Additionally, batch sorption experiments were performed with two sorbents (powdered activated carbon (PAC) and a sandy sediment). In general, sorption tendency towards the PAC was higher than towards the sand. Besides, both oxazepam and diazepam were completely removed from the aqueous phase by sorption to the PAC within 72 h of contact time, whereas elimination of the remaining compounds was less effective (20-58 %). Finally, experimental results were used to calculate sorption parameters with the aim to evaluate the future risk for drinking water production at the DWTP FRI. This assessment suggests that the investigated pharmaceuticals will remain in the aquifer for several decades up to centuries despite their rather good mobility.

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## Zusammenfassung

Das Grundwasser im Einzugsgebiet des Wasserwerkes Friedrichshagen in Berlin (Deutschland) ist in erhöhtem Maße mit einer Vielzahl anthropogener Schadstoffe belastet. Die Verunreinigung des Grundwassers an diesem Standort ist eine Folge der jahrzehntelang andauernden Verrieselung von Abwasser auf dem nahegelegenen Rieselfeldbezirk Münchehofe. Der Rieselfeldbetrieb wurde im Zuge der Errichtung einer Kläranlage bereits in den 1980er Jahren eingestellt. Die Böden und das angrenzende Grundwasser sind jedoch auch heute noch stark kontaminiert.

Anhand von gaschromatographisch-massenspektrometrischen Screenings von Grundwasser unterhalb und abstromig des ehemaligen Rieselfeldes wurde im Vorfeld dieser Arbeit das Vorkommen mehrerer Psychopharmaka festgestellt. Dabei wurden die folgenden Wirkstoffe identifiziert: Primidon und seine beiden Metaboliten Phenobarbital und Phenylethylmalonamid sowie Meprobamat und Pyrithyldion. Ihr Nachweis im Grundwasser, welches auch für die Trinkwasserproduktion genutzt wird, war besorgniserregend und daher der Auslöser für die vorliegende Studie.

Ziel der Arbeit war es, das Vorkommen und das Verhalten dieser Psychopharmaka im Grundwasser sowie in anderen Stufen des Berliner Wasserkreislaufes detailliert zu untersuchen und die sich daraus möglicherweise ergebenden Risiken abzuschätzen. Hierfür wurden die gegenwärtigen Schadstoffkonzentrationen in der aquatischen Umwelt in umfangreichen Feldstudien erhoben und Laborexperimente durchgeführt.

Insbesondere stellte sich die Frage, ob die gesundheitlichen Orientierungswerte, die vom Umweltbundesamt für humantoxikologisch nur teil- oder nicht bewertbare Substanzen im Trinkwasser empfohlen werden, sowohl heute als auch zukünftig eingehalten werden können. Laut einem Bericht von Dieter (2011) ist in Bezug auf Primidon eine Höchstkonzentration von 3 µg/L im Trinkwasser gesundheitlich lebenslang duldbar. Für Phenobarbital wird eine Konzentration von maximal 0,3 µg/L im Trinkwasser empfohlen. Die humantoxikologische Relevanz der anderen untersuchten Arzneimittel wurde bisher nicht ausreichend bewertet. Für diese Substanzen gilt entsprechend ein gesundheitlicher Orientierungswert von 0,1 µg/L.

Zunächst bestand die Notwendigkeit, ein zuverlässiges Verfahren zu erarbeiten, welches die routinemäßige Bestimmung der Pharmakarückstände ermöglicht. Daher wurde in einem ersten Schritt eine **analytische Methode** entwickelt und validiert, die eine sensitive und simultane Quantifizierung der ausgewählten Verbindungen sowie zusätzlich der beiden weitverbreiteten Psychopharmaka Oxazepam und Diazepam in wässrigen Proben erlaubt. Das Verfahren beinhaltet eine Aufbereitung der Proben durch Festphasenextraktion und die anschließende Messung mittels Hochleistungsflüssigkeitschromatographie und Tandem-Massenspektrometrie. Die Bestimmungsgrenzen der Psychopharmaka im entwickelten Analysenverfahren liegen bei 0,02 bis 0,03 µg/L für Grundwasser und zwischen 0,10 und 0,15 µg/L für Abwasserproben. Unter Verwendung von Internen Standards können Wiederfindungsraten der Analyten erzielt werden, die generell über 80 % betragen. Das beschriebene Verfahren wurde in einer ersten Untersuchung in Bezug auf das Vorkommen der Substanzen angewendet. Dabei konnte das Vorhandensein einiger der Zielverbindungen in rieselfeldbeeinflusstem Grundwasser bestätigt werden. Die höchsten nachgewiesenen Konzentrationen im Grundwasser reichten dabei bis zu 1,35 µg/L (Phenobarbital).

Diese Ergebnisse waren Anlass für weitere Untersuchungen am Standort. Das Ziel bestand darin, das Auftreten und die Verteilung der Psychopharmaka in dem vorwiegend anoxischen **Grundwasser** unterhalb und im Abstrom des ehemaligen Rieselfeldes umfassend zu untersuchen. Außerdem galt es, das aktuelle und zukünftige Risiko einer Trinkwasserkontamination zu beurteilen. Dazu wurden zahlreiche Grundwassermessstellen und Förderbrunnen im Einzugsgebiet des Wasserwerkes Friedrichshagen beprobt. Das Monitoring ergab, dass fünf der sieben Verbindungen in erhöhten Konzentrationen bis zu 1 µg/L vorliegen. Die Ergebnisse deuten darauf hin, dass die nachgewiesenen Substanzen unter den vorliegenden Redoxbedingungen in der Umwelt persistent sind. Die Kontaminationsfahnen dehnen sich bis hin zu einigen Trinkwasserbrunnen aus und beeinflussen die Rohwasserqualität. Darüber hinaus lässt sich aus den Ergebnissen ableiten, dass die vor Jahrzehnten praktizierte Rieselfeldbewirtschaftung die Qualität des geförderten Grundwassers auch in Zukunft weiterhin beeinträchtigen wird. Erfreulicherweise liegen die Psychopharmaka-Konzentrationen im Reinwasser des Wasserwerkes Friedrichshagen unterhalb der Bestimmungsgrenze, was in erster Linie auf Verdünnungseffekte zurückzuführen ist. Um ein besseres Verständnis in Bezug auf die vorliegenden

hydrogeologischen Bedingungen zu erhalten, wurde das Grundwasseralter mit Hilfe der Tritium-Helium-Datierung ( $^3\text{H}$ - $^3\text{He}$ -Datierung) ermittelt. Dabei wurde festgestellt, dass das Grundwasser in einer Tiefe von 40 m unter Geländeoberkante bis zu 40 Jahre alt ist, während flaches Grundwasser ein Alter von ein bis zehn Jahren aufweist. Außerdem zeigten die Ergebnisse, dass die Konzentrationen der Psychopharmaka mit dem Grundwasseralter zunehmen.

Aufgrund der besonderen Merkmale des **Berliner Wasserkreislaufes** können vor allem polare, schwer abbaubare Schadstoffe, die in Klärwerksabläufen und/oder in Oberflächengewässern vorliegen, über Uferfiltration oder künstliche Grundwasseranreicherung potenziell auch Rohwasserressourcen erreichen. Daher befasst sich ein weiterer Teil dieser Arbeit mit dem Vorkommen und Verhalten der Psychopharmaka in den verschiedenen Stufen des partiell geschlossenen Wasserkreislaufes. Zu diesem Zweck wurden Klärwerksabläufe, Oberflächengewässer, Uferfiltrat, rieselfeldbeeinflusstes Grundwasser sowie Roh- und Reinwässer der Berliner Wasserwerke untersucht. Primidon und Phenylethylmalonamid kommen ubiquitär vor und konnten in allen Stufen des aquatischen Systems von Berlin nachgewiesen werden. Die höchsten Konzentrationen wurden in Klärwerksabläufen gemessen (0,87 bzw. 0,42  $\mu\text{g/L}$ ). Beide Verbindungen werden im Fließverlauf des Wasserkreislaufes nicht entfernt und die beobachteten Konzentrationsabnahmen sind lediglich Verdünnungsprozessen zuzuschreiben. Diese Substanzen erreichen somit die Trinkwasserressourcen und können in das zur Trinkwasserversorgung bereitgestellte Reinwasser gelangen. Mit Ausnahme von Roh- und Reinwasser konnte auch Phenobarbital in allen Bereichen des Berliner Wassersystems nachgewiesen werden. Die höchsten Konzentrationen wurden dabei in rieselfeldbeeinflusstem Grundwasser festgestellt (bis zu 0,96  $\mu\text{g/L}$ ). Oxazepam wurde nur in Klärwerksabläufen und in Oberflächenwasser gefunden (bis zu 0,18  $\mu\text{g/L}$ ), wohingegen Diazepam in keiner der untersuchten Matrices gemessen werden konnte. Positivbefunde von Meprobamat und Pyridylidion wurden nur in rieselfeldbeeinflusstem Grundwasser (bis zu 0,50 bzw. 0,04  $\mu\text{g/L}$ ) und in Bezug auf Meprobamat auch in zehn Jahre altem Uferfiltrat (0,03  $\mu\text{g/L}$ ) bestimmt. Diese Ergebnisse unterstreichen erneut die hohe Persistenz einiger der untersuchten Verbindungen in der aquatischen Umwelt.

Auf der Grundlage der gesammelten Ergebnisse, vor allem der Befunde der Psychopharmaka im Einzugsgebiet des Wasserwerkes Friedrichshagen sowie von Primidon

und Phenylethylmalonamid im Reinwasser eines Berliner Wasserwerkes, erschien es notwendig, das **Umweltverhalten** der Schadstoffe anhand von Laborexperimenten detaillierter zu erforschen. Um das Verhalten der Substanzen unter verschiedenen Redoxbedingungen (oxisch und anoxisch) zu untersuchen, wurden Belüftungsversuche mit anoxischem Grundwasser durchgeführt. Oxazepam und Diazepam wurden von diesem Experiment ausgeschlossen, da beide Stoffe nicht in dem verwendeten Grundwasser vorlagen. Die Versuchsergebnisse zeigen, dass die untersuchten Verbindungen weder unter oxischen noch unter anoxischen Bedingungen abgebaut werden, und deuten auf eine von dem vorliegenden Redoxmilieu unabhängige Persistenz hin.

Weiterhin wurden Batch-Sorptionsversuche mit zwei Sorbenten (Pulveraktivkohle und Sand) durchgeführt. Im Allgemeinen war die Affinität zur Pulveraktivkohle größer als zu dem sandigen Sediment. Außerdem wurde sowohl Oxazepam als auch Diazepam vollständig durch Sorption an der Pulveraktivkohle innerhalb einer Kontaktzeit von 72 h aus der wässrigen Phase entfernt, wohingegen die Elimination der anderen Verbindungen weniger effektiv war (20-58 %). Schließlich wurden die experimentell bestimmten Werte zur Ermittlung von Sorptionsparametern genutzt. Die Berechnungen hatten auch das Ziel, das zukünftige Risiko für die Trinkwassergewinnung des Wasserwerkes Friedrichshagen besser beurteilen zu können. Die Risikobewertung lässt vermuten, dass die untersuchten Arzneimittel trotz ihrer recht guten Mobilität noch über mehrere Jahrzehnte bis zu Jahrhunderten in dem Grundwasserleiter verbleiben werden.

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## Abbreviations

B	Boron
BEE	Beelitzhof
BGS	Below ground surface
BIOXWAND	Acronym for the research project entitled „Entwicklung und Erprobung einer Bio-Oxidationswand im Abstrom eines hoch mit Ammonium kontaminierten Grundwasserleiters“
BMBF	Federal Ministry of Education and Research
BWB	Berliner Wasserbetriebe
$C_0$	Initial concentration
$C_s$	Equilibrium concentration of the dissolved pharmaceutical
$C_w$	Equilibrium concentration of the sorbed pharmaceutical
CDB Fe	Citrate-dithionite-bicarbonate extractable iron
CE	Collision energy
$CEC_{pot}$	Potential cation exchange capacity
$Cl^-$	Chloride
$C_{org}$	Organic matter
CV	Cone voltage
$d$	Distance
DOC	Dissolved organic carbon
DVWK	German Association for Water Resources and Land Improvement
dw	Drinking water
DWTP	Drinking water treatment plant
DZP	Diazepam
EC	Electric conductivity
eff	Effluent
Eh	Redox potential
ESI	Electrospray ionization
$f_{oc}$	Organic carbon content
$Fe_t$	Total iron content
FRI	Friedrichshagen
FUB	Freie Universität Berlin
GC-MS	Gas chromatography-mass spectrometry
gw	Groundwater
$^3H$	Tritium
$^3He$	Helium-3

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$^3\text{He}_{\text{tri}}$	Tritiogenic helium-3
$^4\text{He}_{\text{rad}}$	Radiogenic helium-4
HPLC	High-performance liquid chromatography
HPV	Health-based precautionary value
inf	Influent
KAU	Kaulsdorf
$K_d$	Distribution coefficient
KLA	Kladow
$K_{\text{OC}}$	Soil/water partition coefficient
$K_{\text{OW}}$	Octanol/water partition coefficient
LOD	Limit of detection
LOQ	Limit of quantification
M	Mass
$M_w$	Monoisotopic molecular mass
$m/z$	Mass-to-charge ratio
MP	Medium level
MPB	Meprobamate
MRM	Multiple reaction monitoring
MS	Mass spectrometry
MS/MS	Tandem mass spectrometry
MÜN	Münchehofe
n	Number of samples
$n$	Soil porosity
n.a.	Not available
n.d.	Not determined
Ne	Neon
$\text{NH}_4^+$	Ammonium
$\text{NH}_4^+\text{-N}$	Ammonium nitrogen
NIDESI	Acronym for the research project entitled „Entwicklung eines gekoppelten Nitrifikations-/Denitrifikations-Verfahrens zur in-situ Reinigung stark stickstoffbelasteter Grundwasserleiter“
$\text{NO}_2^-$	Nitrite
$\text{NO}_2^-\text{-N}$	Nitrite nitrogen
$\text{NO}_3^-$	Nitrate
$\text{NO}_3^-\text{-N}$	Nitrate nitrogen
$\text{O}_2$	Oxygen
OP	Upper level
OZP	Oxazepam



---

PAC	Powdered activated carbon
PB	Phenobarbital
PEMA	Phenylethylmalonamide
PRM	Primidone
PTD	Pyrihydione
<i>p</i> -TSA	<i>Para</i> -toluenesulfonamide
$\rho_b$	Bulk density
$R_f$	Retardation factor
RSD	Relative standard deviation
RT	Retention time
RUH	Ruhleben
SCH	Schönerlinde
SO <sub>4</sub> <sup>2-</sup>	Sulfate
SPA	Spandau
SPE	Solid phase extraction
SRM	Single reaction monitoring
STA	Stahnsdorf
STO	Stolpe
sw	Surface water
SWTP	Surface water treatment plant
<i>t</i>	Residence time
T	Temperature
TEG	Tegel
TIE	Tiefwerder
TOC	Total organic carbon
TU	Tritium unit
UBA	German Federal Environmental Agency
UHPLC	Ultrahigh-performance liquid chromatography
UHPLC-MS/MS	Ultrahigh-performance liquid chromatography-tandem mass spectrometry
UP	Lower level
<i>v</i>	Groundwater flow velocity
V	Volume
WAS	Waßmannsdorf
WDF	Wansdorf
WUH	Wuhlheide
WWTP	Wastewater treatment plant

# 1. Introduction

## 1.1 Background and problem definition

For more than a century, land disposal of untreated wastewater as well as its application for irrigation of agricultural land has been a common practice worldwide (Blume et al., 1980; Aboulroos et al., 1989; Siebe and Fischer, 1996; Hoffmann et al., 1999). Today, sewage – treated and untreated – is still widely used for irrigation purposes or groundwater recharge, especially in arid and semi-arid regions (e.g., Bouwer, 1991; Siebe and Fischer, 1996; Abdul-Ghaniyu et al., 2002; Asano and Cotruvo, 2004; Ensink et al., 2004; Scott et al., 2004; Pedersen et al., 2005). The benefits of using sewage, in particular arising for peasant farmers (Abdul-Ghaniyu et al., 2002; Scott et al., 2004), are countered by several drawbacks. Human health risks caused by pathogens and heavy metals are of major concern (Aboulroos et al., 1989; Siebe and Fischer, 1996). Another key issue is the environmental impact of wastewater irrigation, which is marked by a severe impairment of the soils and the adjacent groundwater by organic and inorganic contaminants (Blume et al., 1980; Hoffmann et al., 1999; Savric, 2001).

In Berlin (Germany), untreated wastewater had been disposed on sewage farms in the city and its surrounding area for almost 100 years (Ginzel et al., 1995; Schmidt, 1995; Hoffmann et al., 1999). This measure was necessary at the end of the 19th century in order to cope with untenable hygienic conditions and associated unpleasant odors in the rapidly growing city (Schmidt, 1995). Irrigation of Berlin wastewater began in 1876. By the year 1920, 20 sewage farm districts with an approximate area of 10,000 ha were operated (SenStadt, 2012). The surface load amounted up to 10,000 m per year (Ginzel et al., 1995). With the construction of WWTPs, sewage farms were gradually relieved (Savric, 2001; SenStadt, 2012). However, most sewage field sites were decommissioned not until the 1970s (SenStadt, 2012).

The decades lasting infiltration of wastewater has left behind large amounts of accumulated nutrients (i.e., P and N), heavy metals (i.e., Pb, Zn, Cd), and organic contaminants (i.e.,

adsorbable organic halogens, polycyclic aromatic compounds, polychlorinated biphenyls) in the local soils and aquifers of Berlin. This is confirmed by numerous previous studies on the occurrence and the dynamics of pollutants in soils and groundwater of former sewage farms in and near Berlin (e.g., Ginzler et al., 1995; Tröger and Asbrand, 1995; Heberer and Stan, 1997; Hoffmann et al., 1999; Scheytt et al., 2000; Savric, 2001; Peschka et al., 2006; Richter et al., 2009a). Particularly alarming in this context is that contaminants potentially reach groundwater supplies used as drinking water resources (Bouwer, 2000; Pedersen et al., 2005).

The DWTP FRI operated by the BWB is located in the southeast of Berlin (Figure 1.1). It is the second largest DWTP of the city and, with a daily output of approximately 125,000 Mio m<sup>3</sup>, provides roughly 22 % of the city's daily drinking water demand (BWB, 2012a). The entire drinking water production at the DWTP FRI is based on groundwater extraction, wherein primarily bank filtrate is used next to artificially recharged groundwater and ambient groundwater. The DWTP and some of its production well galleries are situated downstream of the former sewage farm district Münchehofe (Figure 1.1). In the period from 1907 to 1976, untreated sewage of domestic and industrial origin was applied to soils by flood irrigation on an area encompassing approximately 104 ha (SenStadt, 2012). Following the construction of the WWTP Münchehofe (MÜN) in 1976, WWTP effluents and temporarily also sewage sludge were applied to the sewage field until its final closure in 1991 (Engelmann et al., 1992). Thus, over decades, high pollutant loads were introduced into the soils resulting in a significant anthropogenic contamination of the sediments and the groundwater below and downgradient of the former sewage farm (Engelmann et al., 1992; Hamann, 2009; Richter et al., 2009a).

Various studies have so far dealt with the local situation and several measures have been developed and are applied in order to guarantee a safe drinking water supply at the DWTP FRI and to efficiently decontaminate the aquifer. Detailed investigations of the hydraulic properties and the state of groundwater quality have been conducted by Fugro Consult GmbH and the BWB from the 1990s on. These studies aimed at achieving a better understanding of the groundwater flow characteristics and subsequently at adjusting the pumping regime of the well galleries to ensure an as far as possible contaminant-free water supply. Since then, the hydraulic and hydrochemical conditions have been evaluated and

reported regularly (Engelmann, 1994, 1995; Engelmann et al., 1998; Schmolke and Padet, 2000; Schmolke, 2003, 2006, 2009). A general appraisal of the study area is provided by Engelmann et al. (1992).

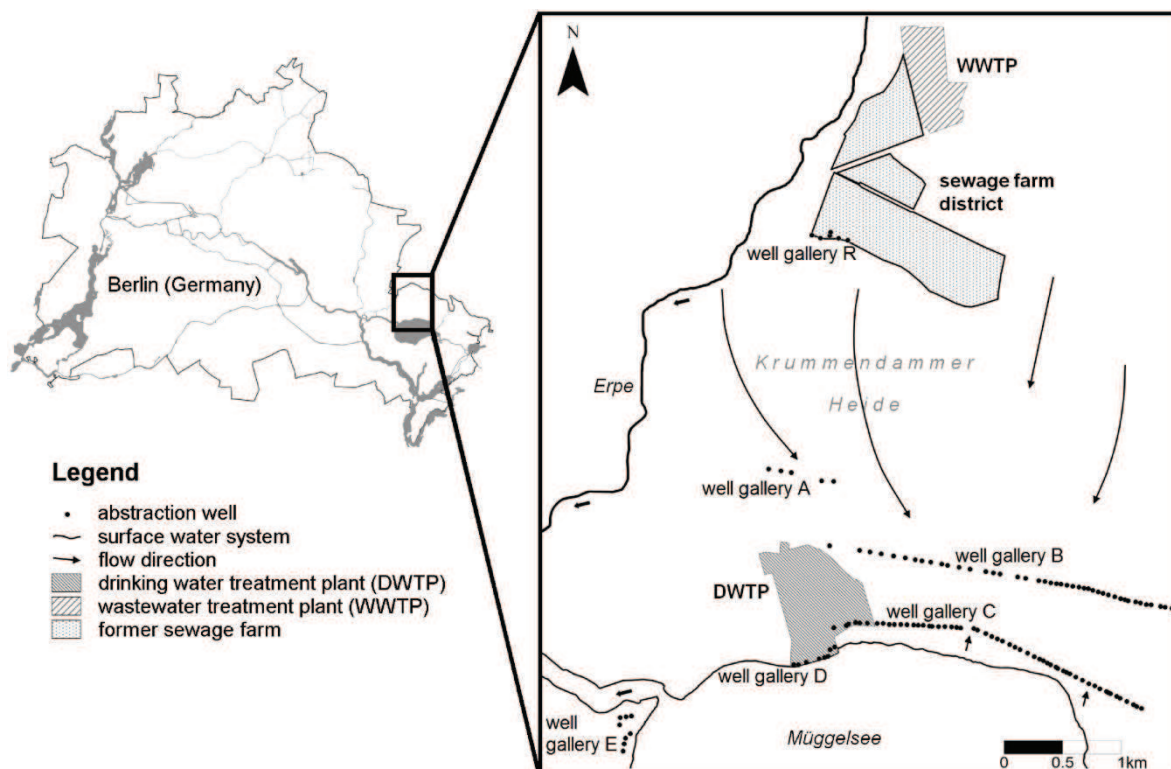


Figure 1.1 Location of the field site in the southeast of Berlin (left). Map of the investigation area Machnow/Krummendammer Heide (right) with locations of the wastewater treatment plant (WWTP), the drinking water treatment plant (DWTP), the former sewage farm, and the abstraction wells (circles). Arrows indicate the main groundwater flow direction at the study site.

High contaminant loads, first and foremost of ammonium ( $\text{NH}_4^+$ ), in the groundwater of the catchment area of the DWTP FRI necessitated the development of protective and remediation measures. The first concept applied involved the decontamination of abstracted groundwater via the nearby WWTP MÜN ("pump and treat"). For this, two protective well galleries (well gallery A: in operation since 1997; well gallery R: operated between 1998 and 2005; Figure 1.1) were established. Furthermore, two research projects were initiated with the objective of an in-situ groundwater decontamination. The examined clean-up technologies consist of the infiltration of highly oxygenated water (NIDESI – "Entwicklung eines gekoppelten Nitrifikations-/Denitrifikations-Verfahrens zur in-situ Reinigung stark

stickstoffbelasteter Grundwasserleiter"; Ehbrecht and Luckner, 2000) and the in-situ gas sparging of oxygen or air (BIOXWAND – "Entwicklung und Erprobung einer Bio-Oxidationswand im Abstrom eines hoch mit Ammonium kontaminierten Grundwasserleiters"; Ehbrecht and Luckner, 2004). Testing of the two methods was funded by the Federal Ministry of Education and Research (BMBF) and the BWB. The promising approach of in-situ oxygen/air gas injection (BIOXWAND) was further tested between July 2007 and September 2010 with a pilot experiment in order to optimize the oxygen transfer and its propagation in the groundwater amongst other things (SENSATEC, 2010). The pilot plant is currently extended to allow a large-scale treatment of the contaminated groundwater (SENSATEC, 2011). The oxidation barrier procedure was evaluated by extensive groundwater monitoring and by reactive transport modeling, which is also used for long-term prognosis of the decontamination process (Horner et al., 2009). Furthermore, another reactive multi-component transport model approach has been performed to study the migration of the  $\text{NH}_4^+$  contamination plume (Hamann, 2009).

In 2003, screenings for organic contaminants via GC-MS also disclosed the presence of three sulfonamides in the groundwater at the field site (Richter et al., 2007). Their occurrence and behavior was investigated intensively by Richter et al. (2007, 2008a; 2009a) and Meffe et al. (2010, 2012; Meffe, 2011).

Further GC-MS screenings that are regularly performed by the BWB revealed in 2009 the presence of several psychoactive drugs in the water. They were identified as meprobamate, primidone, its metabolites phenobarbital and phenylethylmalonamide, as well as pyrithyldione (Hass et al., 2011). The discovery of these partly "legacy pollutants", that is substances whose use was banned or strictly regulated years ago (TNRCC, 2000), initiated the present study.

## 1.2 Objectives of the thesis

The general objective of this thesis is to investigate the occurrence and behavior of seven psychoactive compounds, namely primidone, phenobarbital, phenylethylmalonamide, meprobamate, pyrithyldione, oxazepam, and diazepam, in the aquatic environment of Berlin. The focus of the work is placed on studying their presence and fate in groundwater influenced by former sewage irrigation. Another major purpose of this study is to evaluate the relevance of the contaminants in view of the local drinking water production.

The tasks and aims of the research include in particular the following:

- Development of a sensitive, reliable and routine analytical method to simultaneously measure the target compounds in water samples (wastewater, surface water, groundwater, and drinking water).
- Determination of the current concentration ranges and distribution patterns of the psychoactive compounds in the aquifer below and downgradient of a former sewage farm.
- Estimation of apparent groundwater ages in the study area using  $^3\text{He}$ - $^3\text{H}$  dating to gain knowledge of the groundwater age distribution throughout the aquifer and assessment of a potential correlation between groundwater ages and contaminant concentrations to obtain better understanding of the transport behavior of the pollutants.
- Determination of present concentration ranges in water samples of several types in Berlin, including wastewater, surface water, groundwater, and drinking water, to examine the fate of the pharmaceutical residues in a partially closed water cycle; in particular, investigation of the elimination during bank filtration.
- Determination of the redox-sensitivity of the compounds and investigation of their sorption affinity by means of laboratory experiments to further study their environmental behavior.
- Evaluation of the relevance of psychoactive compounds in the study area and in Berlin and assessment of the current and future risk with regard to contamination of the local drinking water on the basis of results from sampling campaigns and laboratory experiments.

### 1.3 Outline of the thesis

This PhD thesis is composed of six chapters. Chapter 1 is the introduction of the thesis. It describes the background and problem definition, provides a short overview on previous studies at the field site, and names the objectives of the thesis. Chapters 2, 3, 4 and 5 comprise the main research work conducted within the thesis. These chapters have been written as manuscripts for publication in international peer-reviewed scientific journals and accordingly, can each be read independently as self-contained pieces of work.

As already mentioned in the Preface, I, as the first author, have been responsible for the substantial scientific work in all four cases. The development, organization and realization of the research work described have been carried out by me. I have been in charge of the composition of the scientific content and of the preparation of the manuscripts. Literature review, data interpretation, data display, and manuscript writing were done by me. Other co-authors have mainly played an advisory and supervisory role.

The papers have been re-edited for a consistent layout. They are as follows:

- Chapter 2: Analytical method

is published as:

Ulrike Hass, Uwe Dünnebier, Gudrun Massmann, Asaf Pekdeger (2011). *Simultaneous determination of psychoactive substances and their metabolites in aqueous matrices by ultrahigh-performance liquid chromatography-tandem mass spectrometry*. *Analytical Methods*, 3 (4), 902-910.

Chapter 2 focuses on the newly developed analytical method. First, the background of the study is roughly described and information on the selected analytes are provided. Above all, the analytical procedure is presented in detail. UHPLC-MS/MS was used and allows a sensitive and simultaneous quantification of seven psychoactive compounds in environmental water samples. Validation of the analytical technique was performed, including the determination of LOQs and recoveries for different aqueous matrices. Furthermore, the influence of matrix effects on measurements was determined

and is discussed. Finally, the analytical method was applied for the first time to groundwater and wastewater samples and first results are presented.

- Chapter 3: Occurrence in polluted groundwater

is published as:

Ulrike Hass, Uwe Dünnebier, Gudrun Massmann (2012). *Occurrence of psychoactive compounds and their metabolites in groundwater downgradient of a decommissioned sewage farm in Berlin (Germany)*. Environmental Science and Pollution Research, 19 (6), 2096-2106.

The emphasis of Chapter 3 lies on the presence of the psychoactive compounds in groundwater downgradient of a former sewage farm. Initially, an overview of the study area is given with details on former sewage farm operation, the groundwater pollutant situation, and prevailing hydrogeological and hydrodynamic conditions. Extensive field sampling was conducted to investigate the occurrence and distribution of the target analytes. Local monitoring revealed elevated concentrations of the pharmaceutical residues throughout the study area. Their distribution is illustrated by means of contaminant plumes. Considering the entry periods of the pollutants, findings suggest long-term persistence in the environment under anoxic aquifer conditions. To obtain better knowledge of the present hydrogeological settings, age dating was performed at selected sampling points. For this, the  $^3\text{He}$ - $^3\text{H}$  dating method, which is described in general terms, was applied. Outcomes exhibit that the apparent groundwater age can be correlated with aquifer depth and with the concentrations of psychoactive compounds. Finally, results are discussed and interpreted in the context of risk assessment for the local drinking water production.

- Chapter 4: Occurrence in the water cycle of Berlin

is published as:

Ulrike Hass, Uwe Dünnebier, Gudrun Massmann (2012). *Occurrence and distribution of psychoactive compounds and their metabolites in the urban water cycle of Berlin (Germany)*. Water Research, 46 (18), 6013-6022.



Chapter 4 initially provides an overview of Berlin's partially closed water cycle. Owing to the nature of the Berlin water system, a number of persistent pollutants may potentially reach drinking water resources via bank filtration and artificial recharge if present in WWTP effluents and/or surface waters. For this reason, the focus of this chapter is placed on the occurrence and fate of the psychoactive drugs in the city's aquatic system. In this connection, WWTP effluents, surface water samples, bank filtrate, groundwater influenced by former sewage irrigation as well as raw and final drinking water were analyzed for the target compounds. Results are discussed for the individual substance taking into account local conditions. A closer look is taken at the behavior of the contaminants during bank filtration and the risk of contamination of raw and final drinking water is evaluated.

- Chapter 5: Redox-sensitivity and sorption behavior

is under review as:

Ulrike Hass, Uwe Dünnebier, Gudrun Massmann. *Redox-sensitivity and sorption behavior of psychoactive compounds in groundwater*. Water Environment Research (submitted on 01 Oct 2012).

Chapter 5 deals with the behavior of the psychoactive compounds in groundwater. The aim is to achieve an advanced understanding of potential processes and to carry out further risk assessment with regard to drinking water production in the study area. To this end, laboratory experiments were conducted to investigate the redox-sensitivity and sorption behavior of the contaminants. The paper provides comprehensive explanations of the experimental designs and procedures. Experimental results are discussed for the individual compounds and resulting calculated sorption parameters are used for further risk estimation.

Chapter 6 summarizes the conclusions of this thesis. It highlights the major outcomes of this work and provides recommendations for future research.

The Appendix contains additional figures and tables that have been included in the original manuscripts as supplementary material (Chapters 3 and 5).

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## 2. Analytical method

An analytical method was developed and validated for the simultaneous determination of six psychoactive compounds (meprobamate, primidone, phenobarbital, pyrithyldione, diazepam, and oxazepam) and a metabolite of primidone (phenylethylmalonamide) in environmental water samples. The method involves pre-concentration and clean-up by solid phase extraction (SPE) followed by ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS), using electrospray ionization (ESI) in both positive and negative modes. Limits of quantification (LOQs) were between 0.02 and 0.03  $\mu\text{g/L}$  in groundwater and between 0.1 and 0.15  $\mu\text{g/L}$  in wastewater. With a few exceptions, relative recoveries of the analytes exceeded 80 %. The described method was used to analyze the selected psychoactive drugs in groundwater that had been affected by sewage irrigation for several decades ago and treated and untreated wastewater from Berlin (Germany). Highest values were found in groundwater with concentrations reaching up to 1.35  $\mu\text{g/L}$  in the case of phenobarbital.

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Ulrike Hass, Uwe Dünnbier, Gudrun Massmann, Asaf Pekdeger (2011)

*Simultaneous determination of psychoactive substances and their metabolites in aqueous matrices by ultrahigh-performance liquid chromatography-tandem mass spectrometry.*

Analytical Methods, 3 (4), 902-910.\*

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## 2.1 Introduction

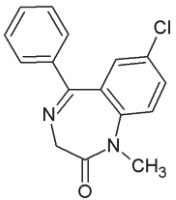
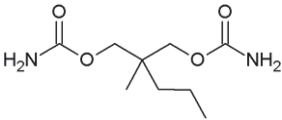
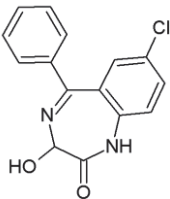
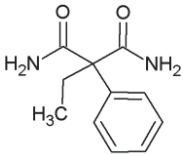
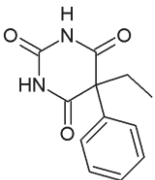
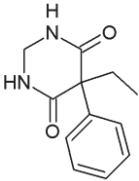
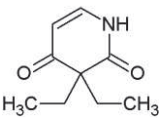
In recent years, the presence of organic micropollutants in the aquatic environment and their potential adverse effects on human and ecological health have raised great scientific and public concerns (e.g., Heberer, 2002a; Schwarzenbach et al., 2006). Discharges of municipal wastewater effluents into the surface water courses are considered as a significant source for various trace contaminants, such as pharmaceutical residues and their metabolites, due to the incomplete elimination during treatment (e.g., Ternes, 1998; Heberer, 2002a; Kreuzinger et al., 2004). In the past, prior to the establishment of wastewater treatment plants (WWTPs), it was a common practice worldwide to disperse untreated wastewater into sewage farms or agricultural lands (e.g., Blume et al., 1980; Aboulroos et al., 1989; Hoffmann et al., 1999). At the end of the 19th century, sewage farms were established in Berlin and its surroundings in order to overcome poor hygienic conditions and odor issues in the fast growing city (Ginzel et al., 1995; Schmidt, 1995). Thus, until the 1980s, untreated wastewater was irrigated directly onto the soils of several irrigation fields (Richter et al., 2008b; SenStadt, 2012). Despite partial removal of pollutants through sorption and degradation during percolation through the soil, it is confirmed that contaminants have been leaching into the local aquifers of Berlin, potentially reaching drinking water sources (Ginzel et al., 1995; Scheytt et al., 2000; Pedersen et al., 2005; Heberer et al., 2008). Recent studies have revealed the presence of anthropogenic organic trace compounds in groundwater as a consequence of wastewater infiltration in, for example, the USA (Drewes et al., 2003), Mexico (Siemens et al., 2008), Austria (Kreuzinger et al., 2004), and Berlin (Heberer and Stan, 1997; Peschka et al., 2006; Richter et al., 2007).

In 2009, several gas chromatography-mass spectrometry (GC-MS) screenings for organic contaminants in groundwater below former sewage farms in Berlin were carried out by the Berliner Wasserbetriebe. These screenings revealed the presence of several psychoactive drugs identified as meprobamate, primidone, its metabolites phenobarbital and phenylethylmalonamide, as well as pyrithyldione in the water. Meprobamate, an anxiolytic drug was introduced in the market in 1955, but was largely superseded by benzodiazepines in the 1960s (Müller and Hartmann, 1995). Since 1970, meprobamate has been listed as a

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controlled substance (Goldberg, 2005) and now has no indication eligibility. Primidone is used as an anticonvulsant and was introduced into the German market in 1950 (Fazekas and Rengei, 1960). In humans and animals, primidone is metabolized into two major pharmacologically active substances, phenobarbital and phenylethylmalonamide (El-Masri and Portier, 1998). Phenylethylmalonamide has no medical application, whereas the barbiturate phenobarbital is widely used as an anticonvulsant itself. Phenobarbital was introduced into the German market in 1912 as a sedative and hypnotic, but was replaced in the 1960s by benzodiazepines for these indications (Linde, 1992; Peschka et al., 2006). Pyrithyldione is also a sedative-hypnotic drug, introduced into the German market in 1949 under the brand name Persedon® (Linde, 1992). Due to adverse effects (Ibáñez et al., 2000) it was withdrawn in 1983. Another two psychoactive drugs that could not be identified during GC-MS screenings but are of interest due to their extensive use since the 1960s were the subject of the investigation. Diazepam and oxazepam, both benzodiazepine derivative drugs, are commonly used for the treatment of anxiety and insomnia. Furthermore, oxazepam is an active metabolite of numerous benzodiazepines (Mutschler et al., 2001). Chemical structures and formulas as well as origin of the compounds are shown in Table 2.1.

Table 2.1 Chemical structures, CAS numbers, and origin/use of the selected pharmaceuticals and metabolites.

Compound	Structure	CAS RN $M_w^a$ (g/mol) formula	Origin/use
Diazepam		439-14-5 284.74 $C_{16}H_{13}ClN_2O$	Tranquilizer
Meprobamate		57-53-4 218.25 $C_9H_{18}N_2O_4$	Tranquilizer
Oxazepam		60475-1 286.72 $C_{15}H_{11}ClN_2O_2$	Tranquilizer
Phenylethyl-malonamide		7206-76-0 206.24 $C_{11}H_{14}N_2O_2$	Metabolite of primidone
Phenobarbital		50-06-6 232.24 $C_{12}H_{12}N_2O_3$	Antiepileptic Hypnotic/Sedative Metabolite of primidone
Primidone		125-33-7 218.25 $C_{12}H_{14}N_2O_2$	Antiepileptic
Pyrithyldione		77-04-3 167.21 $C_9H_{13}NO_2$	Hypnotic/Sedative

<sup>a</sup> Monoisotopic molecular mass.

So far, various analytical methods for the individual determination of the investigated psychoactive drugs and metabolites in biological matrices, such as urine or blood plasma, have been published, including GC-MS and LC-MS techniques (e.g., Maurer, 1990; Subramanian et al., 2008). Some methods also exist for detection in environmental water samples. Applying LC-MS/MS, Vanderford and Snyder (2006) detected meprobamate in wastewater (1.44  $\mu\text{g/L}$ ), surface water (0.59  $\mu\text{g/L}$ ), and in source drinking water (0.02  $\mu\text{g/L}$ ) in the USA, whereas diazepam concentrations were lower than 0.01  $\mu\text{g/L}$  or below the LOQ (0.0025  $\mu\text{g/L}$ ). Van der Ven et al. (2004) reported concentrations of diazepam in the wastewater in Belgium of up to 1.18  $\mu\text{g/L}$ . Several authors investigated the occurrence of oxazepam in water samples from Germany and found oxazepam was present in wastewater and surface water but could not be detected in drinking water (e.g., Reddersen, 2004; Hummel et al., 2006). The presence of the anticonvulsant primidone in environmental water samples has frequently been studied (Drewes et al., 2003; Hummel et al., 2006; Guo and Krasner, 2009) and a few reports exist on the quantification of primidone in the water cycle of Berlin. For instance, primidone has been reported to be present in the municipal wastewater in concentrations ranging from 0.2 to 1.32  $\mu\text{g/L}$  (Heberer, 2002b; Drewes et al., 2003; Reddersen, 2004) while Massmann et al. (2007) quantified primidone in two lakes at maximum concentrations of 0.25 and 0.48  $\mu\text{g/L}$ , respectively. To our knowledge, the metabolite phenylethylmalonamide and the sedative pyrithyldione have so far not been investigated in aqueous matrices, and no routine method has been described for the combined quantitative analysis of meprobamate, primidone, phenylethylmalonamide, phenobarbital, pyrithyldione, diazepam, and oxazepam in water.

The presence of psychoactive substances in the Berlin water cycle and most importantly in groundwater used for drinking water production raised concerns. Therefore, a sensitive and reliable analytical method for the simultaneous detection and quantification of the described psychoactive compounds was developed and is presented in this paper. The analytical method was applied to water samples from various compartments of the Berlin water cycle (groundwater, as well as untreated and treated wastewater) in order to determine the performance and limitations of the method. First results are presented in this paper. The method forms the basis for future studies planned to evaluate the environmental relevance of the selected compounds and to monitor their occurrence and behavior in the aquatic environment.

## 2.2 Materials and methods

### 2.2.1 Materials

The reference compounds diazepam (99 %), meprobamate (98 %), oxazepam (99 %), and phenobarbital (99 %) were purchased from Cerilliant (Round Rock, TX, USA). Primidone (98 %) was obtained from Sigma-Aldrich (Steinheim, Germany), and phenylethylmalonamide (98 %) from Toronto Research Chemicals (Toronto, ON, Canada). Pyrithyldione was kindly provided by the Institute of Doping Analysis and Sports Biochemistry Dresden in the form of a tablet of Benedorm® containing 200 mg of the active pharmaceutical ingredient.

The surrogate standards meprobamate-*d*7 (99 %) and phenobarbital-*d*5 (99 %) were derived from Cerilliant (Round Rock, TX, USA). Oxazepam-*d*5 (98 %) was supplied by Sigma-Aldrich (Steinheim, Germany) and primidone-*d*5 (98 %) was acquired from Toronto Research Chemicals (Toronto, ON, Canada). Individual stock solutions (0.1 mg/mL or 1 mg/mL) were prepared in methanol, except primidone which was dissolved in dimethyl sulfoxide. Mixed standard solutions were prepared at the 10 ng/mL level in methanol and subsequently diluted as necessary. All solutions were stored in darkness at -20 °C.

Methanol, acetone, acetic acid, and dimethyl sulfoxide were of HPLC grade or higher quality. Ultrapure water was prepared in a Milli-Q system (Millipore, Billerica, MA, USA). Distilled water was delivered by a water purification system from WAT-membratec (Erkrath, Germany).

### 2.2.2 Sample origin, collection and storage

Drinking water samples, which were used for method validation, were collected from taps in the waterworks after treatment. The investigated groundwater samples were taken as grab samples in several areas downstream of former sewage farms located within the city boundaries or just outside of Berlin. These groundwater resources are known to be contaminated by organic trace components due to the direct irrigation of untreated wastewater for decades (Richter et al., 2008b). Overall, 109 groundwater samples were pumped from observation wells between April and May 2010. Groundwater sample

retrieval was in accordance with the official guidelines of the German Association for Water Resources and Land Improvement (DVWK guidelines) (DVWK, 1992). Wastewater influent and effluent samples were collected as 24 h composite samples from six municipal WWTPs of Berlin. All investigated WWTPs involve mechanical treatment, an activated sludge system with enhanced nutrient (phosphorus and nitrogen) removal, and a final clarification step. Sampling took place during May and June 2010 using an automatic sampler. Sample collection of the effluent was delayed relative to the influent to account for the residence time of the wastewater in the WWTP.

Samples were taken in glass bottles and, as far as possible, extracted immediately or stored in the dark at 4 °C for less than 14 days. Wastewater samples were extracted and analyzed as soon as possible to avoid analyte losses by microbial degradation.

### 2.2.3 Sample preparation

All analytes were extracted simultaneously using 6 mL RP-C18 sorbent cartridges (500 mg) obtained from Mallinckrodt Baker (Deventer, The Netherlands). SPE was performed on an automated extraction system (AutoTrace SPE Workstation) from Zymark (Hopkinton, MA, USA). The SPE cartridges were sequentially preconditioned with 4 mL of 80/20 (v/v) methanol/acetone, 4 mL of methanol, and 4 mL of distilled water. 250 mL sample aliquots were spiked with 50 µL of a surrogate standard solution (phenobarbital-*d5* at 2.0 ng/µL, primidone-*d5* and meprobamate-*d7* at 1.0 ng/µL, and oxazepam-*d5* at 0.5 ng/µL) and percolated through the cartridges at a flow rate of 15 mL/min. For the analysis of influent samples, 100 mL sample aliquots were filtered through 0.45 µm filters (Macherey Nagel, Germany) and subsequently filled to a volume of 250 mL using ultrapure water. Dilution was performed to minimize signal suppression effects during UHPLC-MS/MS analysis caused by matrix-components. The cartridges were then rinsed with 4 mL of distilled water. After drying the cartridges for 15 min with a stream of nitrogen, the analytes were eluted twice with 2 mL of 80/20 (v/v) methanol/acetone. Subsequently, the eluates were concentrated to a volume of 500 µL by a gentle nitrogen flow at 25 °C using a Turbo Vap II Workstation from Zymark (Hopkinton, MA, USA). Finally, the extract was brought to a final volume of 1 mL with acidified ultrapure water (0.4 % acetic acid, v/v), transferred into a vial, and stored in the dark at 4 °C for up to two weeks prior to analysis.



#### 2.2.4 Ultrahigh-performance liquid chromatography-tandem mass spectrometry

Sample extracts were analyzed by UHPLC-MS/MS. Chromatographic separation was performed on a Waters ACQUITY UPLC system (Waters, Milford, MA, USA) equipped with a degasser, a binary pump, an autosampler, and a column heater. Analytes were separated by gradient elution at 40 °C using a Waters ACQUITY UPLC BEH C<sub>18</sub> column (50 x 2.1 mm, 1.7 μm) and an ACQUITY UPLC column in-line filter unit (0.2 μm) (Waters, Milford, MA, USA). Eluents were ultrapure water (A) and methanol (B), each modified with 0.2 % (v/v) acetic acid. The flow rate of the mobile phase was set to 0.2 mL/min. The composition of the elution gradient was as follows: 30 % (B) held for 0.6 min, increased linearly to 90 % (B) by 6 min and held for 2 min. A 3 min equilibration step at 30 % (B) was applied at the beginning of each run to bring the total run time per sample to 11 min. A sample volume of 5 μL was injected in the 'partial loop with needle overflow' mode using a loop size of 10 mL. Ultrapure water/methanol (80/20, v/v) and methanol served as needle wash solvents.

A Quattro Micro tandem mass spectrometer (Waters/Micromass, Manchester, UK) equipped with ESI was used for MS/MS detection. The system was controlled from MassLynx 4.1 (Waters/Micromass, Manchester, UK). All analytes were determined either in positive or negative mode by multiple reaction monitoring (MRM). The ESI source was operated at a temperature of 120 °C, and desolvation was performed at 400 °C with a desolvation gas flow of 650 L/h and a cone gas flow of 30 L/h. Desolvation and nebulization were achieved using high-purity nitrogen. Argon (99,998 %) served as the collision gas. The capillary voltage was adjusted to 2.8 kV.

MS/MS parameters (precursor ions, product ions, collision energy, cone voltage) were optimized by infusing a 500 pg/μL solution of each individual compound dissolved in acidified ultrapure water/methanol (50/50 v/v) and delivered by a syringe pump at a flow rate of 20 mL/min with a background mobile phase of acidified ultrapure water/methanol (50/50 v/v) at 0.05 mL/min.

Retention times, precursor and product ion masses, and the individually optimized parameters, cone voltage and collision energy, are compiled in Table 2.2. Product ions of higher signal intensities are listed first. Data acquisition was carried out using retention

time windows with dwell times for single reaction monitoring (SRM) set to 0.05-0.20 s, depending on the signal intensity of the product ions. An example of extracted MRM chromatograms for the investigated compounds in spiked WWTP influent is shown in Figure 2.1.

Table 2.2 Retention times, precursor ions, product ions, and MRM conditions for UHPLC-MS/MS measurements.

Compound	RT (min)	Precursor ion <sup>a</sup> ( <i>m/z</i> )	Product ions ( <i>m/z</i> )	CV <sup>b</sup> (V)	CE <sup>b</sup> (eV)
<b>ESI +</b>					
Diazepam	5.10	285.0	193.0	35	33
		287.0	193.0	35	33
Meprobamate	2.97	219.0	158.1	15	7
			97.1	15	15
Meprobamate- <i>d7</i>	2.95	226.2	165.1	10	10
			104.0	10	15
Oxazepam	4.52	287.0	241.0	25	20
		289.0	243.0	28	20
Oxazepam- <i>d5</i>	4.49	291.9	246.0	24	24
			274.0	24	15
Phenylethylmalonamide	1.24	207.0	161.9	17	12
			91.0	17	25
Primidone	2.22	219.1	162.0	17	12
			91.0	17	25
Primidone- <i>d5</i>	2.19	224.0	167.0	22	12
			124.1	22	16
Pyrithyldione	1.94	168.1	140.1	17	17
			122.1	17	17
<b>ESI -</b>					
Phenobarbital	2.82	231.0	41.8	40	12
			85.0	40	12
Phenobarbital- <i>d5</i>	2.77	236.0	41.7	40	25

<sup>a</sup> ESI+ [M + H]<sup>+</sup>, for diazepam and oxazepam chlorine isotopes <sup>37</sup>Cl; ESI- [M - H]<sup>-</sup>.

<sup>b</sup> Cone voltages and collision energies for the individual product ions.

RT = retention time; CV = cone voltage; CE = collision energy.

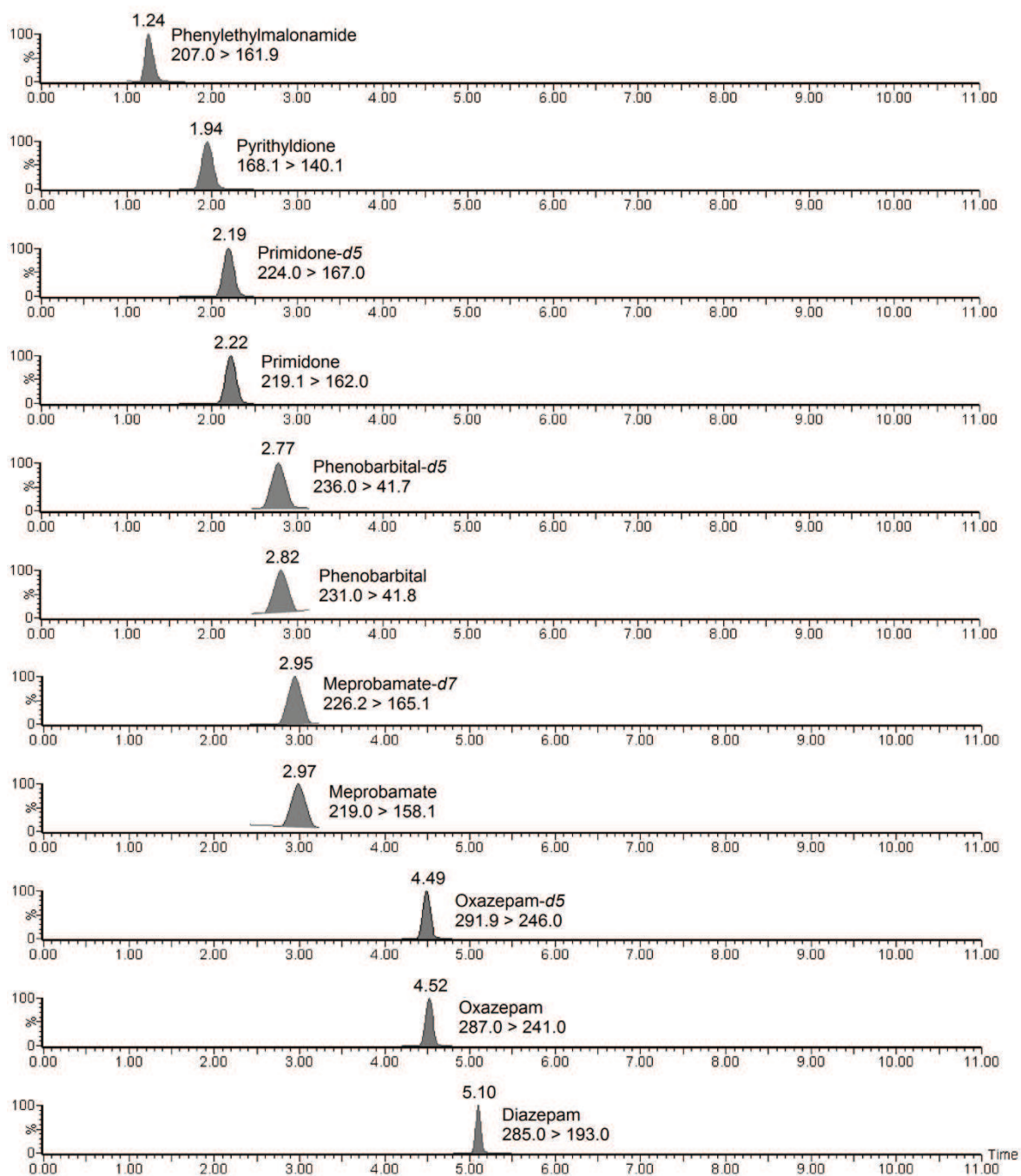


Figure 2.1 Extracted multi-reaction monitoring (MRM) chromatograms for target compounds and surrogates in a spiked WWTP influent sample at 0.4 µg/L. Only the most intense trace is shown. Time scale is minutes.

### 2.2.5 Confirmation and calibration

Together with the retention times, two MRM transitions for each substance were monitored for identification and quantification of the analytes, except phenobarbital-*d5* with only one transition. Quantification of the analytes was performed with QuanLynx (Waters/Micromass, Manchester, UK) using the most intense product ion.

For quantification, internal standard calibration over the complete analytical method, including sample preparation, was employed. Calibration curves with six calibration levels ranging from 0.02 to 2.0 µg/L and a blank matrix were prepared by spiking drinking water collected from taps in the waterworks after treatment. The used drinking water showed no detectable residues of the analytes. A concentration range of two orders of magnitude was covered and concentrations in the environment were expected to fall within this range. Calibration curves were generated by linear regression of peak areas of standard solutions (spiked drinking water) against their respective concentrations, corrected with the appropriate surrogate standards (Table 2.3). A 1/x weighting factor was applied to compensate for heteroscedasticity. The intercept was not forced through zero. Calibration curves were analyzed at the beginning and end of each sample batch.

## 2.3 Results and discussion

### 2.3.1 Method sensitivity and linearity

The sensitivity of the method was evaluated by determination of the limits of detection (LOD) and LOQs for each of the investigated compounds. LODs and LOQs were calculated according to the German Industrial Norm DIN 32645 (2008) with a  $\alpha$ -error of 1 % and a relative confidence interval ( $1/k$ ) of 33.3 %. For the estimation of the LODs and LOQs, non-contaminated drinking water and groundwater samples were spiked with a standard mixture of the selected pharmaceuticals at the low concentration range from 0.01 to 0.1 µg/L using equidistant concentration levels. Thus, LOQs were between 0.02 and 0.03 µg/L for all analytes (Table 2.3). Obtained LODs and LOQs for drinking water were identical to those calculated for groundwater. As suggested by Ternes et al. (2001), LOQs

for wastewater were calculated by multiplying the LOQs for groundwater by a factor of five, which is an empirical worst-case value appropriate even for extremely polluted waters.

The linearity of the method was investigated by calculating regression lines as described in the Materials and methods and is expressed by correlation coefficients ( $r^2$ ). All calibration graphs were linear between 0.02 and 2.0  $\mu\text{g/L}$  and correlation coefficients were typically greater than 0.991 indicating good linearity (Table 2.3).

To examine the reproducibility on repeated injections, groundwater samples spiked at two concentration levels (0.04 and 0.4  $\mu\text{g/L}$ ) were re-injected ten times within one batch. The precision was expressed as percent relative standard deviation (RSD) of replicate measurements using the peak areas for calculation and all individual values ( $n = 10$ ) were weighted equally. Repeatability of replicate measurements was satisfactory, with RSD values ranging from 0.8 to 9.4 % at 0.04  $\mu\text{g/L}$  and from 0.4 to 2.1 % at 0.4  $\mu\text{g/L}$ .

Table 2.3 summarizes the LODs, LOQs, calibration correlation coefficients, and results from replicate measurements at 0.04  $\mu\text{g/L}$  for each of the studied psychoactive compounds.

*Table 2.3 Limits of detection (LOD), limits of quantification (LOQ), calibration correlation coefficients ( $r^2$ , 0.02-2.0  $\mu\text{g/L}$ ), and repeatability of replicate measurements (% RSD, 0.04  $\mu\text{g/L}$ ,  $n = 10$ ) for groundwater.*

<b>Compound</b>	<b>Surrogate standard</b>	<b>LOD (<math>\mu\text{g/L}</math>)</b>	<b>LOQ (<math>\mu\text{g/L}</math>)</b>	<b><math>r^2</math></b>	<b>% RSD</b>
Diazepam	Oxazepam- <i>d5</i> <sup>a</sup>	0.01	0.02	0.996	0.8
Meprobamate	Meprobamate- <i>d7</i>	0.01	0.02	0.997	3.2
Oxazepam	Oxazepam- <i>d5</i>	0.01	0.02	0.997	1.8
Phenylethylmalonamide	Primidone- <i>d5</i>	0.01	0.03	0.991	2.6
Primidone	Primidone- <i>d5</i>	0.01	0.02	0.998	2.6
Pyrrithyldione	Primidone- <i>d5</i>	0.01	0.02	0.996	1.7
Phenobarbital	Phenobarbital- <i>d5</i>	0.01	0.03	0.996	9.4

<sup>a</sup> Oxazepam-*d5* is inappropriate as surrogate standard.

### 2.3.2 Recovery experiments

To determine analyte recoveries, two types of extracts (E1 and E2) were prepared for all matrices investigated, including drinking water and groundwater, as well as untreated and treated wastewater using the method described above. Extract 1 (E1) was prepared by processing 250 mL of sample spiked with analytes at a concentration of 0.4 µg/L and surrogate standards. Wastewater samples were spiked at individual concentrations of 1.0 µg/L. The second extract (E2) was spiked after SPE elution and subsequently processed throughout the rest of the sample treatment procedure. Four recovery experiments were performed for each type of aqueous matrix. Unspiked samples were used as a control.

Extraction recoveries of the analytes from the matrices were calculated by comparing the respective analyte response factors in E1 to those in E2 (Weiss and Reemtsma, 2005; Ye et al., 2007). Absolute recoveries for the entire method were estimated by comparing the respective E1 response factor to that in a non-enriched standard solution E3 at 0.4 µg/L and 1.0 µg/L. Relative recoveries were determined by correcting absolute recoveries with the recovery of the spiked surrogate standards (Ternes et al., 2001; Hummel et al., 2006). Results from recoveries experiments are shown in Table 2.4.

The obtained extraction recoveries for drinking water, groundwater, and wastewater samples were satisfactory for most of the compounds, typically ranging from 84-102 % (Table 2.4). However, lower recoveries (52-71 %) were generally observed for phenylethylmalonamide, and also for oxazepam and phenobarbital in groundwater and wastewater, respectively. Phenylethylmalonamide was integrated into the analytical method at a later stage, and thus the selected SPE material might not be appropriate for the extraction of this analyte.

*Table 2.4 Extraction and overall (absolute and relative) recoveries (%) and relative standard deviations (% RSD) of target compounds in different aqueous matrices (drinking water and groundwater were spiked with 0.4 µg/L, and untreated and treated wastewater samples were spiked with 1.0 µg/L; n = 4).*

Compound	Recovery ± RSD (%) <sup>a</sup>															
	Drinking Water				Groundwater				WWTP Influent				WWTP Effluent			
	SPE <sup>b</sup>	Overall Recovery <sup>c</sup>	Relative <sup>d</sup>		SPE <sup>b</sup>	Overall Recovery <sup>c</sup>	Relative <sup>d</sup>		SPE <sup>b</sup>	Overall Recovery <sup>c</sup>	Relative <sup>d</sup>		SPE <sup>b</sup>	Overall Recovery <sup>c</sup>	Relative <sup>d</sup>	
Diazepam	100 ± 2	88 ± 2	113 ± 1	99 ± 2	86 ± 1	157 ± 3	84 ± 11	37 ± 9	146 ± 8	95 ± 8	64 ± 7	128 ± 8				
Meprobamate	102 ± 3	85 ± 3	101 ± 3	100 ± 3	80 ± 2	97 ± 2	94 ± 4	25 ± 5	73 ± 3	93 ± 10	49 ± 11	82 ± 11				
Oxazepam <sup>e</sup>	97 ± 2	77 ± 3	99 ± 1	71 ± 3	53 ± 4	97 ± 2	91 ± 6	21 ± 5	85 ± 2	91 ± 7	43 ± 6	85 ± 7				
Phenylethylmalonamide	64 ± 9	65 ± 10	83 ± 11	63 ± 17	59 ± 15	77 ± 15	52 ± 21	8 ± 17	24 ± 15	64 ± 18	30 ± 19	62 ± 21				
Primidone	100 ± 2	79 ± 2	101 ± 2	98 ± 3	72 ± 2	95 ± 0	90 ± 11	23 ± 6	69 ± 3	97 ± 6	43 ± 6	86 ± 4				
Pyrrithyldione	95 ± 2	82 ± 1	104 ± 1	91 ± 6	77 ± 5	102 ± 4	84 ± 5	43 ± 7	127 ± 4	87 ± 8	48 ± 10	100 ± 9				
Phenobarbital	98 ± 3	84 ± 1	95 ± 5	97 ± 5	79 ± 3	89 ± 3	59 ± 16	60 ± 17	92 ± 3	67 ± 10	40 ± 13	83 ± 1				

<sup>a</sup> Mean values from n = 4 determinations.

<sup>b</sup> E1/E2.

<sup>c</sup> E1/E3.

<sup>d</sup> Calculated using the recovery of the spiked surrogate standard.

<sup>e</sup> Oxazepam-d5 is inappropriate as surrogate standard.

Recoveries of the entire method take into account both the loss of analytes during sample preparation as well as matrix effects during LC-MS/MS analysis. Absolute “overall” recoveries were considerably influenced by the sample matrix as further discussed below. Thus, for drinking water and groundwater, absolute recoveries exceeded 72 % with the exception of phenylethylmalonamide (59-65 %) and oxazepam in groundwater (53 %), whereas distinctly lower recoveries were observed for WWTP influent and effluent samples. Besides matrix effects, leading to signal suppression and thus being a major cause for low absolute recoveries down to 21 % (oxazepam) and 8 % (phenylethylmalonamide), degradation processes might occur during sample preparation and have to be taken into consideration. For most compounds these losses were partially compensated by using selected deuterated surrogate standards. As illustrated in Table 2.4, this practice greatly improved spike recoveries. However, at the beginning of the study, no isotope-labeled standards for pyrithyldione and phenylethylmalonamide were available from commercial suppliers. The use of primidone-*d5* as a surrogate standard for phenylethylmalonamide is not optimal and still leads to an underestimation of the compound. On the other hand, the application of primidone-*d5* for the quantification of pyrithyldione leads to a significant improvement of recovery results, since both compounds exhibit a comparable elution behavior. Elevated relative recoveries of up to 157 % indicate oxazepam-*d5* is not an appropriate surrogate standard for the determination of diazepam, although both substances show similar chromatographic properties. Therefore, subsequent analysis will be carried out with an additional deuterated surrogate standard for diazepam.

Considering the reproducibility of the procedure, good results were obtained for most of the analytes and all sample matrices with RSDs equal to or less than 17 %, except for phenylethylmalonamide with RSDs of up to 21 % (Table 2.4).

### 2.3.3 Matrix effects

One adverse aspect associated to LC-ESI-MS/MS analysis is the existence of matrix effect problems, especially for complex matrices such as environmental samples and wastewater (Annesley, 2003). The phenomena of matrix-related ion suppression or enhancement during ESI, which can severely affect the quantitative performance of a mass detector, are suggested to result from a change in droplet formation and evaporation efficiency caused by



the presence of less volatile coeluting matrix components (Annesley, 2003). However, several approaches can be employed to compensate for signal suppression effects. Amongst others, a widespread method is the removal of interfering matrix components prior to LC-MS analysis via effective sample cleanup steps (Annesley, 2003; Hummel et al., 2006). Signal enhancement can also be achieved through the utilization of buffer additives in the mobile phase, such as ammonium formate, acetic acid, and formic acid (Annesley, 2003). In the current method, acetic acid was found to be the most effective additive for the compounds determined. A suitable option to ensure accurate analyte quantification is the use of appropriate internal/surrogate standards (Annesley, 2003). Therefore, in this study, four deuterated surrogate standards were utilized. Additionally, matrix-containing WWTP influent samples were diluted by a factor of 2.5 with ultrapure water in order to suppress interfering matrix effects.

To evaluate the presence of matrix effect problems an approach similar to that described by Weiss and Reemtsma (2005) and Ye et al. (2007) was used. The influence of the matrix during ESI was determined for all investigated aqueous matrices by comparing the response of the analyte in E2 to that in E3, thus calculating analyte recoveries excluding losses caused by SPE. Results from the determination of matrix effects are illustrated in Figure 2.2.

Matrix effects in drinking water and groundwater were acceptable since they did not exceed 20 % in most cases. However, ion suppression in sample extracts from WWTP effluents and influents was of major relevance and varied between 33 and 56 %, and 49 and 84 %, respectively. A slight signal enhancement (103 %) was observed for phenylethylmalonamide in drinking water and phenobarbital in wastewater influent. The largest degree of ion suppression was found for phenylethylmalonamide, which is the first analyte to elute from the chromatographic column and is therefore more affected by matrix effects (Niessen et al., 2006).

The obtained results demonstrate that the use of suitable surrogate standards for quantification is recommended for all types of samples and is absolutely essential for wastewater samples. Additional work is necessary to achieve enhanced recovery for phenylethylmalonamide. However, the described method will be tested using real samples

to assess its suitability until a better method for phenylethylmalonamide detection can be developed.

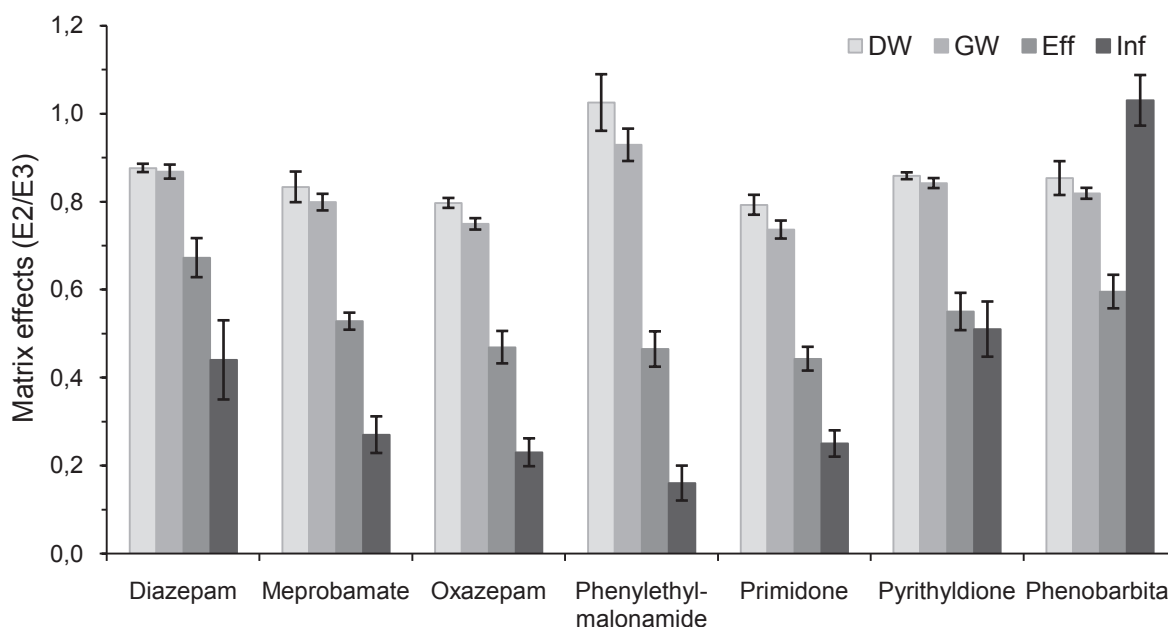


Figure 2.2 Matrix effects of the target compounds in drinking water (DW), groundwater (GW), WWTP effluent (Eff) and influent (Inf).

### 2.3.4 Application to environmental water samples

The analytical method described above was successfully applied to investigate the occurrence of diazepam, meprobamate, oxazepam, phenylethylmalonamide, primidone, pyrithyldione and phenobarbital in groundwater and wastewater influents and effluents from six WWTPs.

As presented in Table 2.5, most of the targeted compounds were detected in the groundwater samples. Maximum concentrations above 1.0  $\mu\text{g/L}$  were determined for meprobamate and phenobarbital with average values of 0.31 and 0.38  $\mu\text{g/L}$ , respectively. Both compounds were present in the majority of samples. Primidone, its metabolite phenylethylmalonamide, and pyrithyldione were measured at lower concentrations of up to 0.4  $\mu\text{g/L}$  (primidone), whereas diazepam and oxazepam were not found in any of the groundwater samples above their LOQs. Results for primidone are in the same order of magnitude of previously reported concentrations in Berlin groundwater at bank filtration sites (Heberer, 2002b) and similar values were reported by Drewes et al. (2003) for

groundwater impacted by wastewater irrigation in the USA. Peschka et al. (2006) included phenobarbital in their investigation of barbiturates and measured concentrations in samples taken at an irrigation field near Berlin corresponding well to those found in the present study. Richter et al. (2007) had previously shown that one of the studied aquifers is contaminated with several sulfonamides originating from former sewage irrigation.

*Table 2.5 Summary of analytical results for psychoactive compounds and metabolites in groundwater and wastewater influents and effluents of the Berlin region.*

Compound	Groundwater (n = 109)			WWTP Influent (n = 6)			WWTP Effluent (n = 6)		
	Values >LOQ <sup>a</sup>	Max (µg/L)	Av (µg/L)	Values >LOQ <sup>a</sup>	Max (µg/L)	Av (µg/L)	Values >LOQ <sup>a</sup>	Max (µg/L)	Av (µg/L)
Diazepam	0			0			0		
Meprobamate	72	1.11	0.31	0			1	0.11	
Oxazepam	0			5	0.18	0.13	4	0.18	0.11
Phenylethylmalonamide	59	0.27	0.09	1	0.18		6	0.42	0.28
Primidone	64	0.40	0.14	6	0.68	0.51	6	0.65	0.54
Pyrithyldione	24	0.16	0.06	0			0		
Phenobarbital	83	1.35	0.38	0			3	0.36	0.12

LOQ = limit of quantification; Max = maximum concentration; Av = average from n samples.

<sup>a</sup> LOQs for WWTP influents and effluents as follows: 0.1 µg/L for diazepam, meprobamate, oxazepam, primidone, and pyrithyldione; 0.15 µg/L for phenylethylmalonamide and phenobarbital.

In all influents and effluents of the investigated WWTPs, primidone was detected with average concentrations of 0.51 and 0.54 µg/L respectively (Table 2.5), indicating that this compound is not eliminated during wastewater treatment. However, its metabolite, phenylethylmalonamide, was found in all analyzed effluents at concentrations ranging up to 0.42 µg/L, while it was generally not present in the corresponding influents. Phenobarbital was found in three effluent samples at a maximum concentration of 0.36 µg/L and never detected in influent samples. Hence, as both compounds originate from primidone and were only present in effluent samples, degradation is likely to occur to some extent. The discrepancy between the results obtained for primidone, phenobarbital, and phenylethylmalonamide may partly be explained by the fact that hydraulic retention times of WWTPs vary greatly, and 24 h composite samples may not reflect the precise elimination profile. Removal efficiencies of 87 % for primidone have been described by Heberer (2002b), whereas Schneider (2004) reported ranges of 0-99 % and emphasized that removal of primidone can be strongly reduced due to precipitation events. High rainfall

during the month of May, and thus shortly before sample collection, could therefore explain the lack of removal during wastewater treatment.

The average concentration of oxazepam in effluent wastewater (0.11  $\mu\text{g/L}$ ) was comparable to the influent concentration. Hummel et al. (2006) also described limited removal efficiency for oxazepam in WWTPs, but reported higher absolute amounts of oxazepam for municipal WWTPs in Germany.

The tranquilizer diazepam and the sedative pyrithyldione were not detected in any of the wastewater in- and effluent samples, and meprobamate was present only in one WWTP effluent sample. Though meprobamate is not in use anymore in Germany (Müller and Hartmann, 1995; Goldberg, 2005), the occurrence of meprobamate in one effluent sample can be explained by the fact that this WWTP receives contaminated groundwater abstracted from below a former sewage farm for remediation purposes, which contains considerable amounts of meprobamate. Concentrations below the LOQ or in the low nanograms per liter range have been reported for diazepam in wastewater (Ternes et al., 2001; Hummel et al., 2006; Vanderford and Snyder, 2006).

## 2.4 Conclusions

The analytical method described above provides a simple and sensitive technique for the simultaneous determination of six psychoactive compounds and a metabolite in various aqueous matrices. It is based on automated SPE followed by UHPLC-MS/MS. It is the first method that allows the analysis of pyrithyldione and phenylethylmalonamide in water. High recovery rates, typically exceeding 80 %, and sensitive and selective UHPLC-MS/MS detection enable the accurate quantification of the pharmaceutical residues at low levels (0.02-0.15  $\mu\text{g/L}$ , depending on the individual analyte and sample origin). However, matrix suppression in both ESI positive and negative modes proved to have a significant impact on recoveries of target compounds. Therefore, appropriate surrogate standards were used to compensate for UHPLC-MS/MS matrix effects and also for losses during sample preparation. To obtain more accurate concentrations in untreated wastewater, the method of standard addition is suggested especially for phenylethylmalonamide.

The developed method was successfully applied to quantify the selected psychoactive drugs in wastewater and groundwater samples. Only two of the seven compounds were continuously present in both influent and effluent samples from WWTPs. Additionally, two degradation products could be detected in treated wastewater. Five of the seven investigated pharmaceutical residues were found in groundwater below former sewage farms at medium-to-high nanograms per liter levels, indicating their long-term stability in groundwater. To verify this hypothesis, degradation studies are currently undertaken.

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### 3. Occurrence in polluted groundwater

Psychoactive compounds – meprobamate, pyrithyldione, primidone, and its metabolites, phenobarbital, and phenylethylmalonamide – were detected in groundwater within the catchment area of a drinking water treatment plant located downgradient of a former sewage farm in Berlin, Germany. The aim of this study was to investigate the distribution of the psychoactive compounds in anoxic groundwater and to assess the risk of drinking water contamination. Groundwater age was determined to achieve a better understanding of present hydrogeological conditions. A large number of observation and production wells were sampled. Samples were analyzed using solid-phase extraction and ultrahigh-performance liquid chromatography-tandem mass spectrometry. Groundwater age was estimated using the helium-tritium ( $^3\text{He}$ - $^3\text{H}$ ) dating method. Concentrations of psychoactive compounds up to 1  $\mu\text{g/L}$  were encountered in the contamination plume. Generally, concentrations of phenobarbital and meprobamate were the highest. Elevated concentrations of the analytes were also detected in raw water from abstraction wells located approximately 2.5 km downgradient of the former sewage farm. Concentrations in the final drinking water were below the limit of quantification owing to dilution. The age of shallow groundwater samples ranged from years to a decade, whereas groundwater was up to four decades old at 40 m below ground. Concentrations of the compounds increased with groundwater age. Elevated concentrations of psychoactive drugs indicate a strong persistence of these compounds in the environment under anoxic aquifer conditions. Results suggest that the heritage of sewage irrigation will affect raw water quality in the area for decades. Therefore, further monitoring of raw and final drinking water is recommended to ensure that contaminant concentrations remain below the health-based precautionary value.

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### 3.1 Introduction

The occurrence of anthropogenic organic contaminants in aquatic ecosystems has drawn the attention of both the public and scientists in recent years, a fact confirmed by the numerous studies published in this field. With respect to pharmaceuticals, many of the investigations have focused on high consumption substances currently being introduced into the environment. These include analgesics (e.g., Drewes et al., 2003; Kim et al., 2007), beta blockers (e.g., Calamari et al., 2003; Scheurer et al., 2010), iodinated X-ray contrast media (e.g., Ternes and Hirsch, 2000; Schittko et al., 2004), anticonvulsants (e.g., Kim et al., 2007; Stein et al., 2008), and antibiotics (e.g., Calamari et al., 2003; Drewes et al., 2003; Heberer et al., 2008). Research studies on the presence of pharmaceutical residues as legacy pollutants in environmental compartments are comparatively rare. “Legacy pollutant” is a general term for a substance whose use was banned or strictly regulated years ago. The previously widespread application of these legacy pollutants has left large amounts of often highly persistent toxins in the environment (TNRCC, 2000).

In previous studies, groundwater within the catchment area of a drinking water treatment plant (DWTP) affected by prior sewage irrigation practices was found to be heavily polluted with a number of anthropogenic contaminants such as ammonium ( $\text{NH}_4^+$ ) (Hamann, 2009) and the trace organic compound *para*-toluenesulfonamide (*p*-TSA) (Richter et al., 2009a). In 2009, gas chromatography-mass spectrometry (MS) screenings of such groundwater also revealed the presence of several legacy pollutants, including the following psychoactive compounds: meprobamate, pyrithyldione, primidone, and its metabolites phenobarbital and phenylethylmalonamide.

Meprobamate was introduced on the market in 1955 as anxiolytic drug but was largely superseded by benzodiazepines in the 1960s (Müller and Hartmann, 1995). Since 1970, meprobamate has been listed as a controlled substance (Goldberg, 2005) and is included in the German Narcotics Law as a non-prescribable narcotic (BtMÄndV, 1991). Pyrithyldione is a sedative-hypnotic drug, introduced in 1949 under the brand name Persedon® (Linde, 1992). Due to adverse effects, pyrithyldione was withdrawn in 1983 (Ibáñez et al., 2000). Primidone has been available on the German market since 1950 and is prescribed as an anticonvulsant for the treatment of psychomotor epilepsy. During *in vivo* metabolism in

both humans and animals, primidone is converted into two major pharmacologically active substances, phenobarbital and phenylethylmalonamide (El-Masri and Portier, 1998). The barbiturate phenobarbital was introduced onto the German market in 1912 as a sedative and hypnotic drug. It was used extensively, but owing to an increased addiction potential and a narrow therapeutic range, it was replaced in the 1960s by benzodiazepines for these indications (Cozanitis, 2004). Nowadays, phenobarbital is still used as anticonvulsant. The primidone metabolite phenylethylmalonamide has, in contrast, no medical application.

The occurrence of the identified psychoactive substances in groundwater intended for drinking water production purposes gave cause for concerns and led to the development of a sensitive and reliable analytical method for their detection (Hass et al., 2011). But the question has arisen as to whether the health-based precautionary values (HPV), which are recommended by the German Federal Environmental Agency for only partially or non-assessable substances in drinking water, can be met today and in the future. For primidone, H.H. Dieter (personal communication, December 8, 2010) has suggested that a maximum concentration of 3 µg/L in drinking water is tolerable for lifetime consumption. With respect to phenobarbital, a HPV of 0.30 µg/L has been recommended (Dieter, 2009). For the other investigated pharmaceuticals, human toxicological relevance has not yet been assessed, and therefore, a HPV of 0.10 µg/L is applicable.

The objective of the present study was (a) to determine the occurrence and distribution of the psychoactive compounds in groundwater downgradient of a former sewage farm by means of extensive field sampling and (b) to provide a risk assessment regarding the current and future contamination of the local drinking water. Furthermore, the age of groundwater at representative sites was estimated using helium-tritium ( $^3\text{He}$ - $^3\text{H}$ ) dating (Tolstikhin and Kamenskiy, 1969) to achieve a better understanding of age distribution (i.e., travel time) throughout the aquifer. This allowed an assessment of the potential correlation between contaminant concentrations and groundwater ages, as well as providing some understanding of the transport behavior of the pollutants.

To date, several studies have dealt with the occurrence and fate of primidone in environmental compartments (e.g., Heberer et al., 2002; Heberer, 2002b; Drewes et al., 2003; Massmann et al., 2007). However, to our knowledge, there has not been a thorough



study of the presence and behavior of meprobamate, pyriithyldione, and phenylethylmalonamide in groundwater thus far, and phenobarbital has been rarely studied in the aquatic environment (Peschka et al., 2006).

## 3.2 Study area

### 3.2.1 Location

The area of investigation, Machnow/Krummendammer Heide, is located to the north of Lake Müggelsee in the southeastern part of Berlin, Germany (Figure 3.1). It covers the former sewage farm district Münchehofe and lies within the catchment area of the DWTP Friedrichshagen. The production well galleries of the DWTP are located along the shores and north of Lake Müggelsee (Figure 3.1). The vertical abstraction wells are screened at depths of 20-40 m below ground and extract a mixture of bank filtrate and ambient groundwater. Gallery B extracts mostly ambient groundwater, whereas galleries C, D, and E extract mainly bank filtrate. In 2010, approximately 125,000 m<sup>3</sup>/day of raw water were purified at the DWTP, which corresponds to roughly 22 % of the total drinking water demand per day in Berlin (BWB, 2011). Generally, only minimal treatment consisting of aeration and rapid sand filtration is required to meet drinking water quality standards (BWB, 2011). Well gallery A is located further inland of the galleries B, C, and D (Figure 3.1) and is not used for production purposes. Instead, it serves as a hydraulic protection to avert the contamination plume originating from the former sewage farm (Schmolke, 2009). Therefore, the pumped groundwater of gallery A is directly discharged to the nearby wastewater treatment plant (WWTP) Münchehofe. To monitor the groundwater quality at the field site, a dense network of 100 observation wells screened at various depths from 3.5 to 87.3 m below ground was established (Figure 3.1, Table A.1).

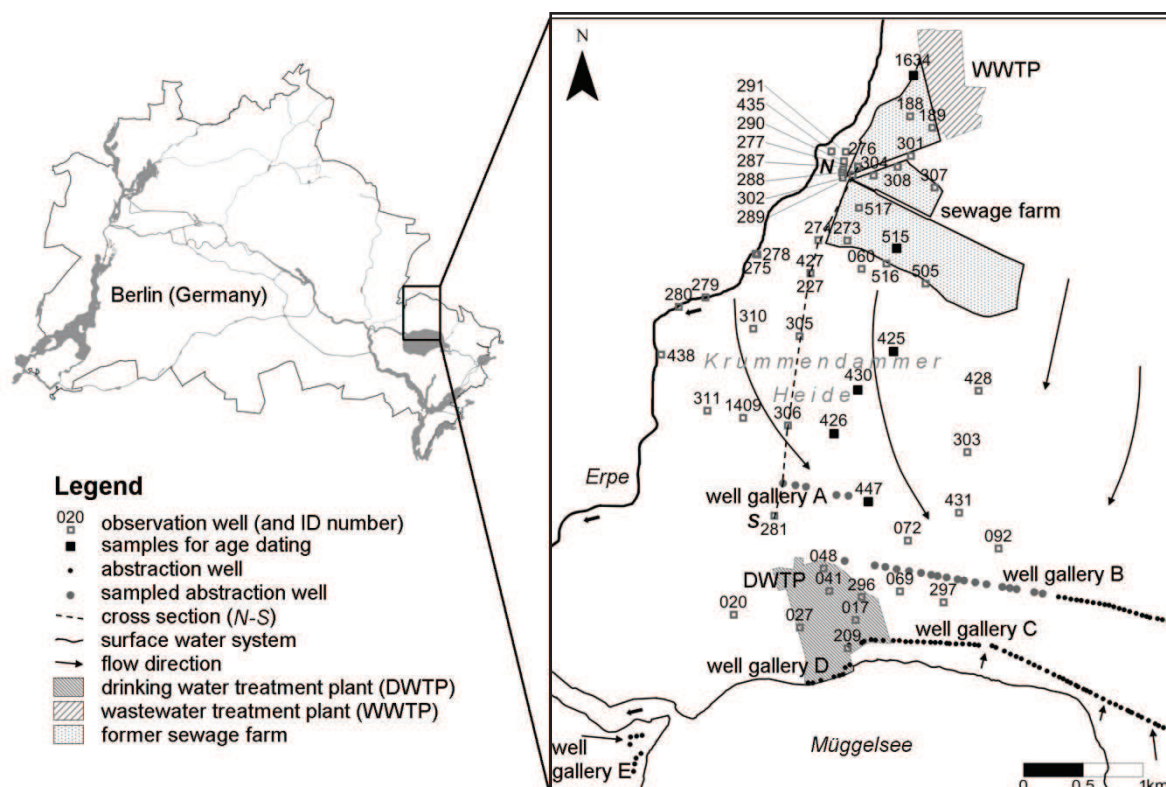


Figure 3.1 Location of the field site in southeast Berlin (left). Map of the investigation area Machnow/Krummendammer Heide (right) with locations of sampled observation wells (gray squares, with corresponding numbers but without acronym FRI), abstraction wells (gray circles), and well galleries A-E. Position of the cross section N-S (dashed line, see Figure 3.3) and observation wells additionally sampled for age dating (black squares) are also given. Arrows indicate the main groundwater flow direction at the study site.

### 3.2.2 Sewage farm operation

The former sewage farm Münchehofe is located at the northern border of the study area and encompasses 1.04 km<sup>2</sup> (SenStadt, 2011a). Untreated sewage of domestic and industrial origin was applied to soil by flood irrigation on horizontal terraces beginning in 1907 (SenStadt, 2011b). From 1955, the sewage field was quantitatively overloaded causing anoxic conditions in the unsaturated zone and resulting in a reduced remediation capacity of the sediments (Engelmann et al., 1992). In the course of the construction of the WWTP in 1976, irrigation of untreated sewage was terminated, and instead treated wastewater was applied to the sewage field until its closing in 1991. Furthermore, between 1978 and 1991, sewage sludge from the WWTP was deposited in basins that were, at least partially, without underground sealing (Engelmann et al., 1992). The high contaminant loads that were

introduced into the sediments over decades led to strongly elevated concentrations of anthropogenic compounds such as  $\text{NH}_4^+$  ( $\leq 59$  mg/L), boron (B;  $\leq 710$   $\mu\text{g/L}$ ), dissolved organic carbon (DOC;  $\leq 31$  mg/L), and *p*-TSA ( $\leq 39$   $\mu\text{g/L}$ ) in the adjacent groundwater (Engelmann et al., 1992; Hamann, 2009; Richter et al., 2009a).

### 3.2.3 Hydrogeology and hydrodynamics

The field site is located in the Warsaw-Berlin glacial valley and is bounded to the north by the Barnim plateau. The origin of the porous, glaciofluvial, and fluvial sediments dates back to the Saale and Weichsel glaciations. The aquifer is comprised primarily of fine- to medium-sized sand and is characterized by a medium hydraulic conductivity of  $10^{-4}$  m/s. It has a thickness of approximately 50 m and is not subdivided by aquitards owing to the absence of glacial till in this area (Engelmann et al., 1992). Groundwater dynamics are affected by the abstraction regime of the northern well galleries of the DWTP, and flow is essentially from north to south (Figure 3.1) at an approximate velocity of 0.15-0.25 m/day (Schmolke, 2009).

## 3.3 Materials and methods

### 3.3.1 Sample collection

Groundwater samples from 100 observation wells and 23 production wells were collected every 6 months from March 2010 to April 2011 ( $n = 3$ ). Retrieval of groundwater samples was in accordance with the DIN 38402-13 (1985). Samples of raw and final drinking water were collected in the waterworks before and after treatment, respectively. All samples were collected in glass bottles and extracted immediately or stored in the dark at 4 °C for less than 14 days. Measurements of redox potential (Eh), pH, oxygen ( $\text{O}_2$ ), temperature (T), and electric conductivity (EC) were carried out in the field in a flow cell.

Groundwater samples for  $^3\text{He}$ - $^3\text{H}$  dating were collected during the sampling campaign in September 2010. Six sites, partly equipped with multi-level wells and distributed over two aquifers, were sampled, encompassing 13 observation wells (Figure 3.1). One observation well (FRI1634OP) was chosen as a reference point because it is located up gradient of the

former sewage farm and therefore has not been influenced by wastewater irrigation. Tritium ( $^3\text{H}$ ) samples were taken in 1,000 mL polyethylene bottles with air entrapment minimized. Water samples for noble gas analysis were collected in 40 mL copper tubes (inner diameter 0.8 cm, outer diameter 1 cm) mounted in aluminum frames. During sample collection, a transparent Teflon hose was attached to the each end of the copper tube and continuously checked for bubbles. Subsequently, the copper tubes were sealed with stainless steel clamps to prevent gas exchange with the atmosphere. Both tritium samples and water for noble gas analysis were collected in duplicate. Further details on the procedure used to collect  $^3\text{H}$  samples and water for noble gas analysis are summarized in Sültenfuß et al. (2009).

### 3.3.2 Analytical program

All water samples, except those for  $^3\text{He}$ - $^3\text{H}$  dating, were analyzed in the laboratory of the Berliner Wasserbetriebe. The analytical method used for the quantification of psychoactive compounds was developed and validated previously and is described in detail in Hass et al. (2011). Briefly, for the extraction of analytes from samples, automated solid-phase extraction was performed using a reverse-phase octadecyl adsorbent. Subsequently, sample extracts were analyzed via reverse-phase ultrahigh-performance liquid chromatography (Waters ACQUITY UPLC) coupled with MS/MS detection (Waters/Micromass Quattro Micro) in multi-reaction monitoring mode. Electrospray ionization was applied in both positive and negative mode. This procedure resulted in limits of quantification (LOQ) between 0.02 and 0.03  $\mu\text{g/L}$  in groundwater and drinking water. Using suitable surrogate standards for quantification, recoveries generally exceeded 80 % (Hass et al., 2011).

Ammonium nitrogen ( $\text{NH}_4^+\text{-N}$ ) in the water was analyzed photometrically (VitalScientific VITALAB Electra S) as described in the DIN 38406-5 (1983). Cations in the water were measured according to the DIN EN 11885 method (DIN EN ISO 11885, 2009) using an inductively coupled plasma optical emission spectrometer (Thermo Scientific iCAP 6000 Series). Determination of anions in the water was carried out by ion chromatography (Dionex ICS 1000) (DIN EN ISO 10304-1, 2009). Measurements of DOC were performed on a DOC analyzer (Elementar) in accordance with the DIN EN 1484 (1997).

For  $^3\text{He}$ - $^3\text{H}$  dating, analysis of  $^3\text{H}$ , He isotopes, and Ne was carried out at the noble gas laboratory of the Institute of Environmental Physics, University of Bremen (Germany). Details on the measurements are given in Sültenfuß et al. (2009).

### 3.3.3 Age dating method

The analysis of  $^3\text{H}$  in groundwater samples combined with the measurement of its decay product,  $^3\text{He}$ , allows the calculation of groundwater age and thus has become a powerful tool in hydrogeological studies in recent years (e.g., Solomon and Cook, 2000; Sültenfuß and Massmann, 2004).  $^3\text{H}$ , the only radioactive isotope of hydrogen, was released to the atmosphere primarily between 1952 and 1963 as a result of atmospheric testing of nuclear devices (Solomon and Cook, 2000). As part of the water molecule,  $^3\text{H}$  is washed out into surface waters by precipitation and vapor exchange. The peak concentration of  $^3\text{H}$  in precipitation, reached in 1963, was three orders of magnitude higher than pre-testing concentrations (Sültenfuß et al., 2011). Since then,  $^3\text{H}$  concentrations have decreased due to dilution and radioactive decay by beta emission (half-life of 12.32 years) which produces the rare and stable helium isotope  $^3\text{He}$  (tritogenic  $^3\text{He}$ ,  $^3\text{He}_{\text{tri}}$ ) (Lucas and Unterweger, 2000). Both isotopes accumulate in groundwater and are unaffected by groundwater chemistry (Sültenfuß et al., 2011). Groundwater age as determined by the  $^3\text{H}/^3\text{He}_{\text{tri}}$  ratio is therefore independent of tritium input concentrations, and this dating technique can be applied to waters recharged since the late 1950s.

### 3.4 Results and discussion

#### 3.4.1 Characterization of the groundwater at the field site

The groundwater at the study area contained high concentrations of  $\text{NH}_4^+$  ( $\text{NH}_4^+\text{-N}$  up to 61.00 mg/L; Table 3.1). In 72 % of sampled observation wells, concentrations exceeded the upper limit of the natural background concentration of 0.5 mg/L (LUA, 2002), indicating the influence of sewage irrigation.

Boron is rarely geogenic and is often used as an indicator of sewage (LUA, 2002). Schleyer and Kerndorff (1992) suggested that concentrations of B above 80  $\mu\text{g/L}$  indicate impairment of groundwater. The high concentrations of B detected in this study (up to 750  $\mu\text{g/L}$ ; Table 3.1) are therefore evidence of impact by urban wastewater.

Likewise, high sulfate ( $\text{SO}_4^{2-}$ ) concentrations (up to 451 mg/L; Table 3.1) are a further sign of anthropogenic contamination as they considerably exceed the natural background values of approximately 100 mg/L typical for this region (LUA, 2002; Hamann, 2009).

DOC values of up to 34.00 mg/L (Table 3.1) (DOC background concentration = 2-4 mg/L; Hamann, 2009) and high concentrations of the trace organic compound *p*-TSA (<0.05-39  $\mu\text{g/L}$ , data not shown) also point to sewage contamination and compromised groundwater quality (Richter et al., 2009a).

Groundwater also contained high amounts of dissolved manganese (up to 2.90 mg/L; Table 3.1) and iron (up to 31.00 mg/L; Table 3.1). As suggested by Berner (1981), redox conditions are classified by the disappearance ( $\text{O}_2$ , nitrate ( $\text{NO}_3^-$ ), and  $\text{SO}_4^{2-}$ ) or the appearance ( $\text{Mn}^{2+}$ ,  $\text{Fe}^{2+}$ ) of reactants. Iron-reducing conditions and high  $\text{SO}_4^{2-}$  concentrations were predominant in the groundwater at the field site. However,  $\text{O}_2$  and  $\text{NO}_3^-$  concentrations above  $\geq 0.5$  mg/L were also encountered in some shallow observation wells located mainly in the vicinity of the former sewage farm or the Erpe River. Results for parameters used for the characterization of the groundwater at the field site are given in detail in Table A.1.

Table 3.1 Maximum and median concentrations of meprobamate, pyrithyldione, primidone, phenobarbital, phenylethylmalonamide, O<sub>2</sub>, nitrate nitrogen (NO<sub>3</sub><sup>-</sup>-N), Fe<sup>2+</sup>, Mn<sup>2+</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>-N, B, Cl<sup>-</sup>, DOC, and EC in groundwater from March 2010 to April 2011.

Parameter	Unit	Observation wells (n = 300)		Abstraction wells (n = 69)	
		Maximum	Median	Maximum	Median
Meprobamate	(µg/L)	1.13	0.05	0.67	0.43
Pyrithyldione	(µg/L)	0.19	<0.02	0.16	0.05
Primidone	(µg/L)	0.49	0.04	0.34	0.20
Phenobarbital	(µg/L)	1.35	0.17	1.23	0.48
Phenylethylmalonamide	(µg/L)	0.48	<0.03	0.54	0.14
O <sub>2</sub>	(mg/L)	6.1	0.2	7.0	0.4
NO <sub>3</sub> <sup>-</sup> -N	(mg/L)	59.00	<0.05	<0.05	<0.05
Fe <sup>2+</sup>	(mg/L)	31.00	3.00	4.20	2.90
Mn <sup>2+</sup>	(mg/L)	2.90	0.54	0.87	0.39
SO <sub>4</sub> <sup>2-</sup>	(mg/L)	451	149	223	153
NH <sub>4</sub> <sup>+</sup> -N	(mg/L)	61.00	2.60	25.00	6.80
B	(µg/L)	750	140	320	220
Cl <sup>-</sup>	(mg/L)	1410	38	330	59
DOC	(mg/L)	34.00	3.40	5.40	3.20
EC (at 25 °C)	(µS/cm)	5370	890	1540	1010

### 3.4.2 Horizontal distribution of the psychoactive compounds

Median concentrations of the investigated psychoactive compounds at depths of 17-33 m below the surface are illustrated as concentration contour maps (Figure 3.2 a-e). Corresponding values for each observation and production well are listed in detail in Table A.1.

The ambient groundwater north of the sewage farm area (FRI1634OP) was unaffected by former irrigation practices. Wastewater indicators (psychoactive compounds, NH<sub>4</sub><sup>+</sup>, B, DOC, SO<sub>4</sub><sup>2-</sup>) were either not detected or represented a typical geogenic background level (Richter et al., 2009a).

Generally, the lowest indicator concentrations were identified along the plume margins, whereas the highest values were observed in the center of the contamination plume extending from the sewage farm area to northern well galleries A and B (Figure 3.2 a-e).

A comparable distribution pattern has already been described by Richter et al. (2009a) for *p*-TSA.

It should be noted that the contamination plumes drift to the southeast. This is explained by the groundwater flow direction (Figure 3.1), which is strongly influenced by the groundwater abstraction of northern well galleries A and B of the DWTP at Friedrichshagen (Richter et al., 2009a; Schmolke, 2009).

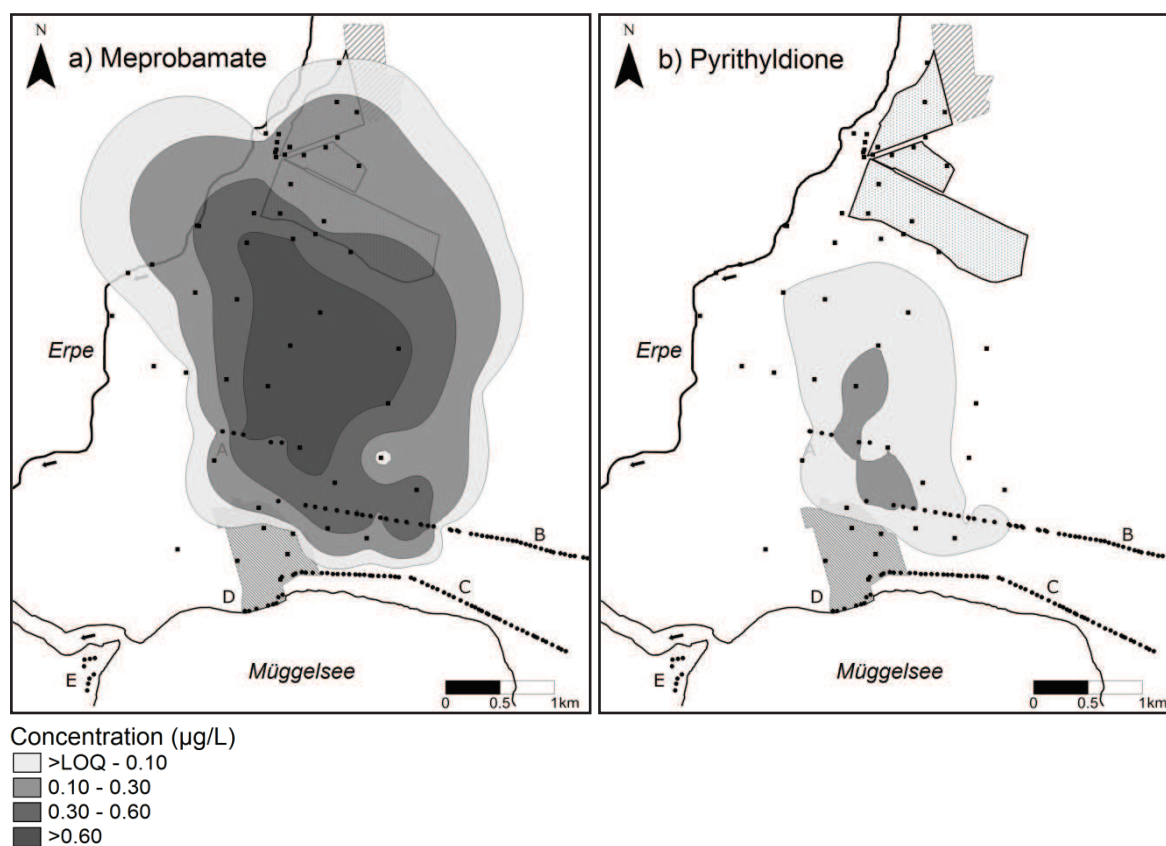


Figure 3.2 Median concentrations of a) meprobamate, b) pyrithyldione, c) primidone, d) phenobarbital, and e) phenylethylmalonamide ( $\mu\text{g/L}$ ) at depths between 17 and 33 m below ground surface from the respective observation wells and abstraction wells ( $n = 3$ ; March 2010 to April 2011) at the field site. Contour lines were drawn using Surfer software (interpolation by kriging). Flow direction of the groundwater is shown in Figure 3.1.



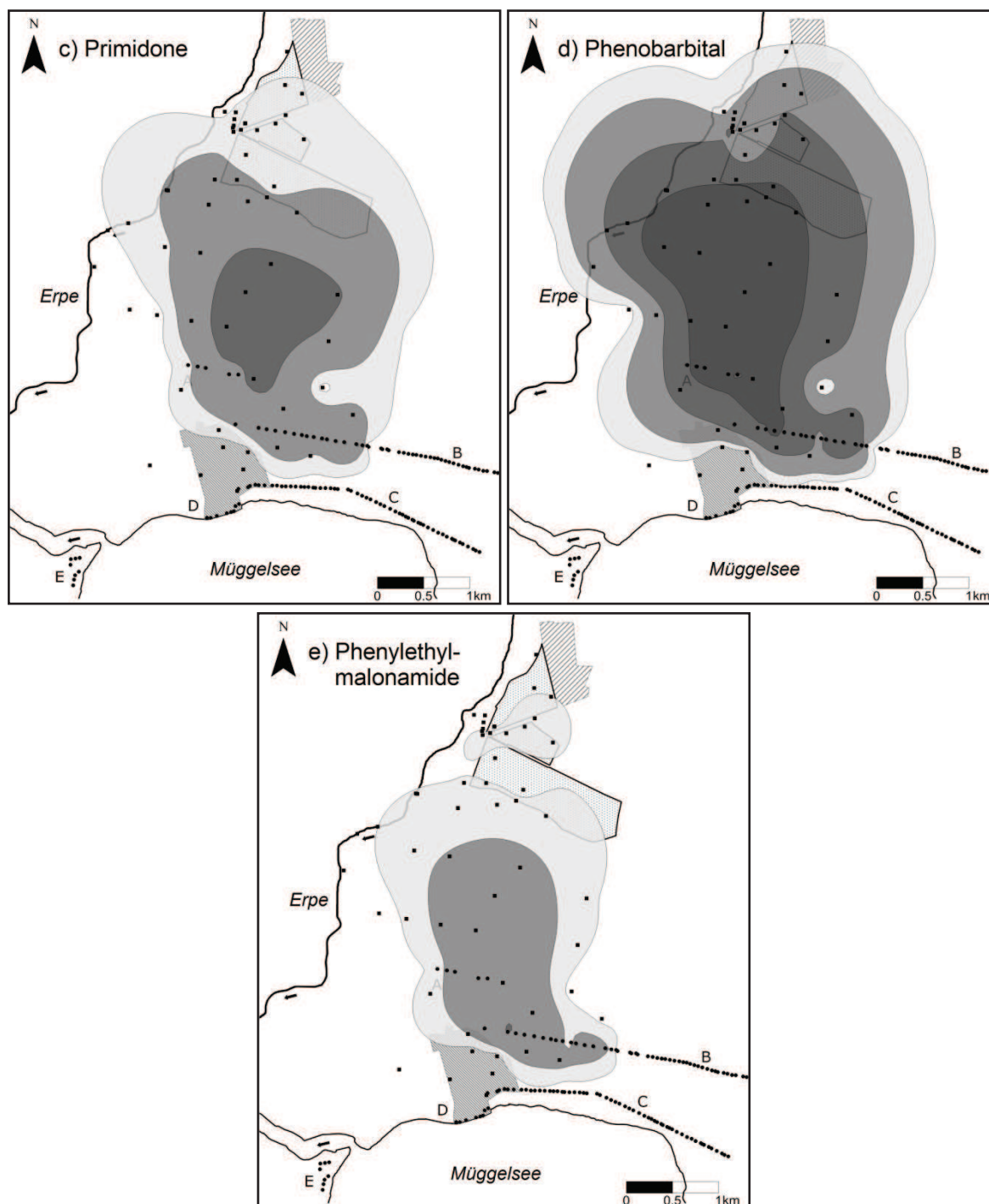


Figure 3.2 continued

In general, all of the investigated psychoactive compounds exhibited similar plume shapes. The different sizes of the plumes were related to the respective concentration maxima of the pharmaceuticals (see Table 3.1). Accordingly, the contamination plumes of phenobarbital and meprobamate, with maximum concentrations of 1.35 and 1.13  $\mu\text{g/L}$ , respectively, show the greatest extent (Figure 3.2 a, d). The north-south extent of the plumes is about 3.5 km

and the east-west extent is about 3.0 km. Considerably lower maximum values were determined for pyrithyldione ( $\leq 0.19 \mu\text{g/L}$ ), primidone ( $\leq 0.49 \mu\text{g/L}$ ), and phenylethylmalonamide ( $\leq 0.48 \mu\text{g/L}$ ) (Table 3.1), resulting in respectively smaller plume sizes (Figure 3.2 b, c, e).

Reference groundwater data for the target compounds only exist for primidone and phenobarbital. Our results for primidone are consistent with previously reported concentrations in Berlin groundwater at bank filtration sites (Heberer et al., 2002; Heberer, 2002b; Massmann et al., 2007), and similar values were described by Drewes et al. (2003) for groundwater in the USA that was impacted by wastewater irrigation. Peschka et al. (2006) included phenobarbital in their investigations of barbiturates and measured concentrations at an irrigation field near Berlin which correspond well to those found in our study.

### 3.4.3 Vertical distribution of the psychoactive compounds

The vertical distribution pattern of the psychoactive compounds along a schematic hydrological cross section (N-S) is exemplified for meprobamate in Figure 3.3. Results for the other compounds are displayed in Figure A.1. Median concentrations ( $n = 3$ ) are given for the respective filter screen depths and wells (Figure 3.3, Table A.1).

The geological section is situated between the former sewage farm district and an observation well (FRI281) located south of the well gallery A (Figure 3.1). The transect consists of several observation wells screened at various depths between 3.5 and 47.5 m and is roughly oriented in the direction of groundwater flow (Figure 3.1).

Elevated concentrations of the investigated psychoactive compounds were encountered in both shallow and deeper groundwater with the exception of pyrithyldione, which was only detected in deeper soil units (Figure A.1 a). Thus, regarded vertically, the contaminant plume extends almost over the entire aquifer with the highest concentrations along the transect observed at the two deep observation wells in the center of the cross section (FRI305UP, FRI306UP) (Figure 3.3, Figure A.1).

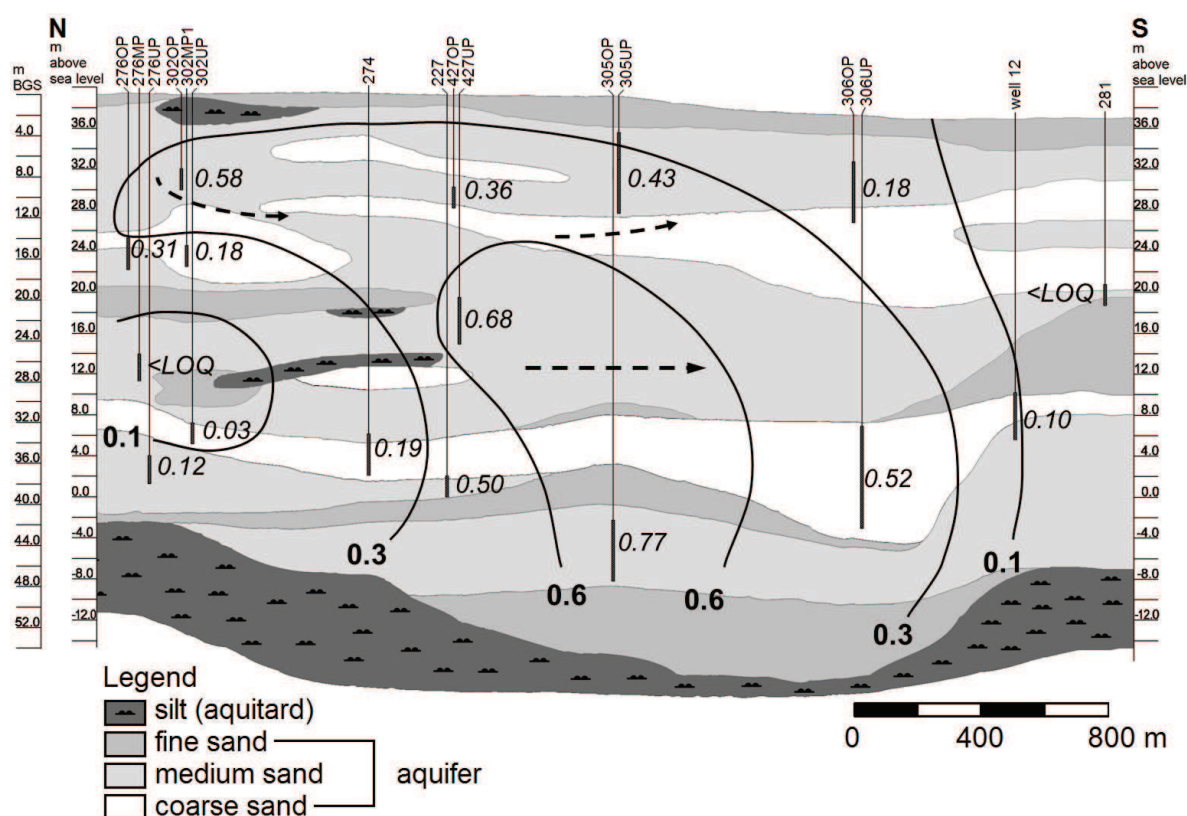


Figure 3.3 Schematic hydrologic cross section along N-S axis of the field site Machnow/Krummendammer Heide (see Figure 3.1 for location). Median concentrations are plotted against the filter screen depth (middle of the screen). Italicized numbers represent median concentrations of meprobamate ( $\mu\text{g/L}$ ) from March 2010 to April 2011 ( $n = 3$ ). Isolines representing different concentration levels (bold numbers) are given with the lines drawn by hand. Arrows indicate groundwater flow direction. Illustrations for other compounds are given in Figure A.1. Modified after Richter et al. (2009a).

Deeper groundwater (e.g., FRI276MP, FRI301UP, FRI302UP, FRI308) in the sewage farm area contained only low concentrations of psychoactive drugs, when they were detected at all, owing to the inflow of uncontaminated deep groundwater (FRI1634OP) from the north, as was already evident from the horizontal distribution patterns. Drug concentrations increased with the flow direction and reached their maximum at the center of the cross section. Elevated values were also detected in shallow groundwater further downgradient from the former sewage farm district (e.g., FRI305OP, FRI425OP, FRI427OP, FRI430OP). This is because the area south of the irrigation fields is widely forested (Krummendammer Heide, Figure 3.1). As a consequence, the groundwater recharge rate is comparatively low, resulting in low dilution by downward discharge.

In the southern part of the cross section, abstraction well 12 displayed elevated concentrations of some drugs, particularly meprobamate (Figure 3.3) and phenobarbital (Figure A.1 c), whereas groundwater further south, at observation well FRI281, was generally free of the investigated pharmaceuticals. This illustrates how well gallery A effectively prevents the expansion of the plume in a southerly direction.

#### 3.4.4 Groundwater age and relation to psychoactive compounds

In general, the apparent age of the shallow groundwater is on the order of years to a decade, whereas at the aquifer base, it is up to four decades old. Apparent  $^3\text{He}$ - $^3\text{H}$  age correlates roughly with groundwater depth, and an increase in age with depth can be observed as illustrated in Figure 3.4. In addition, groundwater age tends to increase in flow direction, as can be expected due to increasing travel times.

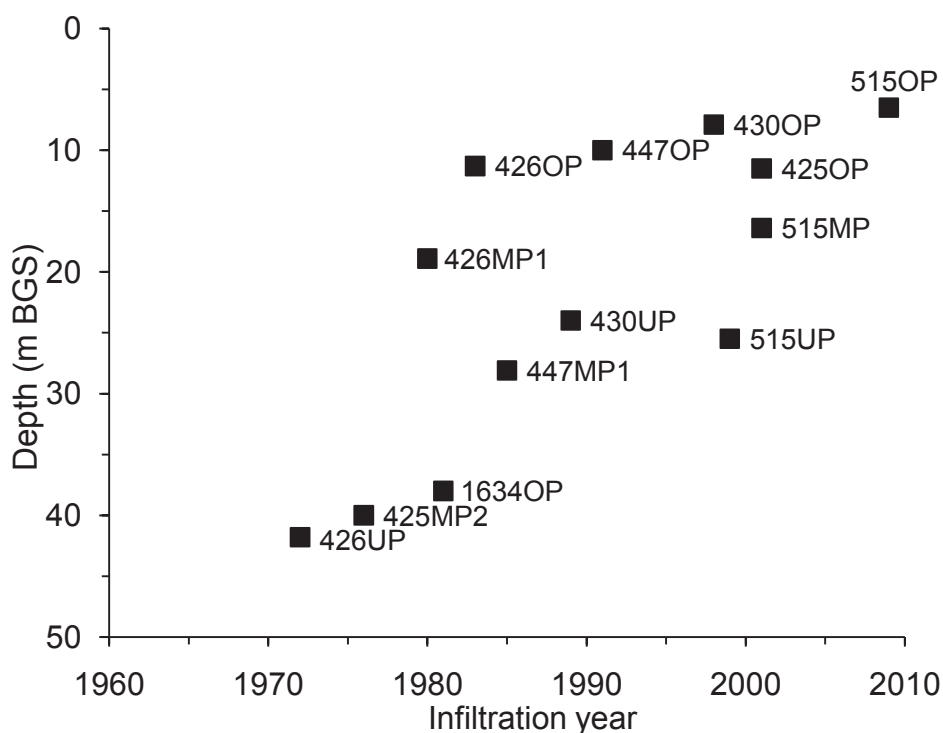


Figure 3.4 Filter screen depths (meters below ground surface; middle of the screen) versus infiltration years (infiltration years = sampling date -  $^3\text{He}$ - $^3\text{H}$  age). The corresponding observation well numbers are also given.

An apparent  $^3\text{He}$ - $^3\text{H}$  age of 1 year was determined for the shallow observation well FRI515OP, directly below the former sewage farm. Here, groundwater contains only 0.5 tritium units (TU) of  $^3\text{He}_{\text{tri}}$  and 7.7 TU of  $^3\text{H}$ , roughly equivalent to current  $^3\text{H}$  concentrations in precipitation (IAEA, 2011). This is due to the high groundwater recharge rate in the forest-free area of the former sewage farm. Such a trend can also be assumed for other observation wells in the vicinity (FRI505OP, FRI516OP, FRI517OP). In contrast, at shallow wells further downgradient (FRI425OP, FRI430OP),  $^3\text{He}$ - $^3\text{H}$  ages are significantly higher (10.7-12.3 years). These older ages suggest that recharge rates are significantly lower within this forested area (Krummendammer Heide), as mentioned previously (see 3.4.3 Vertical distribution).

For three samples (FRI1634OP, FRI426UP, FRI425MP2), the data indicate that apparent groundwater age is the result of mixing between two (or more) waters of very different age. This is illustrated either by samples lying below the  $^3\text{H}$  input curve in a plot of  $^3\text{H}+^3\text{He}_{\text{tri}}$  versus time (Figure A.2) or by high concentrations of the radiogenic helium isotope  $^4\text{He}_{\text{rad}}$  (Hudson, 1994; Solomon et al., 1996).

Groundwater from the deep observation well FRI1634OP, located north of the sewage farm district, contained the largest amount of  $^4\text{He}_{\text{rad}}$  ( $4.63 \cdot 10^{-5}$  N mL/kg), indicating water presumably over 100 years old (J. Sültenfuß, personal communication, May 5, 2011). Furthermore, the low initial  $^3\text{H}$  (sum of  $^3\text{H}$  and  $^3\text{He}_{\text{tri}}$ ) level of 5.8 TU approximated the pre-bomb  $^3\text{H}$  level of 3-6 TU in European rainfall (Roether, 1967), and gives additional evidence of old groundwater (>60 years). Most of the initial  $^3\text{H}$  has already decayed to  $^3\text{He}_{\text{tri}}$ , resulting in a very low  $^3\text{H}$  level of 1.1 TU. However, the estimated apparent age at well FRI1634OP is only 29.1 years, suggesting an admixture of older and younger water, while the proportion of old water predominates.

The maximum apparent  $^3\text{He}$ - $^3\text{H}$  age was 38.7 years (FRI426UP), which also corresponded to the highest initial  $^3\text{H}$  concentration (45.1 TU) encountered at the field site. Again, most  $^3\text{H}$  has decayed, as demonstrated by the large ratio of  $^3\text{He}_{\text{tri}}$  to  $^3\text{H}$ . In addition,  $^4\text{He}_{\text{rad}}$  values were elevated, a not unexpected result as observation well FRI426UP was located in the center of the contamination plume (horizontal) (Figure 3.1 and Figure 3.2) and mixing of water of different ages would be expected. Meffe et al. (*submitted*) found that at a nearby

observation well (FRI447UP), intrusion of deeper and older groundwater from a saltwater-bearing aquifer resulted in strongly elevated chloride ( $\text{Cl}^-$ ) concentrations. Increased  $\text{Cl}^-$  concentrations (Table A.1) were also detected at well FRI426UP, affirming the presence of older fractions.

An admixture of recent groundwater and water dating from before the 1960s can also be presumed for observation well FRI425MP2, which has an apparent age of 34.5 years. This is again indicated by the large ratio between  $^3\text{He}_{\text{tri}}$  and  $^3\text{H}$ . The relatively low amount of  $^4\text{He}_{\text{rad}}$  ( $0.49 \text{ 1E-5 N mL/kg}$ ), however, suggests that the water is probably younger than 100 years. Calculated  $^3\text{He}$ - $^3\text{H}$  ages are summarized in Table 3.2.

Table 3.2 Results of noble gas analysis and age dating.

Sample ID	Filter screen		$^3\text{He}$ - $^3\text{H}$ age (yrs)	$^3\text{H}$ (TU)	$^3\text{He}_{\text{tri}}$ (TU)	$^3\text{H} + ^3\text{He}_{\text{tri}}$ (initial $^3\text{H}$ ) (TU)	$^4\text{He}_{\text{rad}}$ ( $\times 10^{-5} \text{ N mL/kg}$ )
	depth (m BGS)	From To					
FRI1634OP	37.0	39.0	29.1	1.1	4.7	5.8	4.63
FRI425OP	10.5	12.5	10.7	5.4	4.3	9.7	0.00
FRI425MP2	39.0	41.0	34.5	1.5	8.6	10.1	0.49
FRI426OP	10.3	12.3	27.2	3.8	14.0	17.8	0.93
FRI426MP1	17.9	19.9	30.3	3.9	18.0	21.9	0.92
FRI426UP	40.8	42.8	38.7	5.1	40.0	45.1	1.10
FRI430OP	7.4	8.4	12.3	5.1	5.0	10.1	0.03
FRI430UP	23.5	24.5	21.8	4.5	9.5	14.0	0.27
FRI447OP	8.0	12.0	19.3	5.0	10.0	15.0	0.31
FRI447MP1	26.1	30.1	25.2	3.8	12.0	15.8	0.22
FRI515OP	5.5	7.5	1.0	7.7	0.5	8.2	0.00
FRI515MP	15.4	17.4	10.6	5.4	4.4	9.8	0.00
FRI515UP	24.5	26.5	11.4	4.9	4.4	9.3	0.15

Date of  $^3\text{He}$ - $^3\text{H}$  sampling: 20-22 September 2010.

Concentrations of psychoactive substances can be related to groundwater ages as an increase in age is associated with an increase in concentrations (Figure 3.5) unless admixture with older water occurs. The apparent age of groundwater in this study is four decades at maximum. This suggests infiltration after 1970. However, the main input of the studied psychoactive compounds was prior to the 1970s, when sewage irrigation took place. In addition, the application of some of the compounds (e.g., meprobamate) occurred even earlier. Assuming an average groundwater flow rate of 0.2 m/day and conservative behavior

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of the compounds, most of the substances should already have been flushed out. The fact that they are still detectable and are at high concentrations throughout the study area could be the result of either (a) dispersive mixing of otherwise conservative compounds, meaning that concentrations were considerably higher in the past, since peak concentrations have already passed through, (b) retardation as a result of sorption, or (c) immobile domains are now acting as a secondary source and releasing psychoactive compounds. Assumption (a) appears unlikely since concentrations are still very high. However, data on the application rates in the past are lacking. Regarding (b), information on sorption behavior to natural sediments is scarce. Therefore, lab experiments are currently being undertaken by the authors. To date, Yu et al. (2009) described a low sorption affinity with soils for primidone. Other studies report minor sorption of meprobamate (Westerhoff et al., 2005) and primidone (Zwickenpflug and Böhrer, 2010) to activated carbon. Thus, we suppose that sorption probably plays a minor role. Assumption (c) has been posted by Meffe et al. (*submitted*) as a source for *p*-TSA in the area, and thus, it may also apply to psychoactive compounds. The main evidence for this presumption was the observed tailing of the conservative ion Cl<sup>-</sup> which could not be reproduced by conventional advection-dispersion modeling by Meffe et al. (*submitted*). We suppose that the adhesive water in low permeable layers (such as silt lenses, Figure 3.3) still contains high concentrations of the contaminants. The pollutants are exchanged gradually into the surrounding mobile groundwater by diffusion which significantly delays the solute transport.

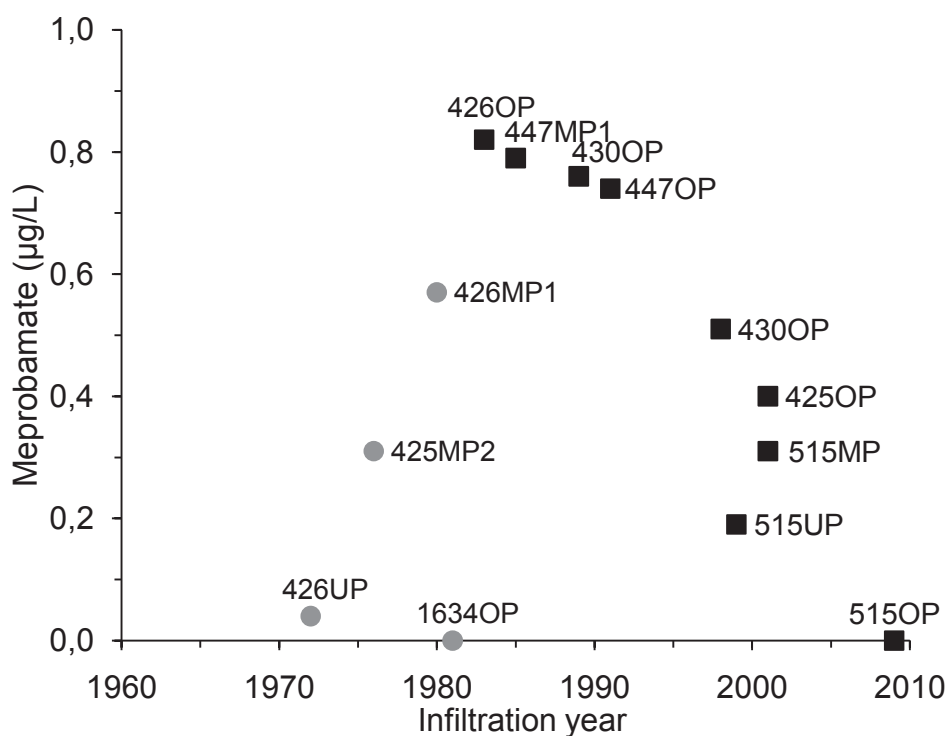


Figure 3.5 Median concentrations of meprobamate ( $\mu\text{g/L}$ ;  $n = 3$ ; March 2010 to April 2011) versus infiltration years as adapted from  $^3\text{He}$ - $^3\text{H}$  dating (infiltration years = sampling date -  $^3\text{He}$ - $^3\text{H}$  age). Corresponding observation well numbers are also given. Gray circles illustrate results for groundwater thought to be a mixture of old and young groundwater. Black squares represent results for presumably unmixed groundwater.

### 3.4.5 Risk assessment

The suspected continuous release of pollutants from immobile domains and the sizes of the contaminant plumes (Figure 3.2 a-e and Figure 3.3) suggest that the heritage of sewage irrigation will affect the raw water quality in the study area for some time into the future. Based on predictive modeling, Meffe et al. (*submitted*) stated that elevated concentrations ( $>0.3 \mu\text{g/L}$ ) of the industrial chemical *p*-TSA can be expected in the groundwater at this site until 2141. Regarding  $\text{NH}_4^+$  at this site, Hamann (2009) predicted groundwater concentrations exceeding the natural background level possibly beyond 2300. These predictions cannot be directly applied to the psychoactive drugs, since concentrations are different and the retardation of  $\text{NH}_4^+$ , owing to sorption as well as degradation, has to be taken into consideration. Nevertheless, we assume that these modeled results demonstrate a tendency that is also applicable to the investigated psychoactive compounds.



In relation to risk assessment for drinking water production, the following aspects should be mentioned. As stated before, well gallery A serves as hydraulic protection and is intended to divert and focus the plume (see 3.2 Study area). However, owing to the high production volume of the eastern wells of gallery B, propagation of the plume is strongly affected and pollutants also reach the western wells of this gallery (gallery B wells 1-15, Table A.1). Raw water from other well galleries (C, D, E) was sporadically examined and did not exhibit concentrations above the LOQ for the psychoactive drugs (unpublished data). Hence, a further expansion of the contamination plume toward the south appears to have been prevented. Due to the strong dilution of the contaminated raw water (gallery B) with the low-pollutant bank filtrate of the other well galleries (galleries C, D, E), concentrations of psychoactive compounds are below the LOQ in the final drinking water of the DWTP (Table A.1). The concentrations are thus also below the HPV of 3.0 µg/L for primidone, 0.30 µg/L for phenobarbital, and 0.10 µg/L for the other psychoactive drugs (Dieter, 2009).

### 3.5 Conclusions

- All of the investigated psychoactive pharmaceuticals and metabolites were detectable in groundwater underneath and downgradient of a decommissioned sewage farm within the catchment area of a DWTP. The detected compounds were phenobarbital, meprobamate, primidone, phenylethylmalonamide, and pyrithyldione (listed in an order of decreasing concentrations). Concentrations ranged up to 1 µg/L.
- The elevated concentrations of these legacy pollutants throughout the study area illustrate their long-term persistence in the environment under anoxic aquifer conditions. Investigations of redox-dependent degradation and sorption behavior are currently being undertaken in lab experiments.
- Dating results confirm the presence of decade-old groundwater. Groundwater gets progressively older as aquifer depth and distance increases.
- At some deeper observation wells elevated concentrations of  $^4\text{He}_{\text{rad}}$  provided evidence for the admixture of younger water with  $^3\text{H}$  and  $^3\text{H}$ -free older water.
- A correlation between concentrations of the investigated psychoactive drugs and the apparent  $^3\text{He}$ - $^3\text{H}$  age can be observed for the unmixed samples. In relation to the entry periods of the pharmaceuticals, determined ages suggest retardation of these

contaminants, either by sorption or due to so-called hydraulic retardation, where immobile domains act as secondary sources as proposed by Meffe et al. (*submitted*).

- The dimensions of the contaminant plumes suggest that the legacy of sewage irrigation will continue to affect the quality of abstracted raw water in the area over the next decades.
- At present, concentrations of the psychoactive compounds in the final drinking water are below the LOQ and thus also below the HPV. This is achieved by (a) the operation of well gallery A as hydraulic protection, (b) an adjusted production regime of the northern well gallery B, and (c) a large dilution of contaminated raw water with raw water from other well galleries that mainly abstract low-pollutant bank filtrate.
- Because of the elevated concentrations of compounds in the groundwater, especially meprobamate and phenobarbital, further monitoring of raw and final drinking water is recommended to ensure that contaminant concentrations remain below the HPV.
- The results of this study highlight the importance of monitoring legacy pollutants in groundwater even if they have been banned from the market for years. The investigated compounds may also be present at similar former wastewater irrigation sites that exist worldwide and which are also often anoxic with regard to their hydrochemical conditions.

## 4. Occurrence in the water cycle of Berlin

The occurrence and distribution of six psychoactive compounds (primidone, phenobarbital, oxazepam, diazepam, meprobamate, and pyrithyldione) and a metabolite of primidone (phenylethylmalonamide) were investigated in wastewater treatment plant (WWTP) effluents, surface water, groundwater of a bank filtration site, raw and final drinking water, and in groundwater affected by former sewage irrigation.

Primidone and its metabolite phenylethylmalonamide were found to be ubiquitous in environmental water samples in Berlin. Maximum concentrations of 0.87 and 0.42 µg/L, respectively, were encountered in WWTP effluents. Both compounds are apparently not removed when passing through the different compartments of the water cycle and concentrations are only reduced by dilution. Phenobarbital was present at nearly every stage of the Berlin water cycle with the exception of raw and final drinking water. The highest concentrations of phenobarbital (up to 0.96 µg/L) were measured in groundwater influenced by former sewage irrigation. Oxazepam was only present in WWTP effluents and surface waters (up to 0.18 µg/L), while diazepam was not detected in any matrix. Due to their withdrawal from the German market years ago, the pharmaceuticals meprobamate and pyrithyldione were only found in sewage farm groundwater (up to 0.50 and 0.04 µg/L, respectively) and, in case of meprobamate, also in decade old bank filtrate (0.03 µg/L).

Our results indicate a high persistence of some of the investigated compounds in the aquatic system. As a consequence, these pollutants may potentially reach drinking water resources via bank filtration if present in WWTP effluents and/or surface waters in partly closed water cycles such as Berlin's.

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Ulrike Hass, Uwe Dünnebier, Gudrun Massmann (2012)

*Occurrence and distribution of psychoactive compounds and their metabolites in the urban water cycle of Berlin (Germany).*

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## 4.1 Introduction

The occurrence of pharmaceuticals from various prescription classes (such as analgesics, antibiotics, beta blockers, iodinated contrast media, and anticonvulsants) in the aquatic environment has been reported frequently in recent years (e.g., Ternes, 1998; Kümmerer, 2001; Drewes et al., 2003; Schneider, 2004; Schwarzenbach et al., 2006; Vanderford and Snyder, 2006). The main source of organic trace pollutants in aquatic systems is wastewater treatment plant (WWTP) effluent. Pharmaceutical residues may not be fully eliminated during sewage treatment and are thus discharged into receiving waters (Ternes, 1998; Heberer et al., 2002; Miehe, 2010). This is particularly problematic in urban areas with a partly closed water cycle such as Berlin (Germany), where drinking water production largely relies on groundwater recharge via bank filtration and/or artificial groundwater enrichment (Heberer and Stan, 1997; Heberer et al., 2004; Massmann et al., 2007). Bank filtration for drinking water production purposes is also common in other countries in Europe and in the USA (Ray et al., 2002). Moreover, especially in emerging countries suffering from high population growth and water scarcity at the same time, bank filtration will be increasingly used in the future to reclaim drinking water (e.g., Egypt; Shamrukh and Abdel-Wahab, 2008; India; Sandhu et al., 2011).

Besides the discharge of WWTP effluents to surface waters, the application of municipal wastewater on sewage irrigation farms may lead to considerable anthropogenic pollution of the environment, in particular of soils and groundwater (e.g., Scheytt et al., 2000; Richter et al., 2009a; Hass et al., 2012a). Irrigation of wastewater is still practiced in many countries of the world and was also common in Berlin until the 1980s (SenStadt, 2012). Although contaminants are diluted or partially removed through sorption and degradation in surface waters and during subsurface flow, they may still reach drinking water resources.

Previous studies by the authors revealed the presence of several psychoactive compounds in groundwater below a decommissioned sewage farm located within the catchment area of a drinking water treatment plant (DWTP) in Berlin (Hass et al., 2011, 2012a). The antipsychotic drugs detected in those studies were further investigated in the current study and include primidone, its metabolites phenobarbital and phenylethylmalonamide, oxazepam, diazepam, meprobamate, and pyrithyldione.

Primidone is an anticonvulsant available on the market since the 1950s. In humans and animals, primidone is converted into two major pharmacologically active substances, phenobarbital and phenylethylmalonamide (El-Masri and Portier, 1998). While phenylethylmalonamide has no medical application, phenobarbital is also prescribed as an anticonvulsant. Moreover, phenobarbital is still one of the most widely used antiepileptic drugs worldwide (Kwan and Brodie, 2004). In the past, the barbiturate phenobarbital was predominantly used as a sedative and hypnotic. Introduced in 1912, phenobarbital was replaced in Germany in the 1960s by benzodiazepines for these indications due to an increased addiction potential and narrow therapeutic range (Linde, 1992). Two benzodiazepine derivative drugs, oxazepam and diazepam, are used extensively worldwide since the 1960s as tranquilizers for the treatment of anxiety and insomnia. Oxazepam is also an active metabolite of numerous benzodiazepines, including diazepam (Klotz, 1995). The anxiolytic drug meprobamate was introduced in 1955 but was soon (1960s) superseded by benzodiazepines (Müller and Hartmann, 1995). Meprobamate is a non-prescribable narcotic in Germany (BtMÄndV, 1991) but is still available, for example, in other European countries and in the USA. Pyrithyldione is a sedative-hypnotic pharmaceutical introduced in 1949 (Linde, 1992). Due to adverse effects (Ibáñez et al., 2000), pyrithyldione was withdrawn from the market in the 1980s.

Although some of these psychoactive compounds are no longer administered in Germany, they were detected in (decade-old) groundwater at concentrations up to 1 µg/L (Hass et al., 2012a). Their presence in the environment raised concerns, initiating the present study exploring the occurrence and fate of these compounds in the entire water cycle of Berlin.

The objectives of this investigation were to: i) determine and monitor the occurrence of the described psychoactive compounds in environmental water samples from Berlin, including WWTP effluents, surface water, bank filtrate, groundwater influenced by sewage irrigation, and raw and final drinking water; ii) study the elimination of these substances during bank filtration and drinking water treatment, and iii) evaluate the risk of contamination of drinking water. This study provides important information on the distribution and the fate of these contaminants in the aquatic environment. At comparable hydrologic settings, the study also gives an insight into the potential negative effects when water supply relies on the indirect reuse of wastewater via bank filtration.

To date, the occurrence and fate of primidone in the environment has been described by several authors (e.g., Heberer et al., 2002; Drewes et al., 2003; Reddersen, 2004; Schneider, 2004; Hummel et al., 2006; Massmann et al., 2007; Guo and Krasner, 2009). Studies describing oxazepam and diazepam in the aquatic environment have also been published (e.g., Reddersen, 2004; Schneider, 2004; Hummel et al., 2006; González Alonso et al., 2010). However, to the best of our knowledge, a comprehensive overview of their behavior in the various stages of an urban water cycle is still lacking. Phenobarbital, phenylethylmalonamide, and meprobamate have rarely been investigated in aquatic environments in Germany and, thus far, no reports exist on the occurrence of pyrithyldione.

## 4.2 The Berlin water cycle

The drinking water supply for the 3.5 million inhabitants of Berlin is comprised completely of groundwater that mainly originates from induced bank filtration (60-70 %) (Massmann et al., 2007; Möller and Burgschweiger, 2008). Owing to the fact that the present hydrologic system can be regarded as semi-closed, Berlin's water production is partially based on the indirect reuse of wastewater (Ziegler, 2001; Massmann et al., 2004).

In the past (1876-1980s) (SenStadt, 2012), untreated wastewater was directly applied to sewage farms located within the city boundaries or in the close surroundings of Berlin (Figure 4.1). These sewage fields were inundated over several decades with high amounts of wastewater and hence accumulated high contaminant loads so that today these fields have to be considered as legacy pollution sites. In a partially closed water cycle such as Berlin's, these sites pose a potential risk for surface and groundwater contamination. Increasing wastewater volume necessitated a reconsideration of wastewater disposal and led to the construction of large-scale WWTPs. Nowadays, household and industrial wastewater from Berlin and its surroundings is processed via six WWTPs (for locations see Figure 4.1). Treatment involves a mechanical stage followed by biological treatment (phosphate and nitrate removal) and a final clarification. In 2011, 238 million m<sup>3</sup> of wastewater were treated and discharged into the receiving surface waters of Berlin (BWB, 2012b).

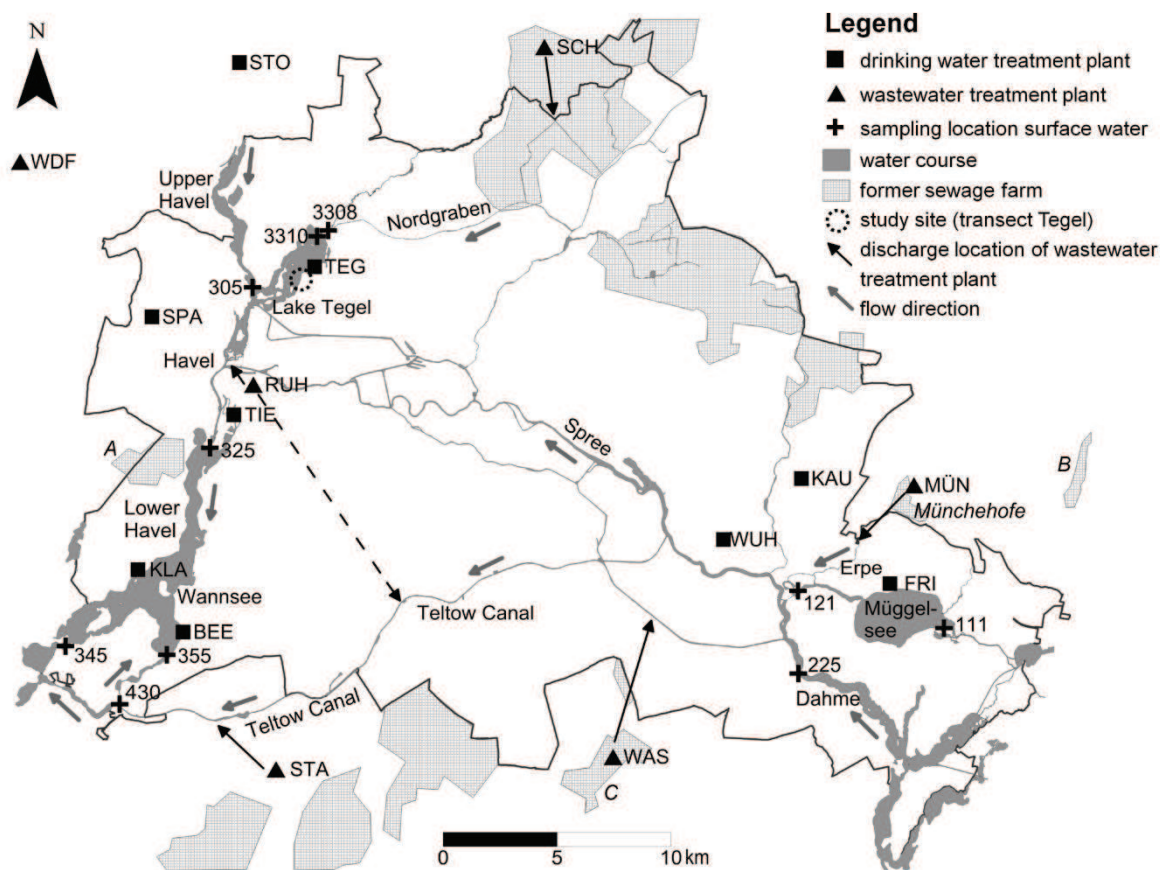


Figure 4.1 Map of Berlin (Germany), showing the waterways and locations of drinking water treatment plants, wastewater treatment plants, and former sewage farm districts. Crosses with corresponding sample IDs mark surface water sampling sites. The dotted circle shows the location of the bank filtration study site (see also Figure 4.3). Surface water flow is directed from south-east and north towards the south-west (gray arrows). Black arrows indicate WWTP discharge points.

The surface water system, primarily formed by the lowland rivers Dahme, Spree, and Havel is characterized by low natural flow rates and small hydraulic gradients (Heberer et al., 2002). As some rivers directly serve as receiving waters for WWTPs (points of discharge are shown in Figure 4.1) locally high proportions of treated wastewater may be found in the surface water. For example, according to Ziegler (2001), Lake Tegel contains 17-35 % treated sewage. Heberer et al. (2002) and Reddersen (2004) reported treated wastewater volumes of up to 84 % at low surface flow in the Teltow Canal, which functions as receiving water for three WWTPs during dry periods (Figure 4.1).

Surface water infiltrates into the ground via induced bank filtration facilitated by production well galleries along lake shores. It mixes with ambient groundwater in the groundwater body and is subsequently withdrawn for drinking water production purposes (e.g., Massmann et al., 2004). After abstraction, minimal, quasi-natural treatment (aeration, rapid sand filtration) is sufficient to meet drinking water quality standards (BWB, 2012c). In this way, the Berliner Wasserbetriebe produced 198 million m<sup>3</sup> of drinking water in 2011 in nine DWTPs (for locations see Figure 4.1; BWB, 2012b).

Owing to the spatial proximity of WWTP discharge points, receiving surface waters, and bank filtration sites, a series of wastewater residues can be found in Berlin surface and groundwater (e.g., Heberer and Stan, 1997; Heberer et al., 2002, 2004; Grünheid et al., 2005; Richter et al., 2008b). Despite natural barriers during underground passage, (e.g., chemical, physicochemical, and biochemical processes) particularly polar, hydrophilic, and persistent compounds can reach abstraction wells and have already been detected in drinking water at measurable but very low concentrations (e.g., Heberer and Stan, 1997; Heberer et al., 2002, 2004; Richter et al., 2008b).

### **4.3 Materials and methods**

#### **4.3.1 Sampling locations and sample collection**

*Wastewater treatment plants.* Effluents from the six municipal WWTPs (Figure 4.1) of Berlin were taken as 24-h composite samples using an automatic sampler. Sampling was conducted in May 2010 and between March 2011 and January 2012 (n = 5-6).

*Surface water.* Surface water samples were taken in temporal proximity to the collection of samples from the WWTPs. Grab samples from ten locations (Figure 4.1) were taken from the middle of the water body at a depth of 1 m using standard equipment (n = 3-5).

*Bank filtration.* Samples along a transect at a bank filtration site on the shore of Lake Tegel (Figure 4.1 and Figure 4.3) were collected quarterly between February and December 2011 (n = 4). The field site was located within the catchment area of the DWTP Tegel (TEG) and was of particular interest, as the adjacent surface water contains a significant amount of



treated wastewater. Hence, this transect had already been subject of several studies (Schittko et al., 2004; Grünheid et al., 2005; Massmann et al., 2008a; Richter et al., 2008b). The research transect follows the flow direction from the lake to a production well (DWTP TEG) and contains a number of observation wells of various depths. One observation well is placed beyond the production well to sample the ambient groundwater (Massmann et al., 2008a). According to Grünheid et al. (2005) the prevailing redox conditions at the bank filtration site, that may have an influence on the degradation, are mostly anoxic (nitrate reduction) to anaerobic (iron and manganese reduction). Further details of the studied bank filtration site have been published by Grünheid et al. (2005) and Massmann et al. (2007; 2008b). A simplified hydrological cross section of the transect in combination with primidone concentrations and travel times is shown in Figure 4.3.

*Groundwater influenced by sewage irrigation.* Groundwater samples were taken in accordance with the DIN 38402-13 (1985) in several areas formerly used as sewage farms within the city boundaries or just outside of Berlin. Some of these groundwater resources were known to be contaminated by organic trace components due to the direct irrigation of untreated wastewater for decades (e.g., Heberer and Stan, 1997; Peschka et al., 2006; Richter et al., 2008b; Hass et al., 2012a).

*Drinking water treatment plants.* Drinking water samples were retrieved from nine DWTPs (Figure 4.1) as grab samples before and after treatment in conjunction with the sampling of the WWTPs. Thus, raw and tap water samples were collected every three months between March and December 2011 (n = 4).

All samples were taken in glass bottles and extracted immediately or stored in the dark at 4 °C for less than 14 days. WWTP effluent samples were extracted within 48 h after collection and extracts were analyzed within a week to avoid changes in the samples (i.e., analyte losses by microbial degradation).

#### **4.3.2 Analysis**

All water samples were analyzed in the laboratory of the Berliner Wasserbetriebe. The analytical method applied for the determination of psychoactive compounds was developed and validated recently and is described in detail in Hass et al. (2011). Briefly, for the

extraction of the analytes from the samples automated solid-phase extraction was performed using a reversed-phase octadecyl adsorbent. Subsequently, sample extracts were analyzed via reversed-phase ultrahigh-performance liquid chromatography coupled to tandem mass spectrometric detection in multi-reaction monitoring mode and the application of electrospray ionization in both positive and negative mode. With this procedure limits of quantification (LOQ) between 0.02 and 0.03  $\mu\text{g/L}$  were obtained for groundwater. LOQs were assumed to be valid for all investigated matrices. Using surrogate standards for quantification recoveries generally exceeded 80 %.

## 4.4 Results and discussion

### 4.4.1 Occurrence in WWTP effluents

Effluents from six WWTPs in Berlin treating a mixture of municipal and industrial sewage were examined for the occurrence of psychoactive compounds ( $n = 5-6$ ). Four of the seven substances investigated, namely primidone, phenobarbital, phenylethylmalonamide, and oxazepam, were frequently found in effluents (Table 4.1, Figure 4.2). Median effluent concentrations for the six WWTPs ranged from 0.43 to 0.71  $\mu\text{g/L}$  for primidone, 0.09 to 0.21  $\mu\text{g/L}$  for phenobarbital, 0.21 to 0.37  $\mu\text{g/L}$  for phenylethylmalonamide, and 0.08 to 0.16  $\mu\text{g/L}$  for oxazepam (Table 4.1). Amongst WWTPs, overall concentrations were within the same order of magnitude. However, values of primidone, phenobarbital, and phenylethylmalonamide were generally somewhat higher in the WWTPs Münchehofe (MÜN) and Wansdorf (WDF) as compared to the other four plants (Table 4.1). This may be explained by a lesser proportion of industrial wastewater and/or less stormwater in the WWTPs MÜN and WDF, both of which could result in less dilution of the water matrix and thus higher concentrations of the investigated compounds. Furthermore, it should be noted that decade-old contaminated groundwater is pumped for remediation purposes from downgradient of a former sewage farm and subsequently discharged to the WWTP MÜN (Hass et al., 2012a). This groundwater is correspondingly also a source of higher primidone, phenobarbital, and phenylethylmalonamide levels and median concentrations of meprobamate of 0.08  $\mu\text{g/L}$  (Table 4.1).

Table 4.1 Sample type (WWTP effluent (eff), surface water (sw), and groundwater (gw)) and filter screen depths of the production and observation wells, number of samples (n) and median concentrations of primidone (PRM), phenobarbital (PB), phenylethylmalonamide (PEMA), oxazepam (OZP), and meprobamate (MPB) ( $\mu\text{g/L}$ ). Concentrations of diazepam and pyriithydione were always  $<0.02 \mu\text{g/L}$ .

Sample ID	Sample type	Filter screen depth (m BGS)	n	PRM ( $\mu\text{g/L}$ )	PB ( $\mu\text{g/L}$ )	PEMA ( $\mu\text{g/L}$ )	OZP ( $\mu\text{g/L}$ )	MPB ( $\mu\text{g/L}$ )
		From To						
<b>WWTP effluents</b>								
RUH	eff Ruhleben		5	0.43	0.09	0.21	0.14	<0.02
WAS	eff Waßmannsdorf		6	0.54	0.11	0.26	0.14	<0.02
SCH	eff Schönerlinde		6	0.43	0.10	0.24	0.08	<0.02
STA	eff Stahnsdorf		6	0.50	0.11	0.25	0.16	<0.02
MÜN	eff Münchehofe		6	0.65	0.21	0.36	0.08	0.08
WDF	eff Wansdorf		6	0.71	0.17	0.37	0.14	<0.02
<b>Surface water</b>								
111	sw Spree		5	<0.02	<0.03	<0.03	<0.02	<0.02
121	sw Spree		5	0.03	<0.03	<0.03	<0.02	<0.02
225	sw Dahme		5	<0.02	<0.03	<0.03	<0.02	<0.02
305	sw Upper Havel		5	<0.02	<0.03	<0.03	<0.02	<0.02
325	sw Havel		5	0.04	<0.03	<0.03	<0.02	<0.02
345	sw Lower Havel		5	0.04	<0.03	<0.03	<0.02	<0.02
355	sw Small Wannsee		5	0.13	<0.03	0.09	0.03	<0.02
430	sw Teltow Canal		5	0.15	0.04	0.11	0.04	<0.02
3308	sw Nordgraben/SWTP influent		3	0.18	0.04	0.11	0.03	<0.02
3310	sw SWTP effluent		5	0.16	0.05	0.11	0.03	<0.02

Table 4.1 continued

Sample ID	Sample type	Filter screen depth (m BGS)	n	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	OZP (µg/L)	MPB (µg/L)
		From To						
<b>Transect Tegel</b>								
5260	sw Lake Tegel		4	0.12	<0.03	0.06	<0.02	<0.02
GWM 3301	gw (bank filtrate)	21.0	4	0.14	0.04	0.07	<0.02	<0.02
GWM 3302	gw (bank filtrate)	22.0	4	0.11	<0.03	0.05	<0.02	<0.02
GWM 3303	gw (bank filtrate)	19.0	4	0.12	<0.03	0.07	<0.02	<0.02
GWM 3304	gw (bank filtrate)	19.0	4	<0.02	<0.03	<0.03	<0.02	<0.02
TEG371OP	gw (bank filtrate)	10.3	4	0.12	<0.03	0.06	<0.02	<0.02
TEG371UP	gw (bank filtrate)	16.2	4	0.09	<0.03	0.07	<0.02	<0.02
TEG372	gw (bank filtrate)	9.7	4	0.11	<0.03	0.07	<0.02	<0.02
TEG374	gw (bank filtrate)	37.0	4	0.14	0.07	0.08	<0.02	0.03
Well 13	gw (bank filtrate, production well)	20.0	4	0.07	<0.03	0.05	<0.02	<0.02

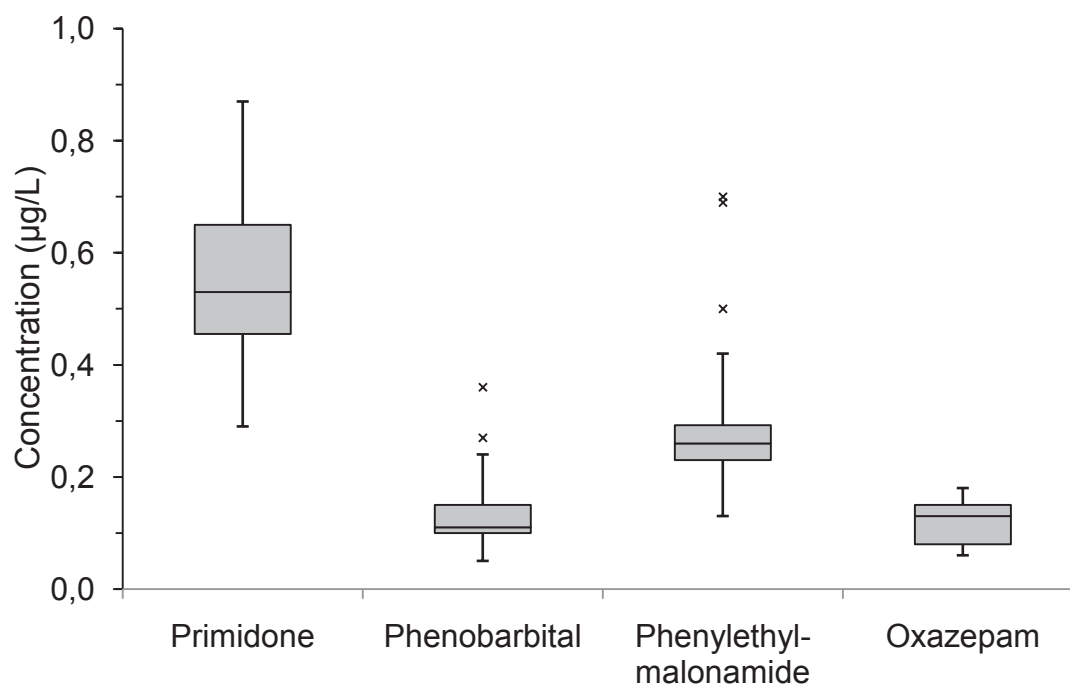


Figure 4.2 Concentrations of primidone (PRM), phenobarbital (PB), phenylethylmalonamide (PEMA), and oxazepam (OZP) in effluents of six WWTPs ( $\mu\text{g/L}$ ;  $n = 35$ ; May 2010 to January 2012). Median values (horizontal center line), the 25 %- and the 75 %-quartiles (box), minimum and maximum values (vertical line), and outliers (crosses) for the respective compounds are shown.

Pyrrithyldione and diazepam were not detected in any of the sewage samples. These results match our expectations. Similar to meprobamate (see 4.1 Introduction), pyrrithyldione is no longer prescribed. Diazepam, which is still in use today, is largely metabolized in the human body and therefore rarely excreted in its original form (Klotz, 1995).

Primidone and oxazepam have previously been quantified in WWTP effluents by several authors. Hummel et al. (2006) observed comparable concentrations of primidone ( $0.42 \mu\text{g/L}$ , median) but slightly higher concentrations of oxazepam ( $0.32 \mu\text{g/L}$ , median) in 12 German WWTP effluents. Somewhat higher levels of primidone ( $0.45\text{--}1.32 \mu\text{g/L}$ ) and oxazepam ( $<\text{LOQ}\text{--}0.55 \mu\text{g/L}$ ) were also reported for WWTP effluents in Berlin in a study carried out between 2000 and 2002 (Reddersen, 2004). In contrast, lower primidone values were measured during studies conducted in Bavaria (Germany) ( $0.1\text{--}0.3 \mu\text{g/L}$ ; LfU, 2010), Switzerland ( $<\text{LOQ}\text{--}0.42 \mu\text{g/L}$ ; Kahle et al., 2009), and the USA ( $0.11\text{--}0.22 \mu\text{g/L}$ ; Drewes et al., 2003).

The occurrence of the primidone metabolites phenobarbital and phenylethylmalonamide in WWTP effluents has rarely been investigated. Mieke (2010) quantified phenobarbital at concentrations between 0.20 and 0.41  $\mu\text{g/L}$  (median) in WWTP effluents in Berlin, while it was not detected during monitoring at 8 WWTPs in Germany and Croatia (Peschka et al., 2006). The levels we describe for phenylethylmalonamide are in agreement with a previous report by the Bavarian Environment Agency (LfU, 2010).

With respect to diazepam, our results are consistent with findings documented in the literature. Accordingly, in WWTP effluents the tranquilizer was either not detected (Hummel et al., 2006; Vanderford and Snyder, 2006) or present at only low concentrations ( $\leq 0.055 \mu\text{g/L}$ ) (Ternes, 1998; Schneider, 2004).

#### 4.4.2 Distribution in surface waters

In the course of this study, ten surface waters that are important components of the partially closed water cycle of Berlin were analyzed for concentrations of psychoactive compounds ( $n = 3-5$ ). Concentrations of the investigated psychoactive compounds are given in Table 4.1.

Samples from the rivers Dahme (sampling point no. 225), Upper Havel (no. 305), and Spree (no. 111) reflect inflow concentrations to Berlin from the north and the southeast, respectively, and did not show measurable concentrations of the psychoactive compounds (Table 4.1).

In contrast, sampling sites located downstream of municipal WWTPs contained elevated concentrations of primidone ( $\leq 0.18 \mu\text{g/L}$ ; median) and phenylethylmalonamide ( $\leq 0.11 \mu\text{g/L}$ ; median), as well as low concentrations of phenobarbital ( $\leq 0.05 \mu\text{g/L}$ ; median) and oxazepam ( $\leq 0.04 \mu\text{g/L}$ ; median) (Table 4.1). These findings are a clear indication of a direct link between WWTP discharges and concentrations of psychoactive compounds in Berlin's surface waters. Meprobamate, pyrithyldione, and diazepam were not detected in any of the surface water samples. This was expected, since these three compounds were also not present in WWTP effluents.

The largest impact of sewage discharges can be observed at the Nordgraben/surface water treatment plant (SWTP) influent (no. 3308) and the Teltow Canal (no. 430). The Nordgraben receives the treated effluents of the WWTP Schönerlinde (SCH), located in the northeast of Berlin (Figure 4.1). A portion of the surface water from the Nordgraben is then treated in a SWTP for elimination of phosphate and suspended matter and subsequently discharged into Lake Tegel. The influent and effluent samples from the SWTP (no. 3308 and 3310) exhibited the same concentration level (Table 4.1), indicating that primidone, phenylethylmalonamide, phenobarbital, and oxazepam are not removed during surface water treatment. As reported in previous studies, the effect of sewage discharges from SCH can be traced further into Lake Tegel and the Havel (Massmann et al., 2004; Richter et al., 2008b). This is also true for primidone, found at 0.04 µg/L in the Havel (no. 325) and Lower Havel (no. 345) (Table 4.1, Figure 4.1). However, in comparison to nos. 3308 and 3310, diluted discharges from the Spree and Upper Havel resulted in considerably lower primidone concentrations further downstream of the WWTP inlets and the remaining psychoactive compounds were not detectable.

As mentioned before, the Teltow Canal serves as a recipient for three WWTPs (Waßmannsdorf (WAS), Stahnsdorf (STA) and Ruhleben (RUH; April to September)) and partially drains into the Small Wannsee (Massmann et al., 2004; Reddersen, 2004). This caused elevated concentrations of primidone ( $\leq 0.15$  µg/L; median), phenylethylmalonamide ( $\leq 0.11$  µg/L; median), phenobarbital ( $\leq 0.04$  µg/L; median), and oxazepam ( $\leq 0.04$  µg/L; median) at sampling point nos. 430 and 355 (Table 4.1, Figure 4.1).

The concentration levels we observed for primidone and oxazepam are within the concentration range reported for some surface waters of the Berlin region by Heberer et al. (2002) and Reddersen (2004). Moreover, Reddersen (2004) reported distribution patterns similar to ours within the water cycle of the city. Thus, the highest concentrations of compounds were found along the Teltow Canal and at the Small Wannsee, whereas the lowest values were measured at the Dahme River. Our results also match well with the primidone concentration (0.06 µg/L) detected in a river located downstream of a WWTP in the USA (Guo and Krasner, 2009). For oxazepam, our findings are consistent with values ( $\leq 0.13$  µg/L) reported by González Alonso et al. (2010) for rivers receiving WWTP

effluents in Spain, whereas Hummel et al. (2006) observed higher concentrations of oxazepam ( $\leq 0.4 \mu\text{g/L}$ ) in rivers and streams in Southwest Germany.

In accordance with our results, diazepam has rarely been detected above a low ng/L level in surface waters (Ternes, 1998; Hummel et al., 2006; Vanderford and Snyder, 2006). Few data are available with respect to the occurrence of phenylethylmalonamide, phenobarbital, and meprobamate in surface waters. In a study by the Bavarian Environment Agency (LfU, 2010) phenylethylmalonamide was detected at comparable concentrations ( $\leq 0.08 \mu\text{g/L}$ ) in rivers in Bavaria. Regarding phenobarbital, in contrast to our results, a significantly higher maximum value ( $\leq 1.5 \mu\text{g/L}$ ) was observed in the river Mulde (Germany) by Peschka et al. (2006). Vanderford and Snyder (2006) reported meprobamate concentrations of  $0.59 \mu\text{g/L}$  (median) in rivers in the USA. However, a comparison with the results obtained here ( $< \text{LOQ}$ ) is not reasonable, as meprobamate is still in use in the USA, while it was declared a non-prescribable narcotic in Germany years ago (BtMÄndV, 1991).

#### 4.4.3 Concentrations in groundwater wells of a bank filtration site

To assess whether the investigated drug residues are eliminated during subsurface flow, samples were taken along a transect at a bank filtration site located at the eastern shore of Lake Tegel (Figures 4.1 and 4.3). Primidone concentrations in combination with travel times according to Massmann et al. (2008b) are shown in Figure 4.3.

Primidone and its metabolite phenylethylmalonamide are obviously not eliminated under present conditions. Both compounds were detected in all observation wells between the lake and the production well at median concentrations of  $0.09$  to  $0.14 \mu\text{g/L}$  and  $0.05$  to  $0.08 \mu\text{g/L}$ , respectively (Table 4.1, Figure 4.3). Concentrations of these compounds in the groundwater are thus in the same range as the surface water of Lake Tegel ( $0.12$  and  $0.06 \mu\text{g/L}$ , respectively), remaining nearly constant during subsurface flow until reaching the production well after a travel time of four to five months (for travel times, see Figure 4.3). Concentrations are somewhat lower ( $0.07$  and  $0.05 \mu\text{g/L}$ ) in the production well, owing to the dilution of the bank filtrate with ambient groundwater. Thus, concentrations in the abstracted water well reflect the percentage of bank filtrate in the production well, which is approximately 75 % (Grünheid et al., 2005). The ambient groundwater (GWM 3304) did not show measurable concentrations of the psychoactive compounds. This was



expected, as the replenishment of the ambient groundwater is caused by natural precipitation.

Results for primidone and phenylethylmalonamide indicate that both compounds may be persistent and mobile in an anoxic aquifer. Concentrations of 0.14 and 0.08  $\mu\text{g/L}$ , respectively, at the deep observation well TEG374 (apparent groundwater age = 25 years; estimated using the  $^3\text{He}$ - $^3\text{H}$  dating method; Massmann et al., 2008a), may suggest that these compounds persist not only for several months, but for decades. This assumption is supported by the results of studies conducted with groundwater from below and downgradient of a decommissioned sewage farm in Berlin (Hass et al., 2012a). Here, elevated concentrations of primidone and phenylethylmalonamide in decade-old groundwater illustrated their persistence in the environment under anoxic aquifer conditions. Our results are also consistent with Drewes et al. (2003), Heberer et al. (2004), and Massmann et al. (2007) who described the persistence and mobility of primidone during subsurface flow. The Bavarian Environment Agency recently conducted column experiments on the transport behavior of primidone and phenylethylmalonamide in the subsurface and also found only minor retention of both compounds. They also documented concentrations of primidone and phenylethylmalonamide in groundwater influenced by bank filtration in Bavaria in the low  $\text{ng/L}$  range (LfU, 2010). Concentrations of primidone of up to 0.11  $\mu\text{g/L}$  in the bank filtrate at the same transect at Lake Tegel were reported by Heberer et al. (2004) and correspond very well with our results.

Phenobarbital was found in Lake Tegel only twice during the investigation (May 2011: 0.03  $\mu\text{g/L}$  and November 2011: 0.05  $\mu\text{g/L}$ , data not shown) but was constantly encountered in low concentrations in two of the groundwater observation wells (GWM 3301 and TEG374). The deep observation well TEG374 also produced the only positive finding of meprobamate (0.03  $\mu\text{g/L}$ , median; Table 4.1). We assume that these findings represent residues of former times, given that the groundwater at this location is more than two decades old (Massmann et al., 2008a).

Oxazepam, diazepam, and pyrithyldione were not detected in any sample.

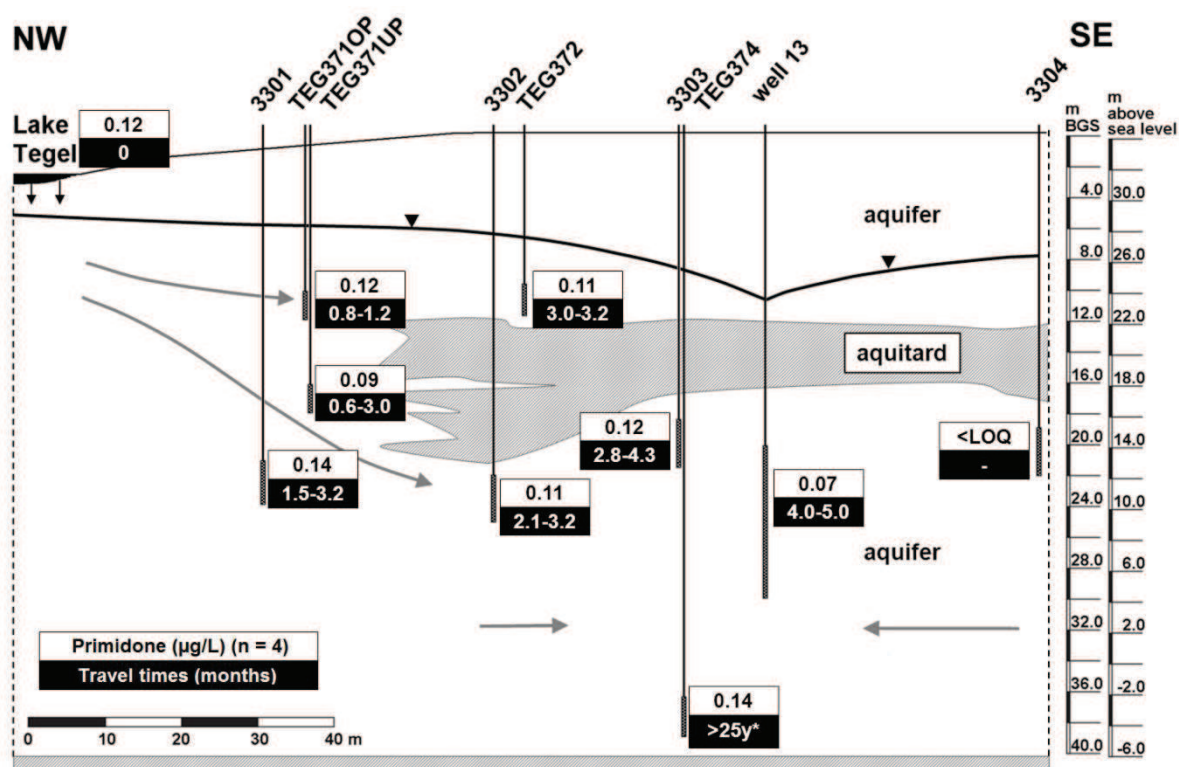


Figure 4.3 Schematic sketch of the transect at Lake Tegel. Black numbers on white background provide median concentrations of primidone ( $\mu\text{g/L}$ ;  $n = 4$ ; February to November 2011; see also Table 4.1) at the depth of the respective filter screen. White letters on black background represent the approximate spectrum of travel times (months) estimated from time-series tracer data (May 2002 to August 2004). An exception is the value (signature\*), giving the apparent  $^3\text{He}$ - $^3\text{H}$  age in years (sampling date 16.03.2004). Possible flow paths and the water level (in winter during pumping) are indicated (modified after Massmann et al., 2008a).

#### 4.4.4 Residues in groundwater influenced by sewage irrigation

The occurrence of five of the investigated psychoactive compounds in groundwater below and downgradient of one of the decommissioned sewage farms of Berlin (Münchehofe; for location see Figure 4.1) has been described in detail in a previous publication (Hass et al., 2012a). To ascertain whether the contamination with psychoactive compounds was an exemption for that specific field site or else is also true for other sewage farm districts, groundwater samples were taken at additional locations formerly used for irrigation of untreated sewage for the present study. Portions of these results are illustrated in Figure 4.4.

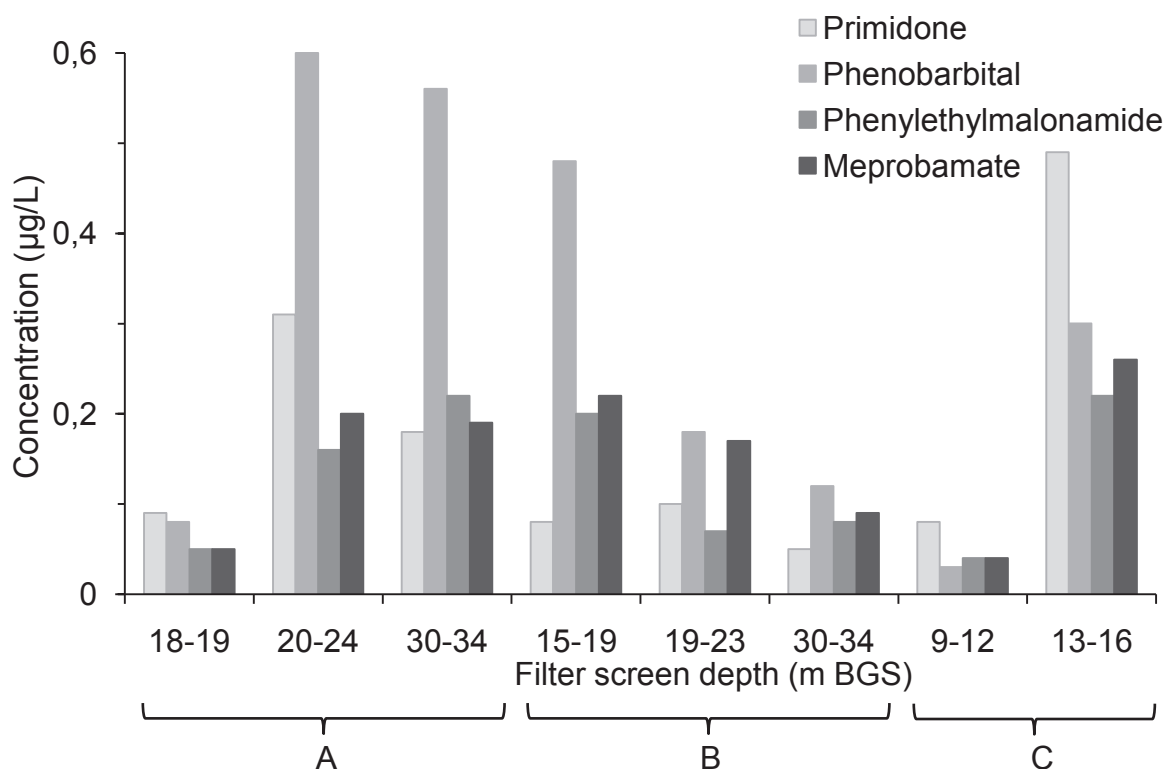


Figure 4.4 Concentrations of primidone, phenobarbital, phenylethylmalonamide, and meprobamate ( $\mu\text{g/L}$ ; single values; March to May 2010) in groundwater below decommissioned sewage farms (A, B, C) in Berlin. Respective filter screen depths (m below ground surface, BGS) of the investigated observation wells are given.

As in other compartments of the Berlin water cycle, primidone, phenobarbital, and phenylethylmalonamide were found in groundwater samples affected by former sewage irrigation. Furthermore, meprobamate and pyrithyldione, both withdrawn from the German market years ago and generally not present in the water cycle, were encountered in these samples. In contrast, oxazepam and diazepam were not detected in any of the groundwater samples.

These findings are in accordance with those from the sewage farm Münchehofe (Hass et al., 2012a). However, concentration ranges of the psychotic drugs in the present study were slightly lower ( $<1 \mu\text{g/L}$ ; data not shown).

As at Münchehofe, the ratio of primidone to its metabolite phenobarbital is often below one. This indicates that water infiltrated when phenobarbital was used extensively, presumably between 1912 and the 1960s (Linde, 1992).

#### 4.4.5 Detection in raw and drinking water

Nine DWTPs in Berlin were analyzed for psychoactive compounds ( $n = 4$ ) to assess whether these reach the DWTPs or final drinking water in measurable concentrations.

Concentrations of the substances studied were generally below the LOQ. Only primidone and its metabolite phenylethylmalonamide were consistently detected in samples of the DWTP TEG (for location see Figure 4.1). Here, primidone and phenylethylmalonamide were present in raw and drinking water at median concentration of 0.08 and 0.04  $\mu\text{g/L}$ , respectively (data not shown). These values reflect the connection between bank filtrate at Lake Tegel (Well 13) and the level of drinking water pollution.

Grab samples were collected from DWTPs and do not allow for the detection of a direct relation between raw and final drinking water. Nevertheless, the results for primidone and phenylethylmalonamide suggest that elimination of these compounds does not occur during locally applied drinking water treatment consisting of aeration and rapid sand filtration. From a toxicological perspective, results for primidone and phenylethylmalonamide raise no safety concerns as drinking water concentrations are well below the health-based precautionary value (HPV) of 3.0 and 0.10  $\mu\text{g/L}$ , respectively (Dieter, 2011). They are, nevertheless, yet another proof that persistent organic pollutants may reach the final drinking water, which is clearly undesired.

Primidone values correspond with previous studies for DWTPs in Germany (Ternes et al., 2002; Reddersen, 2004; Hummel et al., 2006; LfU, 2010) and the USA (Guo and Krasner, 2009). In an earlier survey on the occurrence of pharmaceutical residues in Berlin's water cycle, Reddersen (2004) investigated the formerly 11 DWTPs of Berlin and also reported the highest primidone concentrations ( $\leq 0.12 \mu\text{g/L}$ ) for the DWTP TEG, whereas oxazepam was never detected. These findings are in accordance with our results. The Bavarian Environment Agency (LfU, 2010) documented concentrations of primidone and phenylethylmalonamide of 0.015  $\mu\text{g/L}$  and 0.01  $\mu\text{g/L}$ , respectively, in raw water in Bavaria. However, observations on final drinking water were not given. Consequently, to our knowledge, the present study provides the first evidence of the occurrence of phenylethylmalonamide in drinking water.

#### 4.5 Summary and conclusions

- Four out of seven investigated psychoactive drugs were found in WWTP effluents in Berlin at concentrations of up to 0.87 µg/L (primidone). The detected compounds were primidone, phenylethylmalonamide, phenobarbital, and oxazepam (listed in order of decreasing concentrations).
- These four analytes were also encountered in surface water samples collected from several sites in Berlin. Elevated concentrations of up to 0.29 µg/L (primidone) were found downstream from WWTP discharges. The decrease in concentrations in the course of the water cycle was mainly due to dilution. The persistence of these contaminants in combination with their worldwide application suggests that they are common constituents in municipal wastewater and in WWTP effluent receiving surface waters.
- Primidone and phenylethylmalonamide were frequently detected in the groundwater of a bank filtration site. Measured concentrations suggest that both compounds remain stable during underground passage. Lower concentrations in the production well were caused by dilution with ambient groundwater.
- “Old” bank filtrate (travel time >25 years) also contained phenobarbital (0.07 µg/L; median) and meprobamate (0.03 µg/L; median). Here, both compounds represented residues of former times.
- Low concentrations of primidone (0.08 µg/L; median) and phenylethylmalonamide (0.04 µg/L; median) were frequently detected in the raw and final drinking water of one DWTP, reflecting the concentrations of the bank filtrate. With respect to the investigated DWTPs, all findings were below the recommended HPV.
- With the exception of oxazepam and diazepam, all analytes were present in groundwater influenced by former sewage irrigation at medium to high ng/L levels. These outcomes indicate that these compounds are common components in anoxic groundwater affected by former wastewater irrigation.
- Results of the occurrence and distribution of primidone and phenylethylmalonamide illustrate their high persistence throughout an urban water cycle and potentially resulting consequences in a partly closed water cycle. Removal of both compounds does not appear to occur at any stage of the water cycle and concentrations are only

reduced by dilution. Hence, these compounds reach drinking water resources and potentially even final drinking water.

- The results generally show that when practicing groundwater recharge via bank filtration in drinking water production, polar, poorly biodegradable compounds can leach from contaminated water courses into the aquifers and may also appear at trace-level concentrations in drinking water.

## 5. Redox-sensitivity and sorption behavior

Recently, several psychoactive drugs have been detected in the aquatic system of the metropolis Berlin. Findings point to a strong persistence of the pharmaceuticals and consequently, they may pose a risk to drinking water production. Therefore, a comprehensive knowledge of their fate in the aquatic environment is essential. The aim of this study was to investigate the behavior of primidone, phenobarbital, phenylethylmalonamide, meprobamate, pyrithyldione, oxazepam, and diazepam under different redox conditions (oxic and anoxic). For this, aeration experiments with anoxic groundwater were conducted in the laboratory. Oxazepam and diazepam were not included in this portion of the study since they were not present in the groundwater used for the experiment. Results showed that the compounds were not degraded under either oxic or anoxic conditions, suggesting recalcitrance independent of prevailing redox condition. Further, batch sorption experiments were performed with two sorbents (powdered activated carbon (PAC) and a sandy sediment). Generally, a much higher affinity was observed with the PAC (removal up to 100 %) than with the sand (removal up to 35 % within 72 h), indicating rather good mobility in comparable sandy sediments and hence an elevated potential for leaching to groundwater. Additionally, in comparison to oxazepam and diazepam, sorption of the other compounds to the PAC was considerably less effective (20-58 %). Finally, sorption parameters were calculated and used for risk evaluation at a local field site. This assessment suggested that the investigated pharmaceuticals could remain in the aquifer for several decades up to centuries despite their mobility.

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*Redox-sensitivity and sorption behavior of psychoactive compounds in groundwater.*

Submitted to Water Environment Research (under review).

## 6. Conclusions

The overall aim of this thesis was to obtain better knowledge on the occurrence, fate, and behavior of seven psychoactive compounds in the aquatic environment of Berlin with particular focus on groundwater affected by former wastewater irrigation practices.

Within this last section, the principal findings and conclusions of the study are summarized. Additionally, some recommendations for further investigations are provided.

### 6.1 Major outcomes and conclusions from individual chapters

#### Chapter 2: Analytical method

- An analytical method has been developed allowing the simultaneous determination of primidone, phenobarbital, phenylethylmalonamide, meprobamate, pyrithyldione, oxazepam, and diazepam in various aqueous matrices. The technique involves sample pre-treatment by SPE and subsequent analysis which is performed via UHPLC-MS/MS.
- It is the first published analytical method that facilitates quantification of phenylethylmalonamide and pyrithyldione in water samples.
- The application of surrogate standards significantly contributes to the compensation of analyte losses during sample preparation and of matrix effects during analysis and is therefore strongly recommended.
- The method has been shown to provide good recoveries (typically exceeding 80 %) and low LOQs (0.02-0.15 µg/L, depending on the individual analyte and sample origin) and is appropriate for measuring the seven trace compounds in WWTP effluents, surface water, groundwater, and drinking water.

#### Chapter 3: Occurrence in polluted groundwater

- Investigations have shown that groundwater underneath and downgradient of a decommissioned sewage farm is contaminated with the target compounds, even though operation was terminated in the 1980s. Five out of the seven studied analytes were detected and concentrations ranged up to 1.35 µg/L (phenobarbital).



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- The measured elevated concentrations of the psychoactive compounds are an indication for their long-term persistence in the environment under anoxic aquifer conditions.
  - Dimensions of the contaminant plumes are considerable (approx. 3000 m x 3500 m x 47.5 m; W x L x D). Effects of the predominant groundwater pollution are also observable at some production well galleries of the nearby DWTP FRI and it can be assumed that the legacy of sewage irrigation will continue to affect the quality of abstracted raw water in the area over the next decades.
  - At present, the studied psychoactive compounds do not constitute a risk with regard to the local drinking water production since concentrations in the final drinking water are below the LOQs and thus also below the respective HPV.
  - Age dating results confirmed the presence of decade-old groundwater. It has been shown that groundwater gets progressively older with increasing aquifer depth and distance from the former irrigation area. The apparent groundwater age of unmixed samples correlates with the concentrations of the pharmaceuticals. In general, it is observable that concentrations are higher with increasing groundwater age.
  - With regard to the entry periods of the pharmaceuticals, determined ages suggest retardation of these contaminants by sorption and/or hydraulic retardation, where immobile domains act as secondary pollutant sources as proposed by Meffe (2011).

#### **Chapter 4: Occurrence in the water cycle of Berlin**

- This investigation represents an environmental study on the occurrence of the seven psychoactive compounds in the aquatic system of Berlin.
- Four analytes (primidone, phenylethylmalonamide, phenobarbital, and oxazepam) were found in municipal WWTP effluents at concentrations up to 0.87 µg/L (primidone). These residues are discharged into the surface waters where they were also detected at concentrations up to 0.29 µg/L (primidone).
- Two compounds, primidone and phenylethylmalonamide, were frequently encountered in the groundwater of the studied bank filtration site. Findings are an indication of their stability during underground passage and concentration decreases are only caused by dilution. "Old" bank filtrate (travel time >25 years) also contained phenobarbital and meprobamate, representing residues of former times.

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- Primidone and phenylethylmalonamide were also detected in the raw and final drinking water of one DWTP, reflecting the concentrations of the studied bank filtrate. Measured concentrations were very low and were below the recommended HPV.
  - All analytes except oxazepam and diazepam were present in groundwater impaired by former sewage farming at medium to high nanograms per liter levels, suggesting that the studied psychoactive compounds are common components in anoxic groundwater affected by former wastewater irrigation.
  - The investigations have shown that particularly primidone and phenylethylmalonamide are apparently not removed at any point of the water cycle and concentrations are only reduced by dilution. As a consequence, they potentially reach the final drinking water. These results demonstrate their persistence throughout the urban water cycle with possibly negative effects in a partly closed water cycle such as Berlin's and confirm the suitability of primidone as an indicator for wastewater contamination.

#### **Chapter 5: Redox-sensitivity and sorption behavior**

- According to the results from aeration experiments, primidone, phenobarbital, meprobamate, and pyrithyldione can be considered as 'non-redox-sensitive' since they were eliminated neither under oxic nor anoxic conditions after 250 days. Hence, results support the assumption from field data that these substances are persistent in the aquatic environment.
- Therefore, it is likely that aeration is an unsuitable technique to remove the investigated compounds, although our findings are not directly transferable to aeration performed during drinking water treatment or to aquifer conditions.
- Batch sorption experiments revealed low to very low affinity of all seven compounds with a sandy sediment. Clearly higher affinity was generally observed with a PAC, wherein oxazepam and diazepam were completely removed from the aqueous phase within the contact time of 72 h.
- Results point to a rather good mobility of the contaminants in sandy sediments as typical for the Berlin region. Nevertheless, according to calculated retardation factors, the pollutants will remain in the studied aquifer for several decades up to centuries and will affect local drinking water production for the foreseeable future.

## 6.2 Suggestions for further research

Investigations have shown that primidone, phenylethylmalonamide, phenobarbital, and oxazepam exhibit a certain environmental relevance due to their ubiquitous or widespread occurrence in the water cycle of Berlin. It can be assumed that they play a role for the aquatic environment not just on a regional basis, but globally. Hence, an improved knowledge of their eco- and human-toxicology is a matter of interest.

The investigated compounds appear to be non-degradable. However, a more detailed study of their behavior during sewage treatment is needed. Different technologies, which may be considered as fourth treatment stage in WWTPs in the future such as membrane filtration (micro-, ultra-, nanofiltration, reverse osmosis), ozonation, UV-disinfection, and advanced oxidation processes (Miehe, 2010), should be examined. For this, the described analytical method is to be optimized to be able to perform more reliable measurements of WWTP influents.

The results of this study underline the importance of monitoring legacy pollutants in groundwater affected by former sewage irrigation even if they have been banned from the market for decades. The investigated compounds may also be present at similar former wastewater irrigation sites that exist worldwide and which are also often anoxic with regard to their hydrochemical conditions. With respect to the study area of this thesis, further monitoring of especially phenobarbital and meprobamate in raw and final drinking water of the DWTP FRI should be carried out to ensure that contaminant concentrations remain below the HPV. Further regular observation of concentrations of the psychoactive compounds is recommended to control their temporally and spatially variable distribution in the aquifer.

As evident from the obtained field data, contaminant concentrations are still elevated in the groundwater in the vicinity of the former sewage farm, although operation was stopped in the 1980s. To further assess the extent of contamination at the original source of pollution, soil and sediment samples from underneath the former sewage farm should be collected and analyzed for the trace organic compounds. To comply with this, an additional analytical

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technique needs to be developed which allows the determination of the sorbed fraction in the solid phase.

Since sorption alone cannot explain the elevated concentrations still present below the former sewage irrigation area, retrieval of a drill core (down to the aquiclude at approx. 50 m BGS) and subsequent classification and analysis of the sediment in combination with the pore water should be done to further pursue the question of the cause of contaminant retardation. Thereby, in particular the hypothesis of hydraulic retardation can be checked.

Furthermore, the transport behavior of the contaminants should be examined in more detail, i.e., by means of column studies. Also, the influence of pH, organic matter content, and texture on the sorption behavior has not been studied in the present thesis.

Besides, to gain a more comprehensive understanding of the transport mechanisms controlling the distribution of the compounds in the aquifer, these substances should be integrated in the two-dimensional non-reactive transport model which has been set up and calibrated by Meffe (2011) for the organic trace compound *p*-TSA. This will also contribute to an improved risk assessment at the field site.

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## **Appendix**

## Appendix I – Figures

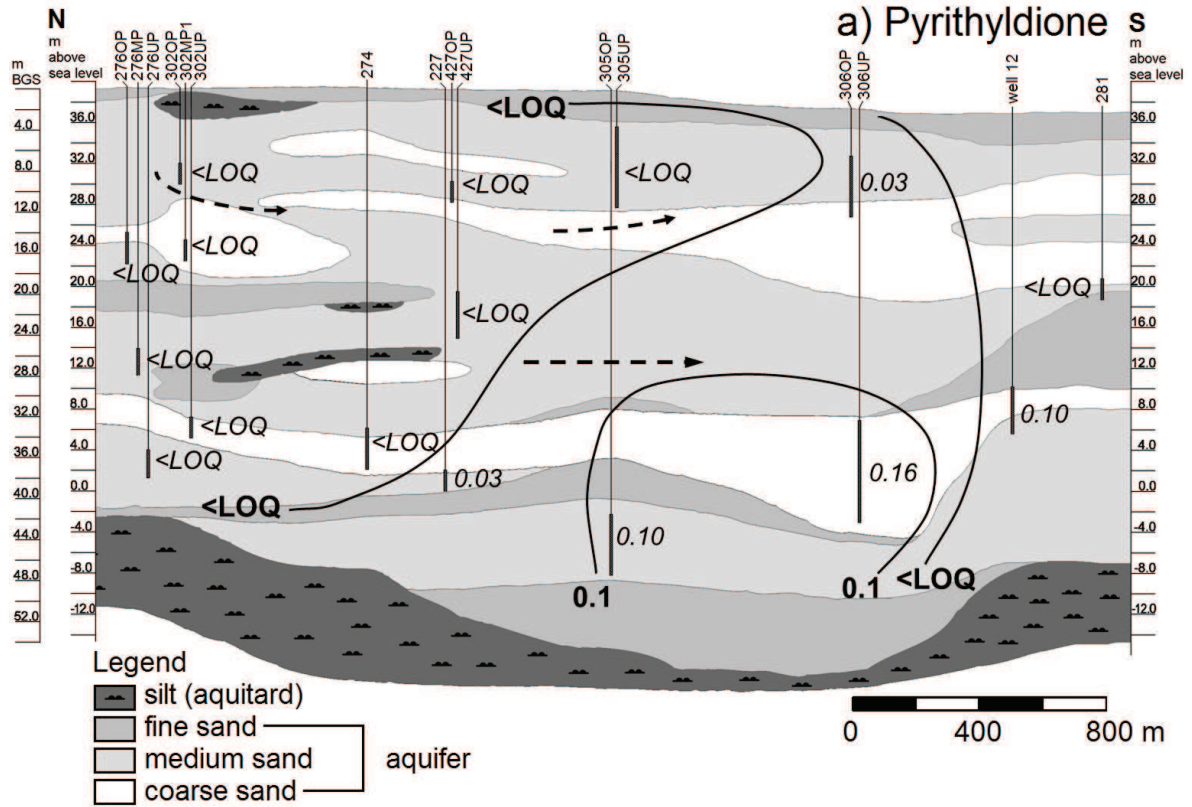


Figure A.1 Schematic hydrologic cross section along N-S axis of the field site Machnow/Krummendammer Heide (see Figure 3.1 for location). Median concentrations are plotted against the filter screen depth (middle of the screen). Italicized numbers represent median concentrations of a) pyriithydione, b) primidone, c) phenobarbital, d) phenylethylmalonamide (all  $\mu\text{g/L}$ ), e)  $\text{NH}_4^+\text{-N}$  ( $\text{mg/L}$ ) and f) B ( $\mu\text{g/L}$ ) from March 2010 to April 2011 ( $n = 3$ ). Isolines representing different concentration levels (bold numbers) are given with the lines drawn by hand. Arrows indicate groundwater flow direction. Modified after Richter et al. (2009a).

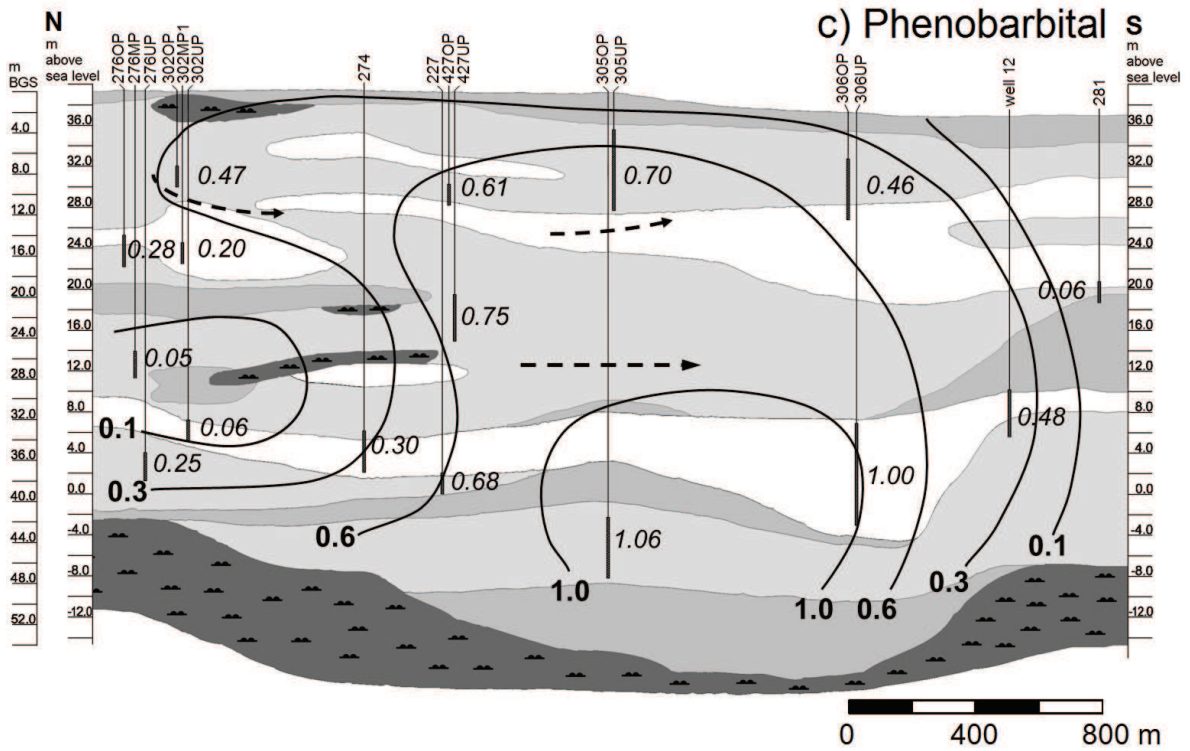
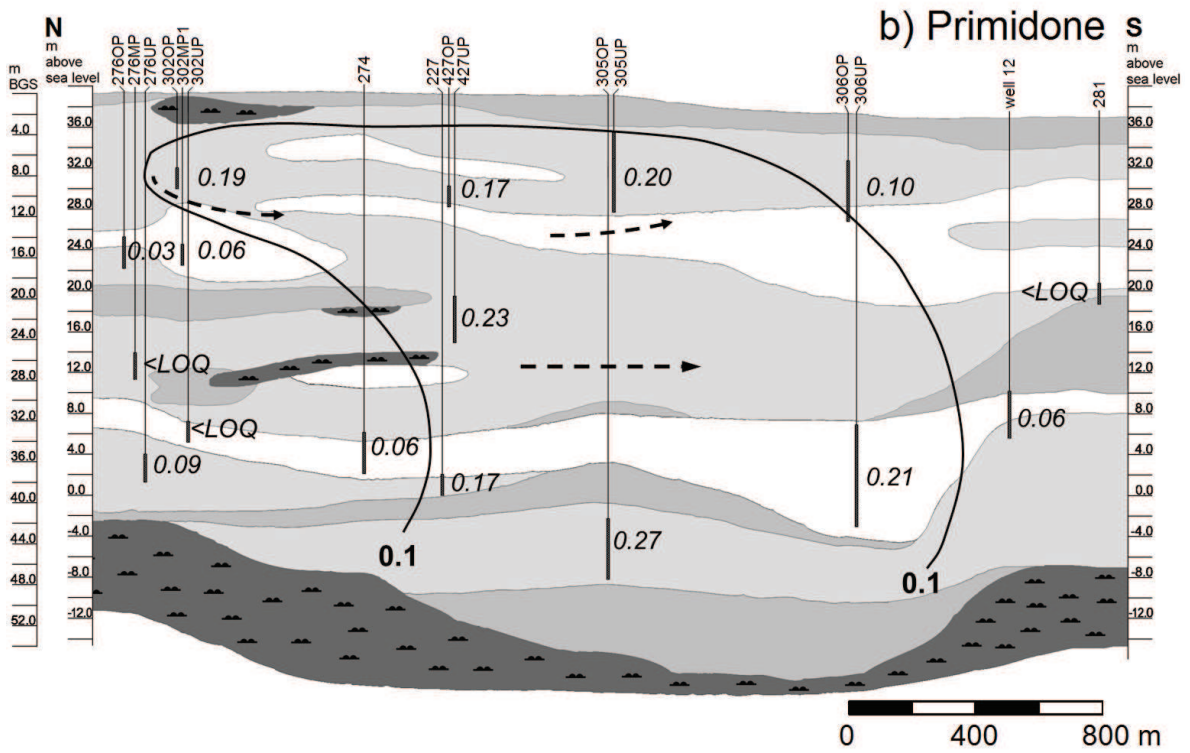


Figure A.1 continued

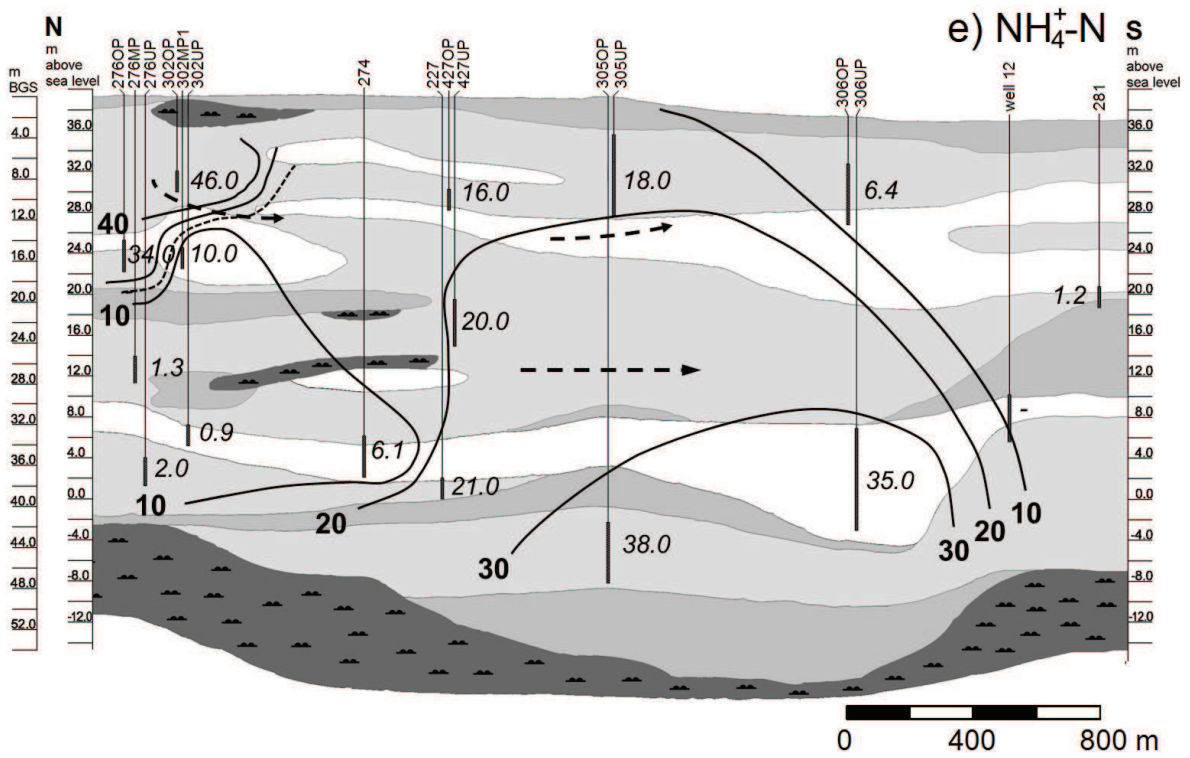
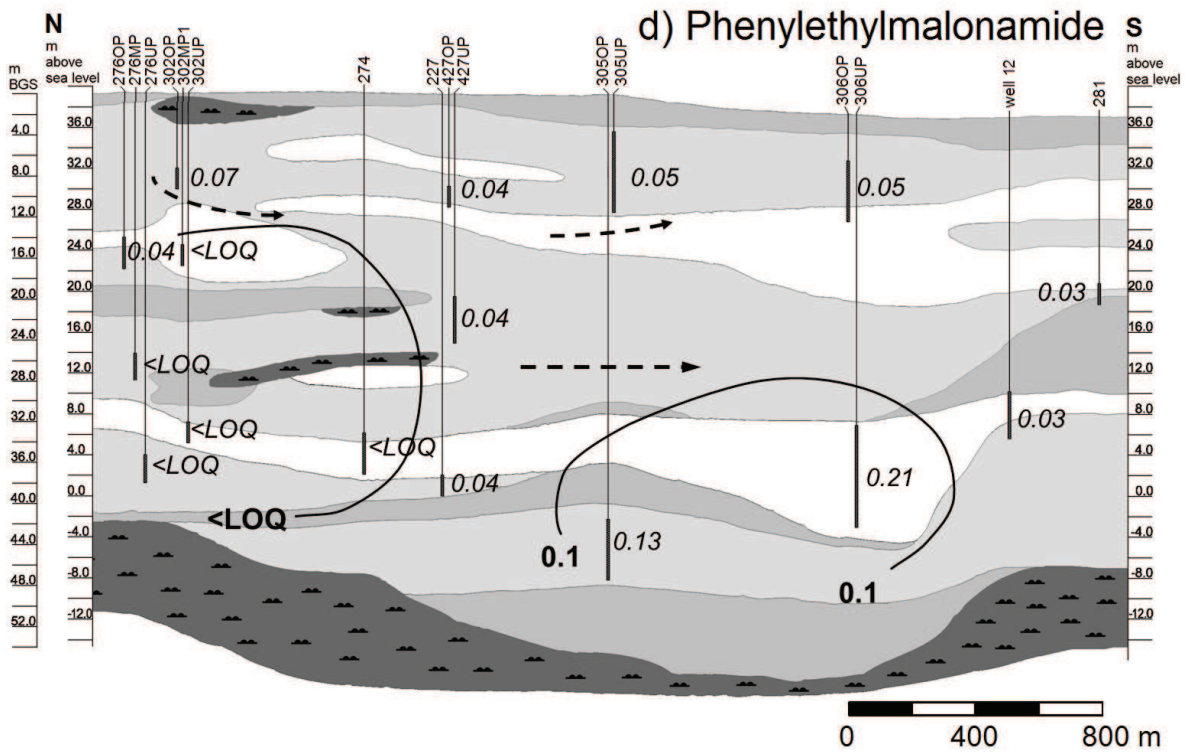


Figure A.1 continued

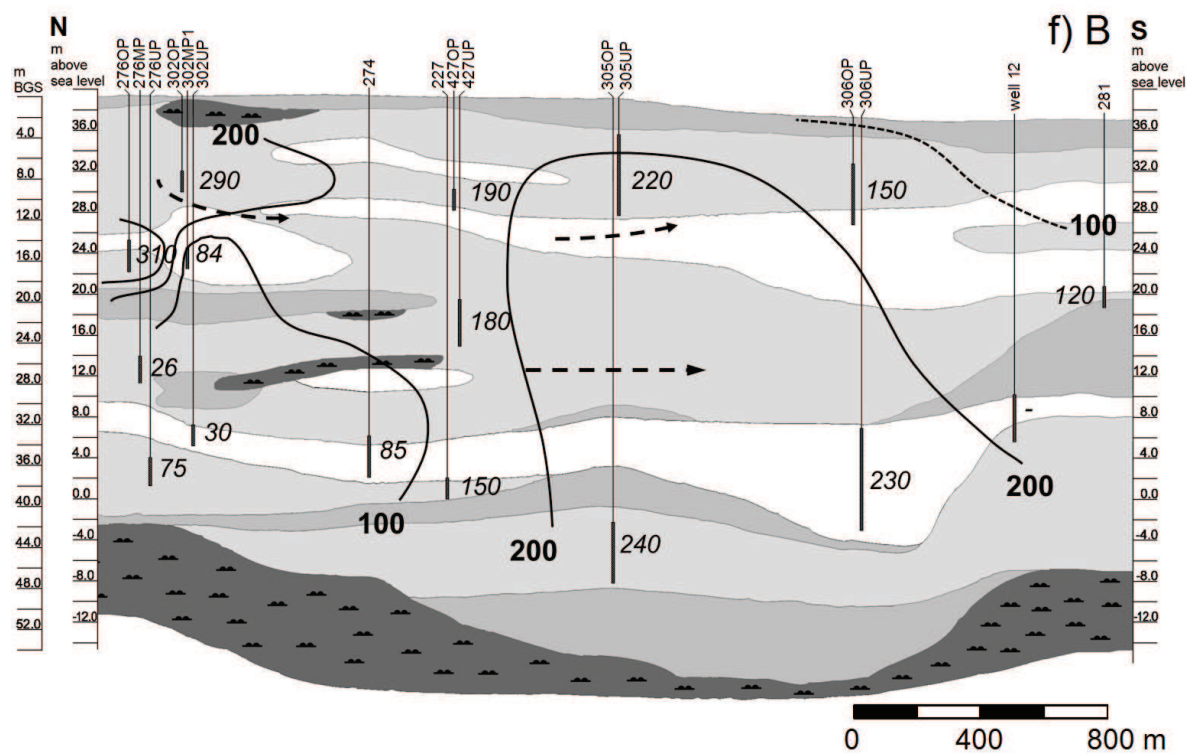


Figure A.1 continued

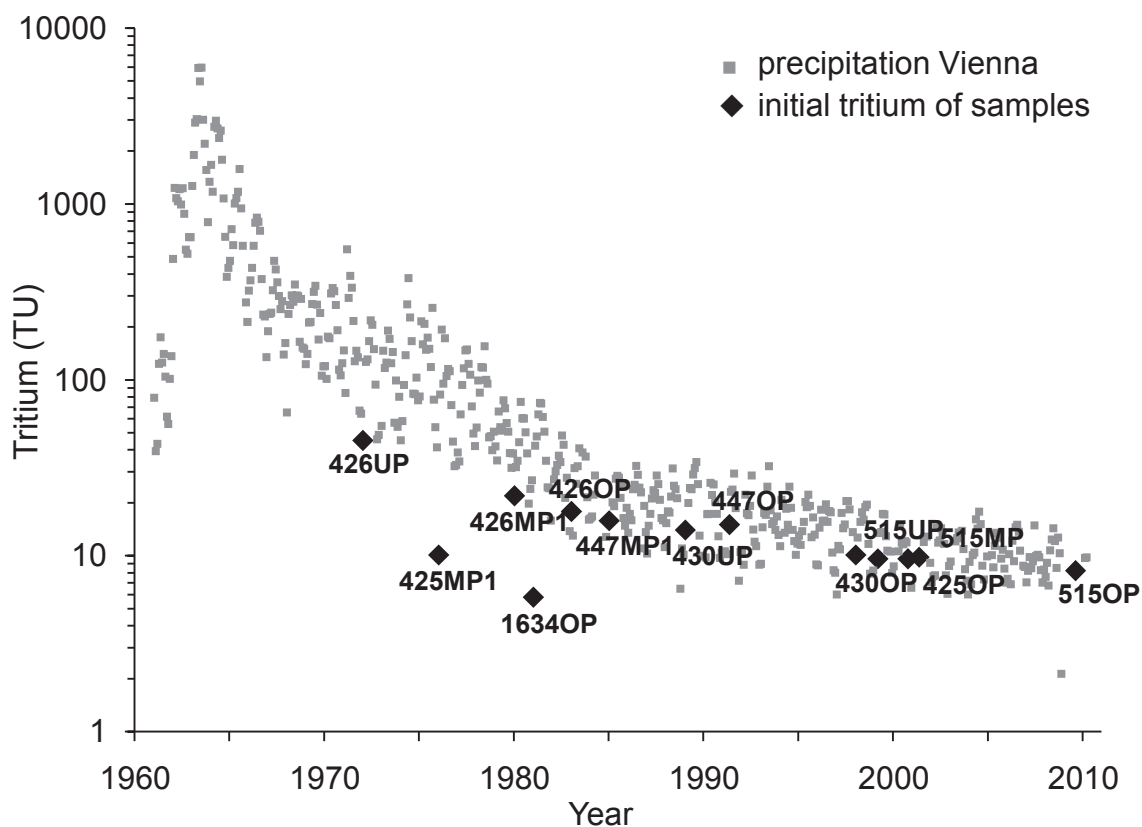


Figure A.2 Initial tritium ( $^3\text{H}+^3\text{He}_{\text{tri}}$ ) concentrations of the groundwater samples for calculated  $^3\text{He}-^3\text{H}$  ages. For comparison, the tritium concentration in precipitation for Vienna (Austria) is shown (data available since 1961). Data source IAEA (2011).

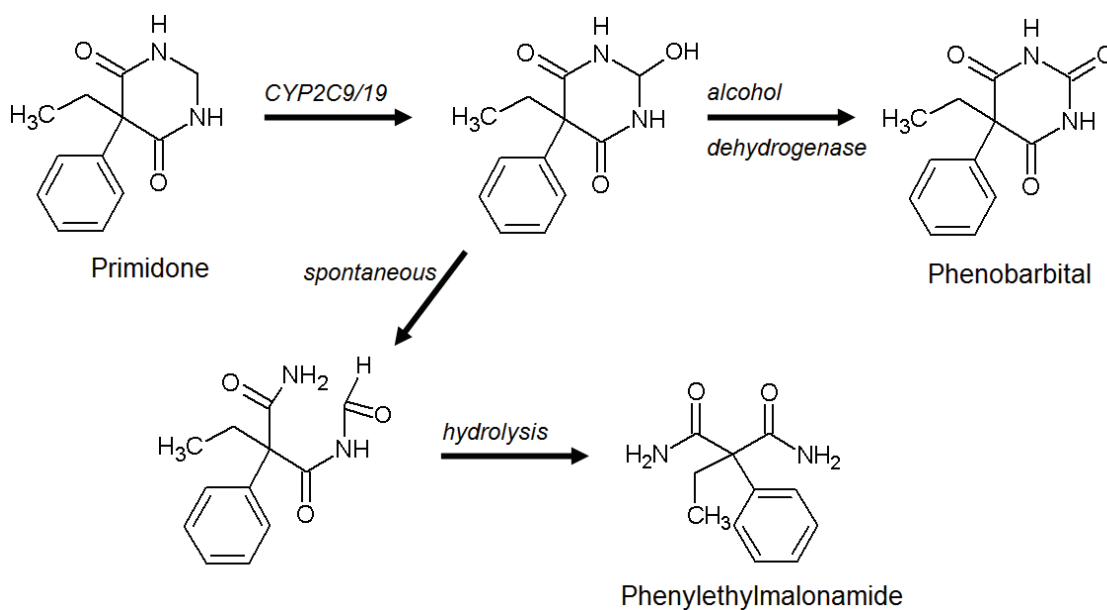


Figure A.3 In vivo metabolism of primidone (modified after Mac Leod et al., 2008).

## Appendix II – Tables

Table A.1 Filter screen depths and x- and y-coordinates (Soldner-Berlin) of the investigated observation and abstraction wells and respective median concentrations of meprobamate (MPB), pyriithydione (PTD), primidone (PRM), phenobarbital (PB), phenylethylmalonamide (PEMA), O<sub>2</sub>, nitrate nitrogen (NO<sub>3</sub><sup>-</sup>-N), Fe<sup>2+</sup>, Mn<sup>2+</sup>, SO<sub>4</sub><sup>2-</sup>, NH<sub>4</sub><sup>+</sup>-N, B, Cl<sup>-</sup>, DOC and EC from March 2010 to April 2011 (n = 3).

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)	
	From	To	X	Y																
<b>Observation wells</b>																				
FRI017	OP	12.0	14.0	41.500	13.792	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.00	0.73	204.0	0.10	150	54	3.60	880
	MP	25.2	27.2			<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.00	0.72	199.5	0.13	145	54	3.25	960	
	UP	33.0	35.0			<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.50	0.43	130.5	0.42	77	48	3.00	860	
FRI020	OP	10.4	10.485	13.837	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	8.50	1.45	0.68	173.5	0.07	130	39	4.25	810	
	MP	20.0	22.0		<0.02	<0.02	<0.02	<0.03	<0.03	0.20	8.00	1.41	0.68	177.5	2.05	125	35	4.25	850	
	UP	27.0	29.0		<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	3.35	0.29	198.0	0.45	160	45	3.55	900	
FRI027		29.8	31.8	41.035	13.730	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	3.50	0.29	141.5	0.64	82	45	3.20	880	
FRI041		28.0	30.0	41.280	14.033	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	1.80	0.89	188.0	0.56	110	69	3.30	1030	
FRI048		35.3	39.3	41.234	14.220	<0.02	0.03	<0.02	0.12	0.04	0.10	<0.05	3.20	0.26	97.0	5.60	110	43	2.70	800
FRI060		21.5	23.5	41.234	14.220	0.59	0.02	0.19	0.84	0.05	0.20	<0.05	3.20	0.42	127.0	8.00	140	25	2.50	760

<sup>a</sup> n = 1 for groundwater from abstraction wells and raw and final drinking water.  
BGS = below ground surface; OP = upper level; MP = medium level; UP = lower level.



Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)
	From	To	X	Y															
FRI069	OP	15.9	41.548	16.708	<0.02	<0.02	0.04	0.13	0.07	0.20	<0.05	3.60	0.47	183.0	0.85	120	37	3.10	870
	UP	33.0			0.16	0.12	0.11	0.39	0.21	0.30	<0.05	3.90	0.40	204.0	11.00	240	82	4.80	1340
FRI072		15.7	41.932	14.452	1.05	0.16	0.47	0.99	0.35	0.20	<0.05	4.10	0.40	182.0	6.70	360	66	3.80	1050
FRI092		17.6	42.686	14.385	0.44	<0.02	0.14	0.39	<0.03	0.20	<0.05	2.70	0.30	138.0	3.60	130	34	1.90	770
FRI1409	OP	20.0	40.564	15.471	<0.02	<0.02	<0.02	0.19	0.05	0.20	<0.05	5.10	0.73	142.0	1.70	140	47	2.90	890
	UP	36.0			<0.02	<0.02	<0.02	0.18	<0.03	0.20	<0.05	5.10	0.33	151.0	2.50	130	77	3.20	1180
FRI1634	OP	37.0	41.975	18.338	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.40	0.19	47.0	0.37	32	39	1.50	660
FRI188		8.0	41.951	17.975	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	0.53	23.00	1.90	66.0	2.30	93	10	4.20	1040
FRI189		8.0	42.136	17.880	<0.02	<0.02	0.09	<0.03	<0.03	1.45	11.00	<0.03	0.02	137.0	0.06	200	34	2.70	1050
FRI209		28.0	41.433	13.558	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	0.53	0.48	142.0	0.12	94	37	3.50	780
FRI227		37.0	41.123	16.674	0.50	0.03	0.17	0.68	0.04	0.20	0.22	2.40	0.96	165.0	21.00	150	30	3.70	910
FRI273		47.4	41.430	16.942	0.18	<0.02	0.08	0.60	0.04	0.10	<0.05	2.10	0.45	133.0	30.00	180	47	3.60	1050
FRI274		34.0	41.190	16.946	0.19	<0.02	0.06	0.30	<0.03	0.10	<0.05	6.10	1.50	136.0	6.10	85	24	2.70	760
FRI275		40.0	40.684	16.828	<0.02	<0.02	<0.02	0.08	<0.03	0.20	<0.05	4.50	0.28	122.0	1.10	99	76	2.70	1100
FRI276	OP	15.0	41.551	18.223	0.31	<0.02	0.09	0.25	0.04	0.10	<0.05	13.00	0.72	192.0	34.00	310	49	15.00	1240
	MP	26.0			<0.02	<0.02	<0.02	0.05	<0.03	0.20	<0.05	9.90	0.64	127.0	1.30	26	27	2.00	710
	UP	37.0			0.12	<0.02	0.03	0.28	<0.03	0.20	<0.05	4.70	0.76	102.0	2.10	75	23	1.80	690
FRI277	OP	4.4	41.522	17.560	<0.02	<0.02	<0.02	<0.03	<0.03	1.55	33.00	0.05	0.16	101.0	0.05	280	19	31.00	770
	UP	8.8			0.09	<0.02	<0.02	0.11	<0.03	0.20	6.60	<0.03	0.73	155.0	0.13	230	27	13.00	840

Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)
	From	To	X	Y															
FRI278	3.7	5.7	40.667	16.832	0.03	<0.02	0.03	0.27	<0.03	0.20	<0.05	1.70	0.50	153.0	0.88	74	41	3.00	820
FRI279	3.7	5.7	40.251	16.471	<0.02	<0.02	0.12	0.06	0.09	0.40	<0.05	11.00	0.41	415.0	2.20	170	63	7.90	1470
FRI280	3.7	5.7	40.029	16.392	<0.02	<0.02	0.05	0.04	0.05	0.30	<0.05	5.90	0.33	263.0	1.80	96	63	4.60	1120
FRI281	15.6	17.6	40.824	14.658	<0.02	<0.02	<0.02	0.06	0.03	0.20	<0.05	2.50	0.35	159.0	1.20	120	42	2.50	830
FRI287	23.7	25.7	43.171	15.064	0.07	<0.02	0.03	0.23	<0.03	0.10	<0.05	5.40	1.10	65.0	3.30	66	20	1.90	610
FRI288	28.2	30.2	41.387	17.510	0.33	<0.02	0.11	0.38	0.05	0.10	<0.05	19.00	2.50	263.0	17.00	120	34	5.50	1330
FRI289	38.3	40.3	41.393	17.465	0.09	<0.02	<0.02	0.22	<0.03	0.20	<0.05	4.00	1.70	88.0	4.00	58	24	2.00	650
FRI290	26.1	28.1	41.401	17.603	0.24	<0.02	0.09	0.27	<0.03	0.30	<0.05	16.00	1.60	151.0	12.00	110	25	3.00	930
FRI291	40.1	42.1	41.417	17.679	0.23	<0.02	0.08	0.33	<0.03	0.10	<0.05	7.50	1.10	59.0	14.00	110	20	2.60	670
FRI296	OP	22.0	41.550	13.981	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.10	0.58	213.0	0.08	120	67	3.10	1050
	UP	35.0	37.0		0.03	0.07	<0.02	0.16	0.13	0.20	<0.05	2.50	0.72	142.0	6.50	120	77	4.20	1160
FRI297	OP	18.0	20.0	42.229	13.940	0.14	0.06	0.09	0.27	0.13	<0.05	3.30	0.56	228.0	0.27	160	50	3.90	1020
	UP	33.0	35.0		0.37	0.10	0.18	0.41	0.22	0.20	<0.05	3.30	0.46	149.0	10.00	260	62	4.20	1110
FRI301	OP	8.4	10.4	41.958	17.645	0.04	<0.02	<0.02	<0.03	0.30	28.00	0.04	0.53	151.0	0.05	200	20	7.10	1220
	MPI	19.7	21.7		0.23	<0.02	0.07	0.32	0.05	0.20	<0.05	1.10	2.00	278.0	0.25	78	37	2.90	1170
	UP	38.2	40.2		<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	0.49	0.67	59.0	0.22	29	19	1.40	590
FRI302	OP	7.3	9.3	41.474	17.487	0.58	<0.02	0.19	0.47	0.07	<0.05	3.90	0.80	207.0	46.00	290	37	14.00	1240
	MPI	14.8	16.8		0.18	<0.02	0.06	0.20	<0.03	0.10	<0.05	17.00	0.69	153.0	10.00	84	27	4.30	830
	UP	32.2	34.2		0.03	<0.02	<0.02	0.06	<0.03	0.10	<0.05	6.30	0.92	118.0	0.86	30	25	1.80	700

Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		PRM	PB	PEMA	O <sub>2</sub> <sup>a</sup>	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup>	Fe <sup>2+</sup> <sup>a</sup>	Mn <sup>2+</sup> <sup>a</sup>	SO <sub>4</sub> <sup>2-</sup>	NH <sub>4</sub> <sup>+</sup> -N	B <sup>a</sup>	Cl <sup>-</sup> <sup>a</sup>	DOC <sup>a</sup>	EC <sup>a</sup> (25 °C)			
	From	To	X	Y																
FRI303	OP	8.3	10.3	42.426	15.186	1.11	0.05	0.49	0.76	0.16	0.20	<0.05	4.00	0.45	212.0	11.00	320	34	3.80	960
	MP1	16.7	18.7			0.63	<0.02	0.26	0.46	0.07	0.20	<0.05	3.40	0.44	180.0	1.10	110	40	2.20	860
	UP	34.1	36.1			0.31	<0.02	0.11	0.29	<0.03	0.20	<0.05	2.00	1.00	179.0	1.40	58	39	2.00	820
FRI304	OP	4.5	9.5	41.648	17.483	0.25	<0.02	0.04	0.09	0.04	0.20	16.00	<0.03	0.70	226.0	8.70	360	105	22.00	1530
	UP	36.5	42.5			<0.02	<0.02	<0.02	0.05	<0.03	0.10	0.49	4.40	0.87	87.0	0.83	43	24	1.70	630
FRI305	OP	3.5	11.5	41.034	16.150	0.43	<0.02	0.20	0.70	0.05	0.20	0.21	2.60	1.80	200.0	18.00	220	51	5.00	1070
	UP	41.5	47.5			0.77	0.10	0.27	1.06	0.13	0.20	<0.05	2.80	0.36	168.0	38.00	240	48	5.40	1130
FRI306	OP	4.5	10.5	40.935	15.408	0.18	0.03	0.10	0.46	0.05	0.20	0.11	1.20	1.90	175.0	6.40	150	34	3.50	830
	UP	30.5	40.5			0.52	0.16	0.21	1.00	0.21	0.10	<0.05	3.20	0.26	192.0	35.00	230	57	5.50	1260
FRI307	OP	4.5	9.5	42.154	17.383	<0.02	<0.02	<0.02	<0.03	<0.03	3.95	4.90	<0.03	<0.005	186.0	0.10	200	77	2.50	1190
	UP	35.5	42.5			<0.02	<0.02	<0.02	<0.03	<0.03	0.10	0.13	1.80	0.24	94.0	0.21	13	30	1.30	670
FRI308		36.0	42.0	41.848	17.556	<0.02	<0.02	<0.02	0.09	<0.03	0.20	<0.05	0.39	0.90	80.0	0.33	61	22	1.60	620
FRI310	OP	5.6	7.6	40.649	16.212	0.02	<0.02	0.10	0.22	0.10	0.20	0.06	2.20	0.25	175.0	1.50	210	78	3.90	1010
	UP	26.6	29.6			0.15	0.04	0.08	0.85	0.08	0.20	<0.05	3.00	0.41	79.0	12.00	140	44	3.40	890
FRI311	OP	5.6	7.6	40.267	15.529	<0.02	<0.02	<0.02	0.03	<0.03	0.30	0.26	0.62	0.10	133.0	0.37	89	82	3.00	870
	UP	28.6	32.6			<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.80	0.21	108.0	0.33	51	36	1.90	740
FRI425	OP	10.5	12.5	41.798	16.026	0.39	<0.02	0.26	0.37	0.12	0.20	<0.05	3.80	1.00	181.0	6.20	420	29	5.60	920
	MP2	39.0	41.0			0.31	0.06	0.14	0.50	0.12	0.10	<0.05	3.70	0.26	106.0	17.00	160	31	2.80	750
	UP	43.5	45.5			0.28	0.03	0.12	0.47	0.07	0.10	<0.05	3.50	0.44	100.0	8.50	130	32	2.60	730

Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)	
	From	To	X	Y																
FRI426	OP	10.3	12.3	41.318	15.346	0.83	0.05	0.36	0.82	0.12	0.20	<0.05	6.10	1.20	216.0	8.40	280	37	4.60	1050
	MP1	17.9	19.9			0.83	0.12	0.41	1.06	0.26	0.10	<0.05	5.70	0.54	220.0	16.00	340	48	5.00	1180
	UP	40.8	42.8			0.04	0.05	<0.02	0.11	0.06	0.10	<0.05	6.00	0.36	119.0	6.60	99	112	5.70	1500
FRI427	OP	9.0	11.0	41.123	16.670	0.36	<0.02	0.17	0.61	0.04	0.20	<0.05	4.40	2.50	264.0	16.00	190	45	5.40	1090
	UP	20.0	24.0			0.66	<0.02	0.23	0.75	0.04	0.40	0.09	3.00	1.10	218.0	20.00	180	36	4.30	1030
FRI428	OP	5.3	7.3	42.520	15.694	0.07	<0.02	0.03	0.04	<0.03	0.50	0.07	2.70	2.50	114.0	0.12	130	16	3.50	630
	MP	10.8	12.8			0.55	<0.02	0.24	0.35	<0.03	0.20	<0.05	6.90	1.30	159.0	1.70	180	28	3.80	920
	UP	20.7	22.7			0.69	<0.02	0.32	0.44	0.04	0.10	<0.05	3.30	0.68	219.0	5.20	200	35	3.10	990
FRI430	OP	7.4	8.4	41.524	15.722	0.56	<0.02	0.29	0.38	0.11	0.20	<0.05	1.20	2.20	188.0	3.30	290	55	5.20	1050
	UP	23.5	24.5			0.84	0.11	0.41	0.87	0.23	0.20	<0.05	4.70	0.64	182.0	8.60	380	54	4.50	1050
FRI431	MP1	19.0	21.0	42.358	14.684	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	1.80	0.17	3.50	0.63	470	87	1.80	820
	UP	43.0	45.0			0.04	<0.02	<0.02	0.05	<0.03	0.20	<0.05	0.65	0.06	<6.0	0.66	290	16	2.90	550
FRI435	MP1	18.6	20.6	41.299	17.683	<0.02	<0.02	<0.02	0.05	<0.03	0.20	<0.05	2.30	0.64	27.0	2.60	54	20	1.80	580
	MP2	31.8	33.8			<0.02	<0.02	<0.02	0.12	<0.03	0.20	<0.05	2.20	0.67	13.0	1.50	56	31	1.50	600
	UP	43.2	45.2			<0.02	<0.02	<0.02	0.05	<0.03	0.20	<0.05	5.00	0.23	67.0	6.00	61	38	3.00	860
FRI438	OP	5.0	7.0	39.883	15.995	<0.02	<0.02	0.12	0.05	0.14	0.20	<0.05	2.40	0.17	171.0	0.21	300	70	3.20	950
	MP	15.2	17.2			<0.02	<0.02	0.03	<0.03	<0.03	0.20	<0.05	2.50	0.28	126.0	0.29	57	49	1.50	750
FRI447	OP	8.0	12.0	41.612	14.777	0.76	0.08	0.36	0.77	0.18	0.20	0.27	5.00	0.82	222.0	10.00	300	67	5.10	1140
	MP1	26.1	30.1			0.79	0.11	0.38	0.88	0.20	0.20	<0.05	4.70	0.43	182.0	15.00	300	70	4.90	1130
	UP	83.3	87.3			<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	2.00	0.17	36.0	1.30	710	1407	2.00	5320

Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)	
	From	To	X	Y																
FRI505	OP	5.0	7.0	42.080	16.586	<0.02	<0.02	<0.03	<0.03	0.20	27.00	<0.03	0.11	37.0	0.05	150	3	23.00	500	
	MP1	15.3	17.3			0.16	<0.02	0.07	0.34	0.10	1.00	4.20	0.66	145.0	8.40	92	45	2.40	880	
	UP	35.0	37.0			<0.02	<0.02	<0.03	<0.03	0.20	<0.05	1.40	0.28	85.0	0.46	22	24	1.40	600	
FRI515	OP	5.5	7.5	41.832	16.871	<0.02	<0.02	<0.03	<0.03	1.10	4.40	0.32	0.04	82.0	0.06	190	24	13.00	540	
	MP	15.4	17.4			0.31	<0.02	0.11	0.46	0.03	0.09	10.00	1.40	156.0	7.80	150	50	4.30	890	
	UP	24.5	26.5			0.19	<0.02	0.06	0.65	0.03	<0.05	2.20	0.33	146.0	4.00	140	46	3.90	830	
FRI516	OP	4.9	6.9	41.754	16.751	<0.02	<0.02	<0.03	<0.03	1.65	8.90	0.84	0.03	43.0	0.06	170	6	16.00	320	
	MP1	14.7	16.7			0.61	0.03	0.25	0.82	0.06	0.29	6.60	1.40	162.0	11.00	190	46	4.60	920	
	UP	44.0	46.0			<0.02	<0.02	<0.03	<0.03	0.10	<0.05	2.10	0.46	82.0	2.00	51	25	1.60	640	
FRI517	OP	4.3	6.3	41.528	17.215	<0.02	<0.02	<0.03	<0.03	0.50	1.80	1.50	0.11	39.0	0.07	85	9	8.30	300	
	MP1	14.0	16.0			0.47	0.03	0.18	0.64	0.08	<0.05	26.00	1.80	209.0	29.00	170	41	6.00	1380	
	MP2	29.0	31.0			0.14	<0.02	0.05	0.19	<0.03	<0.05	10.00	0.99	121.0	17.00	73	26	2.70	810	
	UP	42.2	44.2			0.10	<0.02	0.04	0.28	<0.03	<0.05	2.10	0.57	37.0	5.20	87	18	1.90	570	
<b>Gallery A - abstraction wells</b>																				
Well 12		26	43	40.901	14.927	0.10	<0.02	0.06	0.48	0.03	<0.05	4.20	0.87	176.0	6.80	140	59	3.70	1060	
Well 13		26	43	41.004	14.911	0.36	0.09	0.16	0.83	0.14	<0.05	3.60	0.83	181.0	19.00	180	60	4.50	1110	
Well 14		27	36	41.092	14.897	0.64	0.10	0.29	0.70	0.17	<0.05	3.60	0.53	197.0	24.00	250	58	5.20	1170	
Well 15		20	38	41.345	14.828	0.56	0.13	0.26	0.79	0.20	<0.05	3.70	0.63	212.0	18.00	260	58	5.10	1220	
Well 16		20	37	41.447	14.823	0.51	0.07	0.27	0.53	0.18	<0.05	3.70	0.54	192.0	10.00	270	61	4.50	1130	

Table A.1 continued

Sample ID	Filter screen depth (m BGS)		Coordinates (Soldner)		MPB (µg/L)	PTD (µg/L)	PRM (µg/L)	PB (µg/L)	PEMA (µg/L)	O <sub>2</sub> <sup>a</sup> (mg/L)	NO <sub>3</sub> <sup>-</sup> -N <sup>a</sup> (mg/L)	Fe <sup>2+</sup> <sup>a</sup> (mg/L)	Mn <sup>2+</sup> <sup>a</sup> (mg/L)	SO <sub>4</sub> <sup>2-</sup> (mg/L)	NH <sub>4</sub> <sup>+</sup> -N (mg/L)	B <sup>a</sup> (µg/L)	Cl <sup>-</sup> <sup>a</sup> (mg/L)	DOC <sup>a</sup> (mg/L)	EC <sup>a</sup> (25 °C) (µS/cm)
	From	To	X	Y															
<b>Gallery B - abstraction wells</b>																			
Well01	24	39	41.414	14.282	0.25	0.12	0.12	0.42	0.18	0.40	<0.05	3.90	0.63	190.0	10.00	220	83	4.80	1250
Well02	22	41	41.665	14.245	0.39	0.12	0.20	0.59	0.21	0.50	<0.05	4.10	0.57	210.0	10.00	290	77	5.00	1290
Well03	26	42	41.752	14.231	0.45	0.12	0.20	0.50	0.22	0.30	<0.05	4.10	0.50	201.0	9.20	290	72	5.40	1230
Well04	27	34	41.847	14.214	0.59	0.11	0.28	0.63	0.28	7.00	<0.05	4.20	0.50	199.0	10.00	320	72	5.10	1250
Well05	19	38	41.951	14.198	0.63	0.08	0.31	0.52	0.20	0.40	<0.05	4.00	0.46	168.0	9.10	320	74	5.00	1180
Well06	19	38	42.049	14.181	0.39	0.09	0.16	0.52	0.19	0.30	<0.05	3.10	0.40	140.0	8.80	280	61	3.90	1010
Well07	25	38	42.133	14.166	0.66	0.05	0.32	0.52	0.15	0.20	<0.05	2.90	0.37	140.0	7.00	250	51	3.20	920
Well08	25	39	42.188	14.155	0.59	0.05	0.30	0.55	0.13	0.30	<0.05	2.80	0.35	122.0	3.70	230	45	2.90	820
Well09	26	39	42.263	14.144	0.40	0.04	0.20	0.36	0.11	0.30	<0.05	2.80	0.34	120.0	1.90	190	49	2.40	820
Well10	26	40	42.354	14.129	0.14	<0.02	0.06	0.12	<0.03	0.20	<0.05	2.40	0.33	39.0	1.10	210	300	1.90	190
Well11	25	30	42.405	14.119	0.33	<0.02	0.14	0.36	0.06	0.30	<0.05	2.20	0.37	71.0	1.60	220	290	2.30	1540
Well12	20	40	42.501	14.102	0.29	<0.02	0.15	0.31	0.05	0.80	<0.05	2.10	0.29	43.0	1.70	160	82	2.10	800
Well13	28	41	42.593	14.088	0.63	0.06	0.29	0.60	0.14	4.00	<0.05	2.80	0.39	167.0	4.70	200	38	2.70	880
Well14	26	39	42.726	14.066	0.48	0.04	0.20	0.47	0.10	0.30	<0.05	2.50	0.31	133.0	2.90	140	34	2.00	770
Well15	25	40	42.789	14.056	0.37	<0.02	0.14	0.33	0.05	0.50	<0.05	2.00	0.33	153.0	3.00	99	36	2.20	780
Well16	20	39	42.844	14.047	0.05	<0.02	<0.02	0.06	<0.03	0.50	<0.05	1.90	0.29	140.0	0.24	28	34	1.80	730
Well17	27	38	42.993	14.021	<0.02	<0.02	<0.02	<0.03	<0.03	0.40	<0.05	1.80	0.27	101.0	0.28	22	39	1.40	670
Well18	28	38	43.060	14.010	<0.02	<0.02	<0.02	<0.03	<0.03	0.40	<0.05	1.70	0.28	100.0	0.31	23	29	1.50	660
<b>DWTP</b>																			
Raw	-	-	-	-	<0.02	<0.02	<0.02	<0.03	<0.03	0.20	<0.05	1.20	0.52	148.0	0.63	78	61	3.90	820
Final	-	-	-	-	<0.02	<0.02	<0.02	<0.03	<0.03	10.10	0.58	<0.03	<0.005	147.0	<0.04	76	60	-	800

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## Appendix III – List of publications

Journal and conference contributions listed in chronological order.

**Hass, U.**, Dünnbier, U., Massmann, G., (*under review*). Redox-sensitivity and sorption behavior of psychoactive compounds in groundwater. *Water Environment Research*.

**Hass, U.**, Dünnbier, U., Massmann, G., (2012). Occurrence and distribution of psychoactive compounds and their metabolites in the urban water cycle of Berlin (Germany). *Water Res.* 46 (18), 6013-6022.

Burke, V., **Hass, U.**, Dünnbier, U., Massmann, G., (2012). Laborversuche zur Redoxsensitivität pharmazeutischer Rückstände im Grundwasser. Posterprint at Jahrestagung der Fachsektion Hydrogeologie der Deutschen Gesellschaft für Geowissenschaften (FH-DGG 2012), 16.-20.05.2012, Dresden, Germany.

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## **Curriculum vitae**

For reasons of data protection, the curriculum vitae is not included in the online version.



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