KOMPETENZZENTRUM
WasserBerlin

REPORT

Cicerostr. 24
D-10709 Berlin
Germany
Tel +49 (0)30 536 53 800
Fax +49 (0)30 536 53 888
www.kompetenz-wasser.de

Integration and Consolidation of Information on Pharmaceutical Residues in the Urban Water Cycle

- IC Pharma -

by
K.Seeber, E.Hoa

Department “SUW”
KompetenzZentrum Wasser Berlin, Cicerostraße 24, 10709 Berlin, Germany
Email: eric.hoa@kompetenz-wasser.de, Tel. +49 (0)30-536-53 808

for
Kompetenzzentrum Wasser Berlin gGmbH

Preparation of this report was financed in part through funds provided by BWB and Veolia

VEOLIA WATER

Berliner Wasserbetriebe

Berlin, Germany

2010

Important Legal Notice

Disclaimer: The information in this publication was considered technically sound by the consensus of persons engaged in the development and approval of the document at the time it was developed. KWB disclaims liability to the full extent for any personal injury, property, or other damages of any nature whatsoever, whether special, indirect, consequential, or compensatory, directly or indirectly resulting from the publication, use of application, or reliance on this document. KWB disclaims and makes no guaranty or warranty, expressed or implied, as to the accuracy or completeness of any information published herein. It is expressly pointed out that the information and results given in this publication may be out of date due to subsequent modifications. In addition, KWB disclaims and makes no warranty that the information in this document will fulfil any of your particular purposes or needs. The disclaimer on hand neither seeks to restrict nor to exclude KWB's liability against all relevant national statutory provisions.

Wichtiger rechtlicher Hinweis

Haftungsausschluss: Die in dieser Publikation bereitgestellte Information wurde zum Zeitpunkt der Erstellung im Konsens mit den bei Entwicklung und Anfertigung des Dokumentes beteiligten Personen als technisch einwandfrei befunden. KWB schließt vollumfänglich die Haftung für jegliche Personen-, Sach- oder sonstige Schäden aus, ungeachtet ob diese speziell, indirekt, nachfolgend oder kompensatorisch, mittelbar oder unmittelbar sind oder direkt oder indirekt von dieser Publikation, einer Anwendung oder dem Vertrauen in dieses Dokument herrühren. KWB übernimmt keine Garantie und macht keine Zusicherungen ausdrücklicher oder stillschweigender Art bezüglich der Richtigkeit oder Vollständigkeit jeglicher Information hierin. Es wird ausdrücklich darauf hingewiesen, dass die in der Publikation gegebenen Informationen und Ergebnisse aufgrund nachfolgender Änderungen nicht mehr aktuell sein können. Weiterhin lehnt KWB die Haftung ab und übernimmt keine Garantie, dass die in diesem Dokument enthaltenen Informationen der Erfüllung Ihrer besonderen Zwecke oder Ansprüche dienlich sind. Mit der vorliegenden Haftungsausschlussklausel wird weder bezweckt, die Haftung der KWB entgegen den einschlägigen nationalen Rechtsvorschriften einzuschränken noch sie in Fällen auszuschließen, in denen ein Ausschluss nach diesen Rechtsvorschriften nicht möglich ist.

Colofon

Title

Integration and Consolidation of Information on Pharmaceuticals Residues in the Urban Water Cycle (IC-Pharma)

Authors

Kristin Seeber, KompetenzZentrum Wasser Berlin gGmbH

Eric Hoa, KompetenzZentrum Wasser Berlin gGmbH

Quality Assurance

Kai Schroeder, KompetenzZentrum Wasser Berlin gGmbH

Publication/ dissemination approved by technical committee members:

Luis Castillo, Veolia Environnement Recherche & Innovation

Christelle Pagotto, Veolia Eau – Direction Technique

Regina Gnirß, Berliner Wasserbetriebe

Yann Moreau-Le Golvan, KompetenzZentrum Wasser Berlin gGmbH

Gesche Grützmacher, KompetenzZentrum Wasser Berlin gGmbH

Bodo Weigert, KompetenzZentrum Wasser Berlin gGmbH

Abstract (English)

Within the study “IC-Pharma” a graphical benchmark of the occurrence of 30 priority pharmaceutical active compounds (PhACs) covering different therapeutic classes such as analgesics, antibiotics, lipid lowering drugs, beta blockers, tranquilizers, and cytostatics in the urban water cycle was conducted. The results are based on an extensive data set collected during several monitoring campaigns in Berlin and the Canton Zurich. This benchmark of the occurrence of priority pharmaceuticals allows water practitioners from other sites to compare detected concentrations of priority PhACs in STP effluents, surface water and groundwater.

The study shows that the occurrence of priority pharmaceuticals at both study sites (Berlin and the Canton Zurich) is primarily dependent on sales/consumption quantities, the dilution of the pharmaceuticals in the waste water system and the dilution in surface water by the natural water flow. At both sites mainly conventional STP with mechanical treatment and biological treatment are in operation.

Major differences in the sales data of priority PhACs, the hydrological setting, the water supply and the sewage disposal of both study sites are presented. Comparing both study sites it can be observed that the rivers in the Canton Zurich in general have a higher natural water flow than the Berlin Rivers. Furthermore, instead of operating 6 large municipal STPs like Berlin does, the Canton Zurich operates 103 small public STPs. However, the annual volume of treated sewage at both sites is similar (~235 M m³/a). In Berlin the drinking water consumption per capita and day is 112 litres whereas the inhabitants in the Canton Zurich use approximately 160 litres per day.

These differences of both study sites are reflected in the detectable concentrations of measured priority PhACs in the different water compartments. In general lower levels of concentration (up to a factor ten) were found in all water compartments in the Canton Zurich. Therefore a separate graphical benchmark of the levels of concentration at the two study sites is presented so that the water practitioner has the possibility to refer either to the Berlin situation or the Canton Zurich situation.

For the Berlin site it was furthermore investigated how the concentrations of pharmaceuticals in surface water are correlated with the proportion of treated sewage. It can be observed that detectable median concentrations of priority PhACs tested in rivers or canals with a proportion of treated sewage higher than 30% are significantly higher (e.g. for the antibiotic sulfamethoxazole) than in rivers with a proportion of treated sewage less than 30%.

Abstract (German)

Ziel der vorliegenden Arbeit war es, ein graphisches Benchmark von potentiell messbaren Pharmakakonzentrationen in verschiedenen Kompartimenten des urbanen Wasserkreislaufes zu erstellen. Dabei dienten experimentell erhobene Daten von mehreren in Berlin und dem Kanton Zurich durchgeführten Untersuchungskampagnen als Grundlage.

Das „Benchmarking“ welches potentiell vorfindbare Konzentrationen von 30 prioritären Pharmazeutika aus diversen therapeutischen Anwendungsbereichen (wie z.B. Schmerzmittel, Antibiotika, Betablocker, Beruhigungsmittel, Zytostatika und Lipidsenker) in Klärwerksabläufen, im Oberflächengewässer und Grundwasser aufzeigt, gibt Fachleuten aus dem Wassersektor die Möglichkeit ihre gemessenen Konzentrationen mit denen aus Berlin und der Schweiz zu vergleichen.

Innerhalb der Studie konnte gezeigt werden, dass die gemessenen Konzentrationen in Berlin und der Schweiz in den verschiedenen Kompartimenten des urbanen Wasserkreislaufes hauptsächlich von Verkaufsdaten bzw. dem Konsum des jeweiligen Stoffes, von der Verdünnung innerhalb des Abwassersystems und der Verdünnung durch den natürlichen Abfluss der aufnehmenden Gewässer abhängig sind. An beiden Standorten kommen konventionelle Kläranlagen mit mechanischer und biologischer Reinigung zum Einsatz.

Vergleiche der beiden Untersuchungsgebiete in Verkaufsdaten der prioritären Pharmazeutika, in der hydrologischen Beschaffenheit, in der Wasserversorgung und der Abwasserversorgung zeigen entscheidende Unterschiede der beiden Gebiete, die sich in den gemessenen Konzentrationen wiederspiegeln. Generell kann man erkennen, dass im Kanton Zurich bis zu 10fach geringere Konzentrationen von jeweiligen prioritären Pharmaka in allen Kompartimenten gefunden werden können.

Ursachen dafür liegen unter anderem im Kanton Zurich, welcher ein höheres natürliches Wasserdargebot vorweisen kann als es in Berlin der Fall ist. Dazu kommt, dass in der Schweiz anstelle von 6 größen Kläranlagen über 103 kleine staatliche Anlagen in Betrieb sind, die auf das gesamte Untersuchungsgebiet verteilt sind. Trotzdem fallen in beiden Gebieten bei unterschiedlicher Einwohnerzahl jährlich etwa 235 Millionen m³ gereinigtes Abwasser an, was über die Kläranlagen in die Gewässer gegeben wird. Ursache dafür ist unter anderem der höhere tägliche Trinkwasserverbrauch von 160 Liter pro Kopf im Kanton Zurich und nur 112 Liter in Berlin.

Um dem Fachmann die Möglichkeit zu geben, sich auf die Konzentrationen zu beziehen, die in dem Untersuchungsgebiet gemessen wurden, welches seinem Gebiet am nächsten kommt, wurde zusätzlich ein seperates Benchmarking für beide Gebiete erstellt.

Ein weiterer Schwerpunkt des Projektes lag darin, gemessene Konzentrationen in Oberflächengewässer von Berlin mit dem jeweiligen Abwasseranteil im Gewässer gegenüberzustellen. Dazu wurde ein monatlicher Abwasseranteil an verschiedenen Punkten des Berliner Gewässernetzes berechnet. Es konnte gezeigt werden, dass Konzentrationen von prioritären Pharmaka in Flüssen oder Kanälen mit einem Abwasseranteil von mehr als 30 % deutlich höher sind als in Flüssen oder Kanälen, die einen Abwasseranteil von weniger als 30 % enthalten.

Abstract (French)

Dans le cadre du projet IC-Pharma, une étude référentielle graphique a été menée sur la détection dans le cycle urbain de l'eau de 30 composés pharmaceutiques (PhACs) prioritaires et utilisés pour différentes actions thérapeutiques : analgésique, antibiotique, réducteur de lipides, bêtabloqueur, tranquillisant et cytostatique. L'étude prend en compte des bases de données enrichies lors de campagnes de surveillance menées à Berlin et dans le Canton de Zürich. Ces résultats peuvent ainsi servir de référence aux professionnels de l'eau afin de pouvoir comparer les concentrations en PhACs dans les effluents de STEP, les eaux de surface et les eaux souterraines.

Il est montré dans cette étude que la présence de PhACs sur les deux sites considérés (Berlin et le Canton de Zürich) dépend principalement des chiffres de consommation/vente et de l'effet de dilution dans les eaux usées ainsi que dans les eaux de surface. Sur les deux sites, le traitement des eaux usées est considéré comme conventionnel avec barrière physique et traitement biologique.

Les différences majeures entre les deux sites sont présentées dans le rapport et incluent les chiffres de vente des PhACs, le contexte hydrologique, le système d'alimentation en eau potable et le système des eaux usées. Ainsi, dans le canton de Zürich, les cours d'eau ont des débits plus élevés qu'à Berlin. De plus, en comparaison à 6 grosses STEPs pour Berlin, 103 petites STEPs fonctionnent à Zürich pour un volume traité d'eaux usées similaire (~235 Mm3/a). La consommation en eau potable diffère également avec 112 L/pers/jour à Berlin et environ 160 L/pers/jour à Zürich.

Ces différences jouent donc sur les niveaux de concentrations de PhACs détectés dans les différents compartiments du cycle de l'eau. En général, des niveaux plus faibles (d'un facteur 10) sont mesurés dans le canton de Zürich que dans Berlin pour tous les compartiments confondus. Dès lors, il a été choisi de représenter séparément les graphiques de référence de Berlin et Zürich. Le professionnel de l'eau pourra alors se référer au site qui correspond au mieux à ses besoins.

L'étude inclut en complément une analyse plus poussée sur les concentrations de PhACs mesurées dans les eaux de surface en fonction de la proportion d'eau traitée rejetée par les STEPs. Il est ainsi montré que les concentrations moyennes dans les cours d'eau qui contiennent plus de 30% de rejet de STEP sont significativement plus élevées que dans des cours d'eau qui en présentent moins de 30%.

Acknowledgements

At this point we want to thank everybody who has supported the IC-Pharma project. Special thanks for constructive advices and supporting with the software go to Kai Schröder and Hauke Sonnenberg.

Furthermore we want to thank the aquatic research institute Eawag, located in Dübendorf Switzerland, especially to Christian Götz, Christa McArdell und Juliane Hollender who provided us with the data from the Canton Zurich.

Moreover thanks to the BWB. This gave us data about the Berlin Water and Waste Water Management. Special thanks go to Gunther Pahl, Thomas Buck, Gloria Abel and Isabelle Kraume.

Best thanks go also to Barbara Kalk from the Berlin Senate who exercised patience in providing us with the average discharge values of Berlin's Rivers.

Table of Contents

List of Figures

List of Tables

Chapter 1
Introduction

Pharmaceutical active compounds (PhACs) are chemicals designed to have a specific mode of action, intended for the use in diagnosis, cure, mitigation, treatment or prevention of diseases. Living without them in today's society is unimaginable as they do not only increase (societies') life expectancy, but also enhance to our quality of life in many situations.

In the European Union (EU) approximately 3000 different pharmaceutical ingredients are used in human medicine such as analgesic and antiphlogistic drugs, antibiotics, antidiabetics, beta blockers, lipid lowering drugs, contraceptives, antidepressants, cytostatics, impotence drugs and many others (Fent et al. 2006).

Since the detection of the pharmaceutical active compound clofibric acid, a metabolite of the parent compound clofibrate, in groundwater samples in Berlin in 1992 (Stan and Linkerhägner 1992), the questions about the fate and the behaviour of PhACs aroused scientific and socio-political interest. Investigations carried out in the last 10 to 15 years all over the world have been driven mainly by advances in environmental residue analysis. Particularly after the fast development and increasing use of a new analytical tool, the liquid chromatograph (LC) coupled with mass spectrometry (MS) enabling the detection of polar organic pollutants such as pharmaceuticals down to relatively low concentration levels in all types of water (sewage, surface water, groundwater, drinking water) and in solid matrices (sewage sludge, manure, soil, sediment).

Studies about the occurrence of PhACs in influents and effluents of sewage treatment plants (STPs) have shown that not all pharmaceuticals are removed during sewage treatment processes. Some PhACs are extremely polar compounds, with very limited sorption properties and are therefore favoured to pass most common treatment processes (currently applied in STPs) unaffected.

Because sewage effluents are commonly discharged into rivers and streams or sometimes irrigated to fields, treated sewage water represents an important point source for PhACs in the aquatic environment. If surface water is contaminated by pharmaceuticals, these substances can leach through the subsoil into groundwater aquifers in case of influent conditions, bank filtration or artificial groundwater recharge.

If drinking water is extracted from groundwater or surface water containing a substantial amount of treated sewage water (e.g. from river water downstream of a STP discharge point) a potential risk of drinking water contamination via PhACs exist.

Although no toxicological risks for humans consuming drinking water contaminated by PhACs have been identified so far, estrogenic effects (Routledge et al. 1998) and renal alterations (Triebskorn et al. 2004) at environmental concentration levels on aquatic organisms have already been reported for the contraceptive 17a-ethinylestradiol and the antiphlogistic diclofenac, respectively. In 2004 an article in Nature demonstrated that

residues of veterinary used diclofenac probably caused renal failure of vultures and hence leads to high mortality among three vulture species and a decline of >95 % of the vulture population in Pakistan (Oaks et al. 2004).

Although, adverse effect concentration of several different PhACs on aquatic organisms such as daphnia, algae or fish were determined during toxicological tests in recent years a considerable lack of information for chronic adverse effects on aquatic organisms exists. Furthermore it is not fully understood which drugs or metabolites undergo a chemical reaction with each other and maybe produce a new, unknown toxicological connection.

Currently pharmaceuticals are not considered in the EU Water Framework Directive, which involves the development of environmental quality standards for pollutants to protect and improve the state of aquatic ecosystem, groundwater and land ecosystems which are directly dependent on water. It can be expected however that in the future environmental quality standards for PhACs will be defined since the methods for scientific risk assessment are currently being developed or existing assessment procedures are being modified.

Objectives

The aim of the study was to create a graphical benchmark of the occurrence of PhACs in the urban water cycle, more precisely in treated sewage water, surface water, and groundwater, using an extensive data set of the city of Berlin and the Canton of Zurich. Therefore this report serving as decision support for the risk assessment of PhACs in the aquatic environment was produced. With the help of this study detected concentrations at different sites can be compared with the results from Berlin and the Canton Zurich.

The first part of the report introduces state of the art knowledge about pharmaceuticals such as excretion rates, exposure routes, analytical methods, sampling methods, the occurrence in different water compartments and information about how to estimate concentrations via models, whereas in a second part detailed information about priority pharmaceuticals, which are relevant for the water cycle and considered in this study are outlined. Furthermore information about the two study sites in Berlin and the Canton Zurich and data about the level of occurrence of PhACs in both sites are given. The main focus therefore laid on the differences of the hydrological characteristics and the water management systems at both sites to draw a conclusion on the occurrence of pharmaceuticals in the water cycle (afterwards).

Because municipal sewage water is quantitatively the most important pathway of PhACs in the environment (BLAC 2003) the study aims to depict the dependency of the level of the contamination in the surface water on the amounts of STP effluents.

The method for calculation the proportion of treated sewage water in surface water samples in Berlin is explained in Chapter 5. The results are implemented in the graphical benchmarking to differentiate the measured concentration ranges of PhACs in surface water via the proportion of treated sewage water (see Chapter 7).

Chapter 2
State of the Art

2.1 Human Metabolism and Excretion Rates

After the intake of pharmaceuticals they are subjected to a xenobiotic metabolism which is also called biotransformation. The aim of the biochemical degradation and transformation processes, which are taken place mostly in the liver but also in other organs like kidney, intestine, spleen, blood and dermis, is a faster excretion of the substances with urine or faeces.

The xenobiotic metabolism can be subdivided in two consecutive phases as shown in Figure 1. Reactions of phase I lead to degradation and changes in the structure of the compound. In phase II conjugates with endogenous molecules are created to obtain elevated water solubility. Important Phase I reactions are oxidation, reduction, hydrolysis, hydration, condensation and isomerisation. At this point products are often more reactive and sometimes more toxic than the parent drug. The major phase II reactions are the formation of conjugates with glucuronic acid, activated sulphuric acid and glutathione which normally results in inactive compounds. Both phases change the physical chemical behaviour of the pharmaceutical compounds.

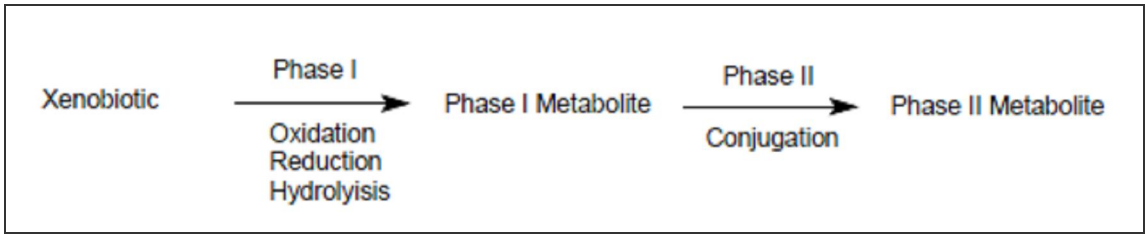


Figure 1: General scheme for the metabolism of a xenobiotic

The metabolism may lower activity and/or enhance water solubility and decreases the toxicity of a PhAC. However, in some cases the metabolism can also lead to a more active compound (Lienert et al. 2007; Kümmerer 2008). Thus, often it is not only the parent compound which is excreted with urine and faeces but also the metabolites of the compound. Therefore main metabolites should be the subject of risk assessment, too.

2.2 Exposure Routes

2.2.1 Human Drugs

PhACs can enter the environment in various ways as shown schematically in Figure 2. Quantitatively, the most import pathway of PhACs in the environment is municipal sewage water (BLAC 2003). Human medical care drugs generally reach the sewage system over excretion products like urine and faeces in private households or hospitals. The vast majority

of PhACs in municipal sewage water, except of radio contrast agents and cytostatic drugs, originate from private households (Schuster 2005). According to the bulletin (DWA 2001) only 10 % of prescribed drugs in Germany are applied in hospitals and medical institutions. The statement that only a low fraction of pharmaceuticals of the total load originate from hospital sewage water was also confirmed by (Heberer 2004) who estimated a proportion of less than 20 %. A study from Switzerland showed that the amount of pharmaceuticals applied and excreted in hospitals varies between different compounds, e. g., radio contrast agents or cytostatic drugs are excreted only to 50 % or 70 % in hospitals, respectively (Weissbrodt et al. 2009).

Depending on their pharmacokinetics the active pharmaceutical ingredients are excreted by the human body in form of metabolites, as conjugates or remain unchanged and end up in municipal STPs after passing the canalisation.

Studies about the occurrence of PhACs in the influents and effluents of STPs have shown that a relevant number of pharmaceutical residues are not completely or only to a low extent eliminated during sewage treatment. According to this, not readily degradable PhACs can enter the environment either as dissolved pollutants by discharging treated sewage water into the receiving waters or by the accumulation of drug contaminated sewage sludge on dumpsites or agriculture areas. In Switzerland it is forbidden to apply sewage sludge on agriculture areas since 2003.

If surface water is contaminated by pharmaceuticals, these substances can leach through the subsoil into groundwater aquifers under influent conditions, by bank filtration or artificial groundwater recharge. Due to their polar structure PhACs are not significantly adsorbed in the subsoil and in case of recharge conditions, they can leach from the contaminated surface waters into groundwater aquifers (Heberer 2002a). Furthermore, direct input of PhACs into the soil, the groundwater or the surface water is either possible due to irrigation fields or can be caused by combined sewer overflow and leaks in sewer systems.

Another pathway for PhACs to enter the environment is the disposal of unused pharmaceuticals by the toilet or domestic waste. For example in Germany about one third of the total amount of the sold drugs are disposed by domestic waste (Zimmer et al. 1992; Zimmer et al. 2000; Rönnefahrt 2005). Although modern dumpsites possess bottom sealing and treatment of percolation water, older waste systems still represent a potential risk for PhACs leaching through the subsoil (BLAC 2003). Additionally, it can be assumed that pharmaceuticals disposed by solid waste are destroyed by incineration, due to chemical oxidation during the burning process (Ternes and Joss 2006).

According to the current (EU)Directive in 1994, out of date drugs are not classified as hazardous waste. Therefore, pharmacies are allowed to deposit them as domestic waste. Some out of date drugs and waste of medical facilities for instant cytostatic drugs and halogenated solvents are excluded from this regularisation and have to be disposed separately.

The production of PhACs follows strict requirements. Hence, the entry of PhACs due to industrial effluents of drug production is graded as relatively low (Kümmerer 2008). Yet accidents and contingency may lead to relevant entries.

In contrast to other organic pollutants such as pesticides, pharmaceuticals are applied during the entire year. Potential steady-state concentrations can thus result in the environmental waters, as they are continuously introduced via the sewage effluents. However, concentration peaks for specific PhACs (e.g. antibiotics) may occur predominantly in the winter period (McArdell et al. 2003).

2.2.2 Veterinary Drugs

Veterinary Drugs are commonly used as grow promoters and therapeutics in livestock production as well as therapeutics for treatment of livestock on fields, as feed additives in fish farms, and as coccidiostatica in poultry production. The medical substances used for animals in stables as growth promoters will mostly end up in manure which is often used as farm fertilizer on fields. It is possible that medical substances dispersed on fields may be mineralized in the soil column or will reach the groundwater as parent compounds and metabolites. A direct exposure of hydrophilic pharmaceutical compounds from the field into surface water can occur during a runoff process caused by a rain event.

A direct input in surface waters also occur by applying medical substances in fish farms, because the most convenient method of treating fish with antibiotics and chemotherapeutics is by using feed additives. Thereby a large portion of the medicated feed administered is not eaten by the fish, but falls through the cages and accumulates on the sea bed.

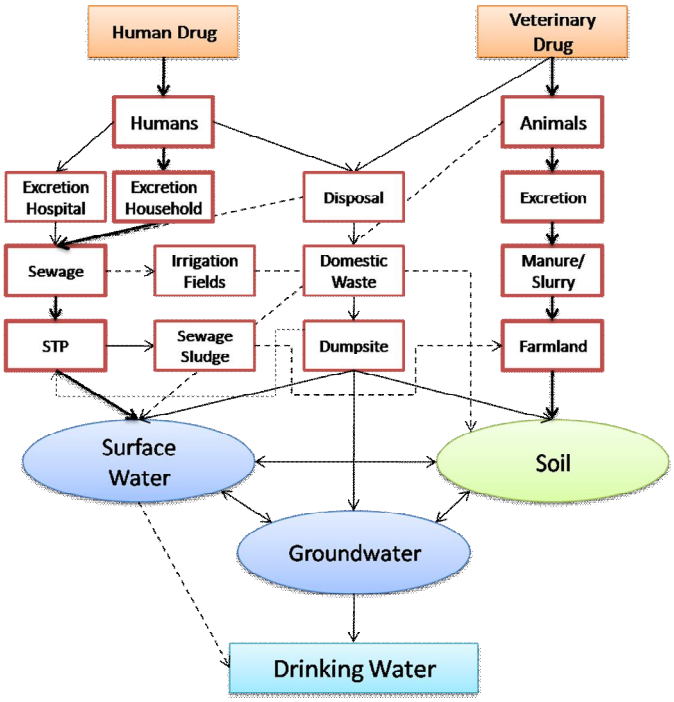


Figure 2: Pathways of Pharmaceuticals in the environment (adapted from Heberer, 2002; LANUV NRV, 2007). Food chain pathways are neglected. Bold arrows symbolise major pathways.

Finally, PhACs may be present in the food chain and in drinking water system and represent a potential risk, not only for the aquatic environment, but also for animals and humans.

2.3 Occurrence and Fate

Pharmaceuticals in the environment first became a focus of scientific interest and public awareness in the 1970s (Tabak and Bunch 1970; Norpoth et al. 1973). Thereafter, first finding of clofibric acid, the active metabolite of blood lipid regulators, in concentrations from 0.8 $\mu g \cdot L^{1-}$ to 2 $\mu g \cdot L^{1-}$ in STP effluents were reported in the USA (Garrison et al. 1976; Hignite and Azarnoff 1977). In the 1980's little research on the occurrence of PhACs was done aside from investigations in Great Britain where analysis about the existence of drugs in STP effluents and river water were realised (Richardson and Bowron 1985; Aherne et al. 1990). In 1986 ibuprofen and naproxen were detected in sewage in Canada (Roger). Later, in 1991, the first detection of a pharmaceutical active compound in groundwater samples was reported. Clofibric acid was measured in concentrations up to 4.2 $\mu g \cdot L^{1-}$ in groundwater samples collected from a former sewage irrigation plant south of Berlin (Stan and Linkerhägner 1992). Since the mid nineties the awareness of the effects of pharmaceutical active compounds and their metabolites and transformation products increased and lot of studies about PhACs and their fate in the aquatic environment were carried out in Austria, Brazil, Canada, Croatia, England, Germany, Greece, Italy, New Mexico, Norway, Romania, Spain, South Korea, Switzerland, Sweden, the Netherlands and the USA. Analyses are mainly driven by advances in environmental residue analysis, particularly after the establishment of chemical analysis methods that were able to determine more polar compounds. More than 100 substances from various prescription classes have been detected up to the $\mu g \cdot L^{1-}$-level in sewage and neighbouring surface water (Heberer & Adam, 2004). Data on environmental concentrations in STPs, surface water, groundwater, sewage sludge up to 2008 have been compiled and reviewed by (Halling-Sörensen et al. 1998; Ternes 1998; Daughton and Ternes 1999; Kümmerer 2001; Kolpin et al. 2002; Heberer 2002c; Kümmerer 2004; Ternes and Joss 2006; Nikolaou et al. 2007; Kümmerer 2008).

In Table 1 the different drugs that have been detected in STP effluents, ordered by prescription class, are listed.

Table 1: Pharmaceuticals and iodinated compounds detected in STP effluents and surface waters in Europe and North America and their therapeutic application (taken from (Ternes and Joss 2006).

Class	Application	Examples
Antiphlogistics (Analgesics, Antiinflammatory Drugs)	Non-prescription: treatment of colds, allergies, pain Prescription: treatment of chronic pain, arthritis, migraines, etc	paracetamol, acetyl salicylic acid, ibuprofen, naproxen (US), codeine, diclofenac, indomethacin, naproxen (EU), propyphenazone
Lipid regulators	Reduce blood cholesterol	atorvastatin, clofibric acid, Gemfibrozil
Antiepileptic	Anti-convulsant	carbamazepine
Psychotropics	Psychopharmacotherapy, antidepressant	diazepam, fluoxetine
Beta Blockers	Heart arrhythmias, hypertension	metoprolol, propranolol
Sympathomimetics	Bronchodilator for treatment of asthma	Salbutamol
Antihistamine	Treatment of stomach acidity	cimetidine
Cytostatic drugs	Cancer chemotherapy	cyclophosphamide, ifosfamide
Contrast Media	Diagnostic aid	Iopamidol
Antibiotics	Treatment of bacterial Infections	ciprofloxacin, sulfamethoxazole, tetracycline, trimethoprim
Hormones	Birth control, post-menopausal therapy	17α-ethinylestradiol

It can be assumed that currently detected concentrations of PhACs and of their metabolites and transformation products in the aquatic environment are just a temporary situation because the medical market changes constantly. Furthermore it is not fully understand which drugs or metabolites undergo chemical reactions with one another and if these substances may even produce new toxicological connections.

2.3.1 Sewage Treatment Plants (STPs)

Pharmaceuticals, mainly used in human medicine can be found regularly in a similar spectrum in sewage and environmental samples. Radio contrast agents are findable in highest maximum concentrations but with biggest fluctuation range, particularly amidotrizoic acid, iomeprol and iopromide, followed by the analgesic diclofenac and the antiepileptic carbamazepine. Next PhACs, occurring in comparable ranges, are lipid lowering drugs bezafibrate and clofibric acid, metoprolol and sotalol (beta blockers) as well as phenazone (analgesic) and its derivates, followed by the antibiotics sulfamethoxazole and erythromycin ((BLAC 2003)). In general, the levels of pharmaceuticals in STP effluents range in high $ng \cdot L^{1-}$ to low $\mu g \cdot L^{1-}$ concentrations. Studies about the occurrence of PhACs in influents and effluents STPs have shown that the fate of pharmaceutical residues during sewage treatment can follow one or a combination of three types of behaviour:

a) (Bio)-**degradation** (mineralization to carbon dioxide and water),

b) **Sorption** of the residues onto sewage sludge,

c) **No elimination** or **retransformation** from conjugates to the parent compound.

The question of which PhAC undergoes what particular behaviour depends among other parameters on the chemical structure of the compound and its physicochemical properties. Some physicochemical properties of each priority PhACs, like the water solubility, the octanol-water partition coefficient log K_{OW}, the adsorption coefficient $K_{OC,}$ and the Henry's law constant K_H are described in the compendium (see annex) and explained in Table 2.

Furthermore, parameters like composition of the sewage, design and operation of the treatment process (biological activity, sludge retention time, hydraulic retention time, additional treatment step) and weather conditions (temperature, rain events) determine the fate of a drug during sewage treatment (Clara et al. 2005; Ternes et al. 2005; Vieno et al. 2005; Gros et al. 2007; Jones et al. 2007).

By comparing incoming and outflowing compound concentrations, specific elimination rates can be calculated. In chapter 3.4 elimination rates of priority pharmaceuticals are presented.

Table 2: Key parameters in studies of the environmental fate of organic chemicals

Physicochemical Property	**Information**
Water solubility	Water solubility is the property of a chemical substance to dissolve in a liquid solvent to form a homogeneous solution. A solute will dissolve best in a solvent that has a similar polarity to itself.
Octanol-water partition coefficient (log K_{OW})	Most widely used physical property for predicting the sorption characteristics of particles and living organisms. It describes the equilibrium concentration between water and a solvent (octanol), with octanol serving as a proxy for the partitioning between the aqueous phase and the more lipid-like biophase. The K_{OW} therefore provides as indication of (1) the uptake potential by organisms (2) the potential for bioaccumulation from the water (3) the residence time of persistent organic pollutants. Chemicals with low K_{ow} values (e.g., less than 10) are considered as relatively hydrophilic; they tend to have high water solubility, small soil/sediment adsorption coefficients, and small bioconcentration factors for aquatic life. Conversely, chemicals with high K_{OW} values (e.g., greater than 104) are very hydrophobic.
Adsorption coefficient (K_{OC})	The organic carbon adsorption coefficient K_{OC} (estimated via $0.41 \times K_{OW}$ (Karickhoff, 1981) is crucial for estimating a chemical compound's mobility in soil and the prevalence of leaching from soil. A low K_{OC} of a compound characterises a high mobility of the compound in the soil and vice versa.
Henry's law constant (K_H)	The Henry's law constant K_H informs about the volatilization capacity of a compound. A compound with a KH higher than 10^{-3} is volatile whereas a compound with a K_H less than 10^{-7} is less volatile than water. (Air stripping is no relevant process for pharmaceuticals due to their low K_H ((Ternes, Joss et al. 2005)).

2.3.2 Surface Water

Studies about the occurrence and fate of priority pharmaceuticals in surface water have shown, that concentrations are rarely above 100 $ng \cdot L^{1-}$ and frequently below 10 $ng \cdot L^{1-}$.

The concentrations in surface waters are very dependent on the dilution factor of the STP effluents. The dilution factor is a critical determinant in order to be able to compare the different studies and predict environmental concentrations (cf. Chapter 5). They are site specific and may vary over several orders of magnitude depending on the location and season.

It is assumed that highest concentrations occur at sites close to point sources, such as near discharges from STP where the effluents are poorly diluted by the natural discharge.

Once entering surface waters biotransformation through biodegradation occurs, but abiotic transformation reactions are probably more important. Whereas hydrolysis is generally negligible, photodegradation plays an important role for some PhACs. For example for the analgesics diclofenac and naproxen photolysis has been shown to be an important removal process (Buser et al. 1998a; Packer et al. 2003). For other compounds such as the antibiotics sulfamethoxazole and ofloxacin and the beta-blocker propranolol, laboratory experiments indicate direct and indirect photolysis as an important removal process (Andreozzi et al. 2003)

2.3.3 Groundwater

Several polar PhACs such as analgesics (diclofenac, phenazone, propyphenazone), lipid lowering drugs (clofibric acid, bezafibrate, gemfibrozil), the antiepileptic drug carbamazepine, sulfonamides, macrolides, beta-blockers and X-ray contrast agents have been detected in trace quantities in groundwater in Denmark, Germany, Switzerland, USA, and Croatia (Holm 1995; Heberer et al. 1998; Seiler et al. 1999; Ternes and Hirsch 2000; Ahel and Jelicic 2001; Sacher et al. 2001; Ternes 2001; Reddersen et al. 2002; Heberer 2002a; BLAC 2003; Blüm et al. 2005; NASRI-project 2005; Hanke et al. 2007).

During the NASRI (Natural and Artificial Systems for Recharge and Infiltration) project, laboratory and field investigations about the behaviour of eight drugs during bank filtration have shown that some PhACs such as the antiepileptic drugs carbamazepine and primidone are rarely attenuated, whereas other drugs like bezafibrate and indomethacine show high removal rates. It was also shown, that the attenuation of organic micro pollutants is mainly effected by the prevailing redox conditions (Massmann et al. 2009).During another study carried out by (Drewes et al. 2003), carbamazepine was not removed during groundwater recharge under either anoxic saturated or aerobic unsaturated flow conditions during travel times of up to eight years. Therefore carbamazepine is thought to be a good indicator for evaluating whether groundwater is influenced by municipal sewage effluents.

2.4 Measuring PhACs

2.4.1 Analytical Methods

The number of available analytical methods for the analysis of pharmaceutical residues in water increased during the last 10-15 years. As yet no standardized analytical method is available to investigate pharmaceutical residues in the aquatic environment.

Measuring PhACs in the environment requires the identification and quantification in complex aqueous media (sewage) and in solid matrices (e.g., sludge, sediment, and biota) down to a low trace level. Thus, analytical methods must be very specific to track pharmaceutical residues among a vast majority of other impurities and sensitive enough to enable sufficiently low quantification limits. Furthermore, the analysis of pharmaceuticals are challenging since many of them are polar and characterized by low molecular weights, so that most state of the art commercial and industrial laboratories took a lot of effort to establish an appropriate method. Such methods should provide both, high sensitivity and high accuracy of the analytical results. The highest potential in trace-level analysis of multiple compounds at coeval low cost is attributed to the so-called multi-step approach (see Figure 3).

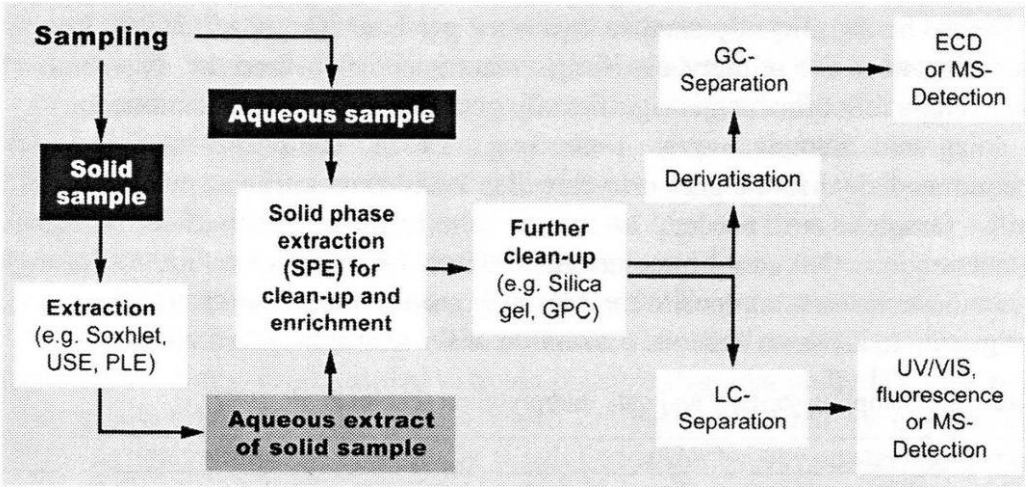


Figure 3: Multistep approaches fort the analysis of organic pollutants (Ternes and Joss 2006)

The sampling is the most important step to get representative data that allow correct conclusions for mass fluxes in natural and technical systems (see chapter 2.4.2). If contaminants are sorbed to solids, the extraction method described by Soxhlet in 1879 has been the general method for many years and is still often applied. More recently other techniques like ultrasonic solvent extraction (USE) or pressurized liquid extraction (PLE) have become increasingly popular. Measuring compounds in an aqueous sample, the compounds first need to be separated from sample matrix and have to be pre-concentrated due to their generally low concentrations. Basically, solid phase extraction (SPE) is applied as extraction and enrichment method for water samples or aqueous extracts. If disturbing matrix components are still present in post-extraction samples further clean-up steps such as

silica gel columns are required. For the quantitative determination of PhACs obtained in the final extraction, chromatographic techniques such as capillary gas chromatography (GC) or liquid chromatography (LC) are used to separate the individual analyte from a complex sample mixture. GC can be directly applied for compounds with higher volatility, whereas molecules with charged groups require a time consuming derivatisation prior to GC detection. Therefore, polar and charged pharmaceuticals are preferable analysed via LC, since no derivatisation is necessary. State of the art is the analysis of polar compounds using high performance liquid chromatography (HPLC) separation, followed by electro spray ionization and tandem mass spectroscopy (MS). Disadvantage of the LC–MS compared to GC–MS is that the ionization of the compounds is not standardized, so that no spectra libraries are available. Hence, the screening of unknown compounds by the interpretation of fragmentation pattern using large spectra libraries (as available for GC-MS) is very difficult. New appendages for LC–MS offer high resolution MS coupled with quadrupole and ion trap. If the exact molecular mass and specific fragmentation can be determined, it is often possible to identify the wanted compound. (Reddersen and Heberer 2003; Hollender 2005; Ternes and Joss 2006; Hollender 2007).

2.4.2 Sampling Method

Effective sampling methods are essential to obtain reliable data of the PhACs concentration and fate in the environment. Before starting a sampling campaign of different environmental compartments, many factors have to be considered and documented.

Resolution in Time

It is known that the occurrence of pharmaceuticals in the urban water cycle varies at different time-scales. Seasonal variation occur when the application of pharmaceuticals is higher in winter, than in summer month (e.g., antibiotics) or when higher temperatures lead to an increase of biological activity in STPs and surface water, and finally result in a higher degradation of some compounds. Other PhACs such as the analgesic diclofenac are subjected to degradation due to radiation of UV-light (Boreen et al. 2003). Furthermore, weekly (school holiday, public events), daily (working days vs. weekend), and diurnal (systematic habits of individuals) changes and variations driven by natural events (e. g., rain) influence the occurrence of substances in the urban water cycle. Additionally, concentrations in sewers of compounds emitted by just a small number of persons can be subjected to considerable short term variations in a range of only a few minutes, even when the flow does not change (Adam 2005; Joss et al. 2005; Ort et al. 2005). The required sampling interval in sewage treatment of these compounds (e. g., radio contrast agents or antibiotics) must be significantly smaller than once per hour (Ort et al. 2004). Furthermore, reliable measurements and adequate sampling strategies are necessary, because it is not yet feasible to perform a high-frequency sampling campaign at reasonable cost and to analyze each sample separately (Ort and Gujer 2005).

To calculate loads or mass fluxes, integrated samples over time (e.g., 24-h composite) are recommended, whereas composite samples may require that aliquots are taken frequently to allow an accurate estimation of the average concentration. Series of grab samples are needed to assess short time distributions or peak concentrations.

Spatial Distribution

The occurrence of pharmaceuticals in different environmental compartments at a specific site is influenced by point sources (e.g., hospitals in catchment areas or medical institution) and different consumption patterns in different regions (due to specific description patterns). Thus, measurements from a wide geographic distribution enable more general interpretation than measurements from single sites only. Additionally, several samples should be collected throughout the area of interest to consider local variability in the analyte concentration. For example spatial inhomogeneity can be caused by incomplete mixing of inflows (Pacini et al. 1997)

Sampling of specific environmental Compartments

Sampling the input of pollutants in a lake within a certain time period, the seasonal stratification of a lake has to taken into account. In summer the upper epilimnion layer has a higher oxygen concentration and higher temperature than the water layers below, whereas in winter upper and lower water layers of a lake are mixed, except for very deep lakes. (Tixier et al.)(2003) detected different concentration profiles of pharmaceuticals such as diclofenac and carbamazepine in the stratified water layers of Lake Greifensee. Furthermore, discharging tributaries of a lake have to be taken into account.

In contrast, concentration of pharmaceuticals in river water may change very quickly. Therefore, flow and time proportional automatic samplers are needed. Water from tributaries or STP effluents, which enter the river, is often not completely mixed over a long distance. Hence, it could be crucial to sample river water over its whole width.

Sampling groundwater requires a constant pH, temperature and conductivity before a sample can be taken.

A tiered research plan for studies in mechanical-biological STPs was conducted by (Alder et al. 1997) (cf. Table 3). The plan can be divided in four distinct levels of sophistication. TIER 1 is most adequate for screening studies to obtain preliminary results. On TIER 2 reliable removal rates and information about mass flows and mass balances are receivable. Samples of the effluent should be taken time-related to the influent. TIER 3 requires an intense sampling program, but produces the most detailed assessment on the behaviour of pharmaceuticals in a STP. TIER 4 integrates mathematical models that extend the monitoring data across space and time. If mass fluxes are calculated aqueous as well as solid samples have to be taken at several places throughout the plant. Usually, grab samples of solid samples are taken, but 24h composite samples are more accurate especially for primary sludge (Ternes and Joss 2006).

Table 3: Research Plan for field studies in STPs (Alder 1997)

TIER 1	monitoring using grab samples of influents, effluents and sludges → screening level
TIER 2	monitoring using composite samples (≥ 24 h) of influents, effluents and grab samples of sludges determining dissolved and sorbed fraction → mass flows in STP, elimination
TIER 3	intensive sampling to determine daily fluctuation and dynamic behaviour
TIER 4	incorporation of TIER 3 data into mathematical model using transport, transfer and transformation processes

Passive Sampling Methods

Currently, sampling methods for PhACs are the same as those routinely used for monitoring priority pollutants in aquatic environment. Samples are taken, based on periodically collection of spot or grab samples of water and are subsequently filtered before extraction and analytical measurements. For some PhACs this may result in mass losses if they are combined with particulate material. This sampling method yields only a momentarily situation of the aqueous concentration and is no representative measurement, if the measured PhAC fluctuate over time. Therefore 24h-composite samples can be used to improve the reliability of the monitoring data. However, the whole sampling techniques rely on the use of expensive, vulnerable equipment that requires regular maintenance. An emerging alternative to these traditional methods is the employing of passive sampling devices.

These devices can be developed over extended time periods and yield time-weighted average concentration. Main operation principle is that a low concentration of a pollutant is maintained at the surface of a receiving phase with high affinity for the compound being measured. This provides continuous diffusion through a diffusion-limited membrane and accumulation of the pollutant from the bulk water phase to the adsorbent receiving phase. The device has to be calibrated for the pollutant of interest. However, calibration data of polar organic pollutants are limited. Calibration studies for 25 pharmaceuticals where carried out by (Mazzella et al. 2007) and (Togola and Budzinski 2007) using the polar organic chemical integrative sampler (POCIS), a passive sampling device which was developed by (Alvarez 1999). Another passive sampling device is the Chemcatcher, which was developed to monitor polar pesticides by (Kingston et al. 2000). Table 4 shows an outline of the advantages and disadvantages of passive sampling devices versus traditionally grab samples or 24-h composite samples. For further details on the principles, the calibration of passive samplers, and application examples, the reader is referred to (Mills et al. 2007) and (Söderström et al. 2009).

Table 4: Currently advantages and disadvantages of passive sampling devices

Advantage	Disadvantage
representative information at relatively low cost (no need of power supply or maintenance)	need for demonstration of their robustness and reliability
can effectively sample significant volumes of water (e.g. for the polar Chemcatcher and POCIS typically between 0.05 and 0..35 L·day^{1-}, depending on compound)	need a combination of laboratory calibration and field studies for this range of emerging contaminants
play a part in protecting watercourses from deliberate sabotage or accidental contamination by providing fingerprint of the background chemical composition of given water systems	some PhACs are labile (photodegradation, hydrolysis) stability on the receiving phase must be known →requires extensive laboratory investigations for target analytes under a range of simulated environmental conditions
provide more representative estimates of total burdens and can sequester chemicals with short residence times	inter-laboratory method validations may be necessary for their acceptance as a regulatory tool
can be used to monitor the effectiveness of water treatment process in the removal of these compounds	selection of suitable receiving phases for PhACs is more difficult and a range will be needed to optimize sequestration for particular classes of compound
time-integrated samples with one sample collection	full understanding of responsiveness of device is required

2.5 Model based Prediction of expected Concentrations

Before realizing a risk assessment, which coincides with an extensive monitoring program of the occurrence of PhACs, exposure assessment is an important step to understand the potential impact of pharmaceuticals in the environment. The occurrence of PhACs in the environment is mainly dependent on the elimination efficiency of pharmaceuticals during sewage treatment as well as on the consumption rates, on the excretion rates of the compound and on the population numbers of STPs. The equations below illustrate a method for predicting pharmaceutical concentration in different water compartments based on the three factors mentioned above and are adapted from (Ternes and Joss 2006).

2.5.1 Prediction of the Pharmaceutical Concentration in STP Influent Water

The calculation assumes that the estimated consumption rate is evenly distributed over the year and throughout the location and that no degradation takes place in the sewer system.

$$PEC_{STPin} = \frac{C_{PhAC} \times 10^9 \times (p+m)}{365 \times P_{total} \times Q_{WW}} \qquad \text{Eq. 1}$$

PEC_{STPin} *predicted concentration in the raw sewage water [µg·L^{1-}]*

C_{PhAC} *consumption of the PhAC per year in the country/area [kg·a^{1-}]*

p *fraction of parent compound excreted and discharge to sewer*

m *fraction of known metabolites excreted and discharge to sewer*

P_{total} *Population within the country/area [cap]*

Q_{WW} *Volume sewage per capita and day (L·cap^{1-}·d^{1-})*

2.5.2 Prediction of the Pharmaceutical Concentration in STP Effluent Water

For predicting the compound concentration emitted by STPs, relevant removal processes have to be considered. In this report we illustrate an equation for the prediction of the concentration of a specific PhAC in STP effluents which combines all occurring elimination processes such as sorption onto sludge, biological degradation, and deconjugation, in one parameter (e), which was determined in many studies by the ratio of incoming and outflowing concentrations of a specific compound. Elimination rates of priority compounds revealed in some studies are presented in chapter 3.4.

For a more detailed equation which implements specific parameters for the different elimination processes, see (Ternes and Joss 2006).

$$PEC_{STPout} = \left(\frac{C_{PhAC} \times 1000 \times (p+m)}{365 \times P_{total} \times Q_{WW}} \right) \times (1-e) \qquad \text{Eq. 2}$$

e *elimination rate during sewage treatment process*

2.5.3 Prediction of the Pharmaceutical Concentration in Surface Water

For estimating environmental concentration in surface water, the dilution factor of the STP effluent in the receiving water as well as the background concentration of the compound in the receiving water body have to be considered.

$$PEC_{Surface\ Water} = \frac{(PEC_{STPout} \times Q_{STPout}) + (C_{Background} \times Q_{Background})}{Q_{Total}} \qquad \text{Eq. 3}$$

$PEC_{Surface\ Water}$	*predicted concentration in the receiving water body [ng·L^{-1}]*
QSTPout	*treated sewage flow [m³·s^{-1}]*
$C_{Background}$	*background concentration in the receiving water body prior to the discharge of treated sewage [ng·L^{-1}]*
$Q_{Background}$	*receiving water flow [m³·s^{-1}]*
Q_{Total}	*total water flow of receiving water after inflow sewage [m³·s^{-1}]*

If the dilution factor of treated sewage is higher than 10 (i.e. the proportion of treated sewage in receiving water is less than 10 %), the equation 3 can be simplified to

$$PEC_{Surface\ Water} = PEC_{STPout} \times R_{Dilution} + C_{Background}, \qquad \text{Eq. 4}$$

where $R_{Dilution}$ is the ratio between treated sewage and the receiving water flow.

2.6 Ecotoxicology - Predicted Non Effect Concentration

The EU Water Framework Directive (WFD), which was adopted in 2000, involves the development of environmental quality standards for pollutants to protect aquatic life in surface water. These quality standards have to be derived by a scientific risk assessment and should not be exceeded. Requirements for the evaluation of quality standards are given by the WFD and the European Medicine Agency (EMEA). The evaluation of the lowest effect concentrations should be conducted in three fundamental toxicological tests (EC_{50}, LC_{50} and NOEC) on standard test organisms like algae (primary producer), daphnia (primary consumer) and fish (secondary consumer).

EC_{50} →effect concentration	50 % of the test organisms show effects when they are exposed to this concentration. Decreasing mobility of invertebrates or the reducing metabolism of micro organism are possible impacts.
LC_{50} →lethal concentration	50 % of the test organisms die by applying of this concentration
NOEC →no observed effect concentration	highest concentration, on which no effects on test organisms are observable

For the risk assessment of PhACs on aquatic organisms the predicted or measured concentration (PEC/MEC) of a PhAC is contrasted with the predicted non effect concentration (PNEC), which is determined on the basis of the lowest detected values of these toxicological tests. However, laboratory conditions during the tests never fully reflect the natural environment conditions. Therefore an uncertainty factor is applied on the concentration of the lowest toxic effect.

$$PNEC = \frac{EC_{50} / LC_{50} / NOEC}{Factor_{Uncertainty}}$$

The more data on toxicological tests are available, the higher is the certainty of the effect of the compound. Therefore, data from long time tests are often more significant than data from acute tests, so that if long time test are available the uncertainty factor can be reduced (cf. Table 5). The uncertainty factor includes the following aspects:

- Extrapolation of acute to chronic toxicity
- Inter-species variation
- Intra-species variation
- Extrapolation of laboratory data to nature.

Table 5: Uncertainty factor for the evaluation of PNEC values after TGD (EC 2001)

Available Data	**Uncertainty Factor**
One short-time-test (L(E)C50) on fish, daphnia and algae as agents of different trophic levels	1000
One chronic-test (NOEC) (fish or daphnia)	100
Two chronic tests on species of different trophic level (fish and/or daphnia and/or algae)	50
Chronic test (NOEC) of at least three species of different trophic levels (fish, daphnia, algae)	10

The quotient of $\frac{PEC(MEC)}{PNEC}$ characterises the risk for the aquatic ecosystem.

If $\frac{PEC(MEC)}{PNEC} < 1$,

it is assumed that no risk for the aquatic organism exists.

If $\frac{PEC(MEC)}{PNEC} > 1$

either improvements of the input data PEC and PNEC are necessary or actions for risk avoidance and risk minimisation are needed.

Chapter 3
Priority Pharmaceuticals considered in this Study

3.1 Selection of priority Pharmaceuticals

When analysing the impact of pharmaceuticals in the aquatic environment, it is helpful, with an existing amount of 50,000 registered compounds(Kümmerer 2008), to concentrate on relevant compounds which have a potential to accumulate in drinking water and/or are toxic for the aquatic environment.

Environmentally relevant compounds are ubiquitously detected in the aquatic environment, because there are either often prescribed and used in human medicine, or prescribed in high doses, or they are highly persistent or resistant to treatment in STPs or waterworks (WWs).

For the current work a priority list, developed by the Global Water Research Coalition (GWRC) in 2008, was taken as a basis for the selection of priority pharmaceuticals on which we focus during the study (de Voogt et al. 2009). After introducing the selection methodology of the GWRC, detailed information about the consumption rates, the excretion rates, the elimination rates and the PNEC of the priority pharmaceuticals is given.

3.1.1 Priority List of the Global Water Research Coalition

Experts belonging to the GWRC evaluated a total of 25 reports and references which had the prioritisation of PhACs used in human medicine as key subject. Although this set of base documents is not exhaustive, it represents an ‘average’ of studies used in various countries and provides a good overview of criteria used in priority setting of human PhACs.

Thus 153 different priority compounds where found based on 17 different criteria.

The criteria employed in the base documents were subjected to expert judgement and evaluation by the project team members, whereupon only scientific considerations were used for the evaluation. Based on this judgement, seven key criteria (see below) were regarded as being of special relevance for the GWRC members and selected as a basis for drawing up a priority list.

I) **regulation**
(pharmaceuticals that are listed in any environmental Directive are of special relevance),

II) **consumption**
(numbers on production and use are directly related to the probability of occurrence in the environment),

III) **physicochemical properties**
(E.g. polarity, water solubility, chemical reactivity determine the behaviour of pharmaceuticals in the environment and thus have a major impact on the relevance of a compound)

IV) **toxicity**
(Protection of the health of humans and wildlife is one of the major objectives of all GWRC members and consequently toxic compounds are of special relevance),

V) **occurrence**
(Occurrence of a compound in surface water, groundwater and sewage is one of the key criteria for its selection because if a compound is found in the environment there is a need for further activities),

VI) **persistence** and
(Degradation of a compound during sewage treatment or in the environment can significantly decrease the environmental relevance of a compound)

VII) **resistance to treatment**
(Pharmaceuticals that are difficult to remove during treatment are of high relevance and thus resistance to sewage treatment and drinking water treatment is an important criterion)

Documents which did not use any kind of the 7 key criteria were omitted and pharmaceuticals that did not score on these criteria were deleted (5 documents). Finally the PhACs were ranked on the number of fulfilled criteria, whereas all criteria were considered as being equally important. Thus, 44 priority PhACs were identified belonging to three classes.

Ten PhACs were identified as Class I (High Priority PhACs).These are PhACs that are mentioned in five or more base documents and that fulfil more than four of the seven criteria mentioned above. They represent the minimum of PhACs which should be determined in any study on pharmaceuticals in water management.

Furthermore 18 PhACs, which are mentioned in more than two documents and that fulfil more than two criteria, were indicated as Class II (Medium Priority). And 16 PhACs that are mentioned in two documents and fulfil two or more criteria are classified as Class III (Low Priority).

3.1.2 Priority Pharmaceuticals considered in this Study

In the current study special focus laid on the priority PhACs (Class I to III) that were tested in at least one water compartment of the study sites, Berlin and Zurich. Out of the 44 priority compounds identified by the GWRC, 30 were considered in this study (see Table 6).

Table 6: 30 priority PhACs and their key criteria implemented in this study. (Site B represents Berlin and Z the Canton Zurich)

Name	Class	Regulation	Consumption / Sales	Physico-Chemical Properties	(Eco) Toxicity	Occurrence	Persistence	Resistance to Treatment	Site
Atenolol	I		X		x	x	x	x	B/Z
Bezafibrate	I		X	x	x	x	x		B/Z
Carbamazepine	I	x	X	x	x	x	x	x	B/Z
Ciprofloxacin	I		X		x	x	x	x	B/Z
Diclofenac	I	x	X	x	x	x	x	x	B/Z
Erythromycin	I		X		x	x	x	x	B/Z
Gemfibrozil	I		X		x	x	x	x	B/Z
Ibuprofen	I		X	x	x	x	x	x	B/Z
Naproxen	I		X		x	x	x	x	B/Z
Sulfamethoxazole	I	x	X	x	x	x	x	x	B/Z
Acetyl salicylic acid	II		X		x	x	x		B
Amidotrizoic acid	II	x	X			x			B/Z
Amoxicillin	II		X		x	x	x		Z
Clarithromycin	II		X	x	x				B/Z
Clofibric Acid	II		X	x		x	x		B/Z
Codeine	II		X		x	x		x	B
Cyclophosphamide	II		X		x	x	x		B/Z
Diazepam	II		X	x	x	x		x	B/Z
Iopromide	II		X	x		x		x	B/Z
Metoprolol	II		X			x	x	x	Z
Ofloxacin	II		X		x	x	x		B/Z
Paracetamol	II		X		x	x	x		B
Sotalol	II		X		x	x			Z
Trimethoprim	II		X		x	x		x	B/Z
Doxycycline	III		X		x	x		x	B/Z
Iomeprol	III		X			x			Z
Iopamidol	III	X				x			Z
Oxazepam	III		X		x	x		x	B
Salbutamol	III		X		x	x	x		B/Z
Simvastatin	III		X		x	x		x	Z

In the following chapters specific information about consumption rates, excretion rates and elimination rates of priority PhACs are listed and finally summarised in chapter 3.6. Physicochemical properties of each priority PhAC are given in the fact sheets (see annex).

3.2 Consumption

In 2001 about 50,000 different pharmaceuticals were registered in Germany, of which 2700 account for 90 % of total consumption and which contain about 900 different active substances (Kümmerer 2008). In Switzerland around 10,000 drugs with 3000 different active ingredients are in use. Whereas 95 % of the total sales volume is allotted to less than 50 active ingredients (Hanke, Singer et al. 2007). Yet, in the water cycle the variety of pharmaceutical active compounds is further enlarged by metabolites or transformation products of the parent compound. For the most pharmaceutical compounds total amounts sold are not available for environmental public authorities, because sales data are collected only in the private industry (BLAC 2003). Up to today no central collection of pharmaceutical sales data exists. However, estimation of the annual quantities prescribed can be obtained based on the accessible number of prescription items multiplied by the defined daily dose of a particular compound. In the case of pharmaceuticals which are available without prescription, also called over the counter drugs (OTC), i.e. the analgesic ibuprofen and diclofenac, this calculation leads to underestimations, since the amounts dispensed in non-prescription products are not considered. Non prescription drugs are generally sold in higher quantities than prescription drugs. In Germany higher amounts of non prescription drugs such as aspirin (902 $t \cdot a^{-1}$), paracetamol (654 $t \cdot a^{-1}$) and ibuprofen (354 $t \cdot a^{-1}$) were sold in 2001 compared to prescription drugs such as the antibiotic clarithromycin (7.2 $t \cdot a^{-1}$) or the lipid lowering drug gemfibrozil (5.2 $t \cdot a^{-1}$). Similarly, patterns of use of OTC in the United States and Canada indicate that OTC analgesics (e.g. aspirin, ibuprofen and paracetamol) are the most highly used drugs (Kaufman et al. 2002; Metcalfe et al. 2004).

Sales data of priority pharmaceuticals sold in Germany and Switzerland are shown in Table 7. Data about annual sales in $t \cdot a^{-1}$ for a broad range of pharmaceuticals in Germany were collected by the private Institute for Medical Statistic (IMS Health GmbH & Co. OHG, Frankfurt/Main) and are summarised in the report of the Federal States Committee of Chemical Safety (BLAC 2003). Sales data for Switzerland are not available for all priority pharmaceuticals. Sales data for different years were found in several studies (Blüm, McArdell et al. 2005; Giger 2005; Ternes and Joss 2006; Hollender 2007; Lienert et al. 2007). The consumption pattern of pharmaceuticals varies between different countries and over time since new products are introduced in different countries and some compounds become less popular. Sales data of PhACs in other countries than Germany and Switzerland can be found in the literature, too (Kümmerer 2004; Ternes and Joss 2006).

Table 7: Sales data in $t \cdot a^{-1}$ of several priority pharmaceuticals in Germany and Switzerland. Sales data in $t \cdot a^{-1}$ of several priority pharmaceuticals in Berlin in 2001 are shown in red and in brackets (Adam 2005).

Compound	Therapeutic Use	Sales Germany (Berlin) in $t \cdot a^{-1}$, 2001	Sales in $mg \cdot cap^{-1} \cdot d^{-1}$ in Germany	Sales Switzerland in $t \cdot a^{-1}$	Sales in $mg \cdot cap^{-1} \cdot d^{-1}$ in Switzerland
Acetyl salicylic acid	Analgesic	902 [a]	30	47 [g]	17.4
Codeine	Analgesic	9.7	0.3	n.a.	n.a.
Diclofenac	Analgesic	85.8(2.231)	2.9(1.8)	3.8 [c]/4.6 [g]/4.3 [h]	1.4/1.7/1.6
Ibuprofen	Analgesic	345(9.835)	11.5(7.95)	15.7 [c]/24 [g]/23.1 [h]	6/8.9/8.5
Naproxen	Analgesic	5.0(0.143)	0.2(0.12)	n.a.	n.a.
Paracetamol	Analgesic	654 [a]	21.9	128 [g]	47.3
Amoxicillin	Antibiotic	115	3.8	11 [e]	4.2
Ciprofloxacin	Antibiotic	18	0.6	n.a.	n.a.
Clarithromycin	Antibiotic	7.2(0.252)	0.2(0.2)	1.7 [f]/1.4 [h]	0.7/0.5
Doxycycline	Antibiotic	12.34	0.4	n.a.	n.a.
Erythromycin	Antibiotic	19(0.568)	0.6(0.46)	0.17 [f]	0.07
Ofloxacin	Antibiotic	2.3	0.08	n.a.	n.a.
Sulfamethoxazole	Antibiotic	53.6(1.794)	1.8(1.45)	2.6 [d]/2,5 [c]/2.1 [h]	1/1/0.8
Trimethoprim	Antibiotic	11.4(0.371)	0.4(0.3)	0.7 [b]	0.3
Carbamazepine	Antiepileptic	87.6(2.832)	2.9(2.29)	4.1 [c]/4.4 [g]/4 [h]	1.6/1.6/1.5
Atenolol	Beta blocker	13.6	0.5	3 [h]	1.1
Metoprolol	Beta blocker	93.0	3.1	n.a.	n.a.
Sotalol	Beta blocker	26.7	0.9	n.a.	n.a.
Salbutamol	Bronchodilator	0.4	0.01	n.a.	n.a.
Bezafibrate	Lipid lowering drug	33.5 (1.462)	1.1(1.18)	1.6 [c]	0.6
Clofibric Acid (Metabolite of Clofibrate, Etofibrate, Etofyllinclofibrate)	Lipid lowering drug	0.002 (1996: 1.8)	$7*10^{-5}$	0.02 (clofibrate) [g]	0.007
Gemfibrozil	Lipid lowering drug	5.2	0.2	n.a.	n.a.
Simvastatin	Lipid lowering drug	0.34	0.01	n.a.	n.a.
Amidotrizoic acid	Contrast medium	60.7	2	0.487 [b]	0.18
Iopamidol	Contrast medium	42.99	1.4	n.a.	n.a.
Iopromide	Contrast medium	64.1	2.1	11 [c]/5.3 [b]/6.9 [g]	4.2/2/2.5
Iomeprol	Contrast medium	83.37	2.8	1.7 [g]	0.6
Diazepam	Tranquiliser	1.1	0.04	0.04 [c]	0.02
Oxazepam	Tranquiliser	n.a.	n.a.	n.a.	n.a.
Cyclophosphamide	Cytostatic	0.39	0.01	0.033 [g]	0.01

a) 1999 (BLAC 2003) b) 2003 Source ISM Health (Blüm, McArdell et al. 2005) c) 2000 (Ternes and Joss 2006) d) 1999 (Göbel 2004a)
e) 1999, Source ISM Health f) 1999 (Giger 2005)
g) 2004 (Lienert, Bürki et al. 2007) h) 2005 Source IMS Health (Hollender 2007)
n.a. no information available

For some priority compounds such as carbamazepine, diclofenac, iomeprol and ciprofloxacin the use in Germany has been increased between 1996 and 2001. Therefore it is likely that concentrations in sewage have been increased during this time period. The opposite should be true for compounds such as gemfibrozil, naproxen and erythromycin of which the consumption has been decreased over the time period (BLAC 2003). The use of the priority compounds iopromide and sulfamethoxazole remained relatively constant. In Switzerland consumption rates of PhACs in different years are difficult to compare, because the data availability is scarce.

By comparing the consumption rates of priority compounds available for both countries it is noticeable that some PhACs are sold in up to 11-fold higher amounts in Germany than in Switzerland (acetyl salicylic acid, amidotrizoic acid, bezafibrate, carbamazepine, iomeprol, and sulfamethoxazole) whereas other priority PhACs such as clarithromycin, paracetamol, atenolol are sold in higher doses in Switzerland.

Here it is to mention that different consumption rates have an influence on the levels of concentration occurring in the aquatic environment.

3.3 Excretion Rates

The excretion rate is, among others, an essential parameter for estimating concentrations of PhACs in the aquatic environment (see chapter 2.5).

In a study carried out in Switzerland an analysis of 212 PhACs and their excretion pathways via urine or faeces, and-if data were available-of their metabolites, were compiled. On average, nearly two-thirds (64 %) of each PhAC was excreted via urine, one-third (35 %) via faeces, and on average, 42 % of each PhAC was metabolized (Lienert, Bürki et al. 2007). In Table 8 the excretion rates either as parent compound or as metabolite are shown for the priority PhACs.

Table 8: Excretion rates of several priority pharmaceuticals; used compendiums (Ternes 1998; Hirsch et al. 1999; Adams et al. 2002; Adam 2005; Ternes and Joss 2006; LANUV 2007; Lienert et al. 2007)

Compound	Therapeutic Use	Excretion as parent compound in %	Excretion as metabolite in %	Reference
Acetyl salicylic acid	Analgesic	8 - 5	83 100 90	(Lienert, Güdel et al. 2007) (HSDB 2001) (Adams, Wang et al. 2002)
Codeine	Analgesic	n.a.	n.a.	n.a.
Diclofenac	Analgesic	15 <1 16	<1 65 100	(Landsdorp et al. 1990) (Roth and Fenner 2000) (Lienert, Güdel et al. 2007) LUA, 2002
Ibuprofen	Analgesic	1-8 30 1	14 97 60-90	(Ternes and Joss 2006) (Lienert, Güdel et al. 2007) (Adams, Wang et al. 2002)
Naproxen	Analgesic	10	88	(Adams, Wang et al. 2002); (Adam 2005)
Paracetamol	Analgesic	4 3-10	79 90	(Lienert, Güdel et al. 2007) (LANUV 2007)

Compound	Therapeutic Use	Excretion as parent compound in %	Excretion as metabolite in %	Reference
Amoxicillin	Antibiotic	75 80-90	17 10-20	(Lienert, Güdel et al. 2007) (Hirsch, Ternes et al. 1999)
Ciprofloxacin	Antibiotic	67 70	17 18.8	(Lienert, Güdel et al. 2007) (Adams, Wang et al. 2002)
Clarithromycin	Antibiotic	>60 50	- -	(Hirsch, Ternes et al. 1999) (Roth and Fenner 2000)
Doxycycline	Antibiotic	>70	-	(Hirsch, Ternes et al. 1999)
Erythromycin	Antibiotic	98 >60 19-30	4	(Lienert, Güdel et al. 2007) (Hirsch, Ternes et al. 1999) (Adam 2005)
Ofloxacin	Antibiotic	n.a.	n.a.	n.a.
Sulfamethoxazole	Antibiotic	~15 20 15-30	 78 60-90	(Hirsch, Ternes et al. 1999) (Lienert, Güdel et al. 2007) (LANUV 2007)
Trimethoprim	Antibiotic	50-80 ~60 40-60	- 10-20	(LANUV 2007) (Hirsch, Ternes et al. 1999) (Adam 2005)
Carbamazepine	Antiepileptic	1-2 2-3 (<1) 12 12-15	~30 >70 39 83-88	(Ternes and Joss 2006) (Adam 2005)(Beyer, 1990);LUA, 2002 (Lienert, Güdel et al. 2007) (LANUV 2007)
Atenolol	Beta blocker	83 >90	5 -	(Lienert, Güdel et al. 2007) (LANUV 2007)
Metoprolol	Beta blocker	3-10 11 3-10	 86 85	(Ternes and Joss 2006) (Lienert, Güdel et al. 2007) (Adams, Wang et al. 2002)
Sotalol	Beta blocker	100 100 75 90	0 0 - -	(Lienert, Güdel et al. 2007) (LANUV 2007) (Khan et al. 2004) (LANUV 2007)(Schüssler&Sengel, 2004)
Salbutamol	Bronchodilator	n.a.	n.a.	n.a.
Bezafibrate	Lipid lowering drug	50 40 51	22 - 43	(Ternes and Joss 2006) (Adam 2005) (Lienert, Güdel et al. 2007)
Clofibric Acid (clofibrate, etofibrate.	Lipid lowering drug	6 0	>90 85	(Ternes and Joss 2006) (Lienert, Güdel et al. 2007)
Gemfibrozil	Lipid lowering drug	 6	50 30	(Ternes and Joss 2006) (Lienert, Güdel et al. 2007)
Simvastatin ß-hydroxy-acid	Lipid lowering drug	n.a.	n.a.	n.a.
Amidotrizoic acid	Contrast medium	100	-	(LANUV 2007)
Iopamidol	Contrast medium	100	-	(LANUV 2007)
Iopromide	Contrast medium	100	-	(LANUV 2007)
Iomeprol	Contrast medium	100	-	(LANUV 2007)
Diazepam	Tranquiliser	8	82	(Lienert, Güdel et al. 2007)
Oxazepam	Tranquiliser	n.a.	n.a.	
Cyclophosphamide	Cytostatic	5-40 10-40	-	(LANUV 2007) (Adams, Wang et al. 2002)

3.4 Elimination Rates during Sewage Treatment

Besides the excretion and the consumption rate, the elimination rate in a STP is also an essential parameter to estimate concentrations of PhACs in surface waters (see chapter 2.5). Therefore, several elimination rates of priority PhACs studied in conventional STPs are presented below. Furthermore a classification of PhACs due to their elimination rates in low removal (< 20%) moderate removal (20% to 80%) and high removal (>80%) is given (see Table 9).

Several studies reported that the elimination of PhACs during sewage treatment by biological degradation is mainly dependent on the sludge retention time. Results of the POSEIDON project recommended a sludge retention time of more than 10 days for efficient removal of personal care products. However, some PhACs such as antibiotics, carbamazepine, and diclofenac can be efficiently removed only by advanced technologies such as effluent ozonation, nanofiltration or activated carbon (radio contrast agents constitute an exception) (Ternes, Joss et al. 2005; Abbeglen et al. 2009).

Table 9: Elimination rates of several priority pharmaceuticals (++ high, + moderate and – low removal.)

Compound	Therapeutic Use	Elimination	Elimination rate in %	Reference
Acetyl salicylic acid	Analgesics	++	81	(Ternes 1998)
Codeine	Analgesics	n.a.	n.a.	n.a.
Diclofenac	Analgesics	+	15-40 -4 17 31-69 60 53-74 0 71	(Ternes, Joss et al. 2005) (Plume et al. 2008) (Heberer 2002c) (Ternes et al. 1999; Strenn et al. 2004; MUNLV 2006);(Metcalfe et al. 2003);(Buser, Poiger et al. 1998a) (Tauxe-Wuersch et al. 2005) (Roberts and Thomas 2006)
Ibuprofen	Analgesics	++	>90 86 96 99 58-90 99 78-100 98 12-86 >90 55 75	(Metcalfe, Koenig et al. 2003) (Jones, Voulvoulis et al. 2007) (Buser et al. 1999) (Plume, Martzinger et al. 2008) (Ternes, Hirsch et al. 1999) (Thomas and Foster 2004) (Lindqvist et al. 2005) (Roberts and Thomas 2006) (Strenn, Clara et al. 2004) (Metcalfe, Koenig et al. 2003) (Castiglioni et al. 2006) (Stumpf et al. 1999)
Naproxen	Analgesics	+	84(46-85) 66+-10 40-100 100 15-78 40-55	(Plume, Martzinger et al. 2008) (Ternes, Hirsch et al. 1999) (Metcalfe, Koenig et al. 2003) (Thomas and Foster 2004) (Stumpf, Ternes et al. 1999) (Carballa et al. 2004)
Paracetamol	Analgesics	++	>99 91 100	(Ternes, Hirsch et al. 1999) (Jones, Voulvoulis et al. 2007) (Roberts and Thomas 2006)
Amoxicillin	Antibiotic	++		(Morse and Jackson 2004)
Ciprofloxacin	Antibiotic	+	82+-3 63	(Golet et al. 2002b) (Castiglioni, Bagnati et al. 2006)

Compound	Therapeutic Use	Elimination	Elimination rate in %	Reference
Clarithromycin	Antibiotic	+	61 70-80 0	(Ternes, Hirsch et al. 1999) (MUNLV 2006) (Castiglioni, Bagnati et al. 2006)
Doxycycline	Antibiotic	n.a.	n.a.	n.a.
Erythromycin	Antibiotic	+	8-85 0	Fanck&Heberer, 2005 (Castiglioni, Bagnati et al. 2006)
Ofloxacin	Antibiotic	+	57	(Castiglioni, Bagnati et al. 2006)
Sulfamethoxazole	Antibiotic	+	50 (39-60) 24	(Plume, Martzinger et al. 2008) (Castiglioni, Bagnati et al. 2006)
Trimethoprim	Antibiotic	n.a.	n.a.	n.a.
Carbamazepine	Antiepileptic	-	0 0 7 10-25 <50 8 4 0	(Ternes, Joss et al. 2005) (Plume, Martzinger et al. 2008) (Ternes 1998) (MUNLV 2006) (Metcalfe, Koenig et al. 2003) (Heberer 2002c) (Clara et al. 2004) (Castiglioni, Bagnati et al. 2006)
Atenolol	Beta Blocker	+	0-10 21 75-80	(Fent, Weston et al. 2006) (Castiglioni, Bagnati et al. 2006) (MUNLV 2006)
Metoprolol	Beta Blocker	+	70 67	(Hirsch et al. 1996) (Ternes, Hirsch et al. 1999)
Sotalol	Beta Blocker	+	40-50	(MUNLV 2006)
Salbutamol	Bronchodilator	++	84 94.6 0	(Hirsch, Ternes et al. 1996) (Jones, Voulvoulis et al. 2007) (Castiglioni, Bagnati et al. 2006)
Bezafibrate	Lipid lowering drug	+	>95 72 75+-9 90-95 27-50 10-97 30	(Ternes, Joss et al. 2005) (Plume, Martzinger et al. 2008) (Ternes, Hirsch et al. 1999) (Stumpf, Ternes et al. 1999; Strenn, Clara et al. 2004; MUNLV 2006), (Metcalfe, Koenig et al. 2003) (Castiglioni, Bagnati et al. 2006)
Clofibric Acid	Lipid lowering drug	+	23 51+-10 30-40 6-50 15-34 91	(Plume, Martzinger et al. 2008) (Ternes, Hirsch et al. 1999) (MUNLV 2006) (Stumpf et al. 1996) (Stumpf, Ternes et al. 1999) (Roberts and Thomas 2006)
Gemfibrozil	Lipid lowering drug	+	69 16-46	(Ternes 1998) (Stumpf, Ternes et al. 1999)
Simvastatin ß-hydroxy-acid	Lipid lowering drug	n.a.	n.a.	n.a.
Amidotrizoic acid	Contrast medium	-	0 (aerobic) 35-45	(Ternes, Joss et al. 2005); (Ternes and Hirsch 2000) (MUNLV 2006)
Iomeprol	Contrast medium	-	0	(Ternes and Hirsch 2000)
Iopamidol	Contrast medium	-	0	(Ternes and Hirsch 2000)
Iopromide	Contrast medium	-	0	(Ternes and Hirsch 2000)
Diazepam	Sedative	-	no significant	(lab scale) (BLAC 2003; Ternes, Joss et al. 2005)
Oxazepam	Sedative	n.a.	n.a.	n.a.
Cyclophosphamide	Cytostatic	-	~0 <1	(Adams, Wang et al. 2002) (Halling-Sörensen, Nors Nielsen et al. 1998)

n.a. no information available

3.5 Predicted Non Effect Concentration (PNEC) for priority Pharmaceuticals

The level of concentration of PhACs in the aquatic environment is elementary for the risk assessment. If concentrations of PhACs exceed the PNEC a potential risk for the aquatic environment exists. PNEC values for priority PhACs presented in this study are based on a literature review (see Table 10). Data derive only from the literature compendiums of the North Rhine – Westphalia State Environment Agency (LANUV 2007) and the Brandenburg Environmental Agency (Adams, Wang et al. 2002), whereas the staff of the Brandenburg Environmental Agency currently works on a new environmental quality standard of pharmaceuticals. Further data about the ecotoxicity of several PhACs are given in (Fent, Weston et al. 2006) and (Webb 2001).

Table 10: PNEC values for the priority PhACs

Compound	Therapeutic Use	PNEC ($\mu g \cdot L^{-1}$)	Toxicological test	Concentration ($\mu g \cdot L^{-1}$)	Uncertainty Factor	Reference
Acetyl salicylic acid	Analgesic	**40**	EC 0 bacteria	8000	200[2]	(Adams, Wang et al. 2002)
Codeine	Analgesic	n.a.	n.a.	n.a.	n.a.	n.a.
Diclofenac	Analgesic	**0.1**	NOEC fish	1	10[1]	(Schwaiger et al. 2004; Triebskorn, Casper et al. 2004)
Ibuprofen	Analgesic	**60**	NOEC daphnia	3000	50[1]	(Halling-Sörensen, Nors
Naproxen	Analgesic	**28**	EC 50 daphnia	140000	5000[2]	(Kümmerer 2001)
Paracetamol	Analgesic	**46**	EC_{50} daphnia	9200	200[2]	(Stuer-Lauridsen et al. 2000)
Amoxicillin	Antibiotic	n.a.	n.a.	n.a.	n.a.	n.a.
Ciprofloxacin	Antibiotic	**0.005**	EC_{50} bacteria	5	1000[1]	(LANUV 2007)
Clarithromycin	Antibiotic	**0.002**	EC_{50} algae	2	1000[1]	(Isidori et al. 2005)
Doxycycline	Antibiotic	n.a.	n.a.	n.a.	n.a.	n.a.
Erythromycin	Antibiotic	**0.02**	EC_{50} algae	20	1000[1]	(Isidori, Lavorgna et al. 2005)
Ofloxacin	Antibiotic	n.a.	n.a.	n.a.	n.a.	n.a.
Sulfamethoxazole	Antibiotic	**0.1**	NOEC duckweed	10	100[1]	(Liebig 2005)
Trimethoprim	Antibiotic	**3**	LC_{50} fish	3000	1000[1]	(Kolpin, Furlong et al. 2002)
Carbamazepine	Antiepileptic	**2.5**	NOEC daphnia	25	10[1]	(Ferrari et al. 2003)
Atenolol	Beta blocker	n.a.	n.a.	n.a.	n.a.	n.a.
Metoprolol	Beta blocker	**7.3**	EC_{50} algae	7300	1000[1]	(Cleuvers 2003)
Sotalol	Beta blocker	n.a	n.a	n.a	n.a	n.a
Salbutamol	Bronchodilator	n.a.	n.a.	n.a.	n.a.	n.a.
Bezafibrate	Lipid lowering drug	**6**	LC_{50} fish	6000	1000 [1]	(Adams, Wang et al. 2002)
Clofibric Acid	Lipid lowering drug	**1**	NOEC daphnia	10 (clofibrate)	10[1]	(Ternes, Hirsch et al. 1999)
Gemfibrozil	Lipid lowering drug	n.a.	n.a.	n.a.	n.a.	n.a.
Simvastatin	Lipid lowering drug	n.a.	n.a.	n.a.	n.a.	n.a.
Amidotrizoic acid	Contrast medium	**1000000**	all test organisms	10000000	10[1]	(Steger-Hartmann et al. 1999)

Compound	Therapeutic Use	PNEC ($\mu g \cdot L^{-1}$)	Toxicological test	Concentration ($\mu g \cdot L^{-1}$)	Uncertainty Factor	Reference
Iopamidol	Contrast medium	n.a.	n.a.	n.a.	n.a.	n.a.
Iopromide	Contrast medium	**100000**	NOEC daphnia	1000000	10[1]	(Steger-Hartmann et al. 1998)
Iomeprol	Contrast medium	n.a.	n.a.	n.a.	n.a.	n.a.
Diazepam	Tranquilizer	n.a.	n.a.	n.a.	n.a.	n.a.
Oxazepam	Tranquilizer	n.a.	n.a.	n.a.	n.a.	n.a.
Cyclophosphamid	Cytostatic	**19680**	NOEC fish	>984000	50[1]	(Adams, Wang et al. 2002)

1 (LANUV 2007)

[2] (Adams, Wang et al. 2002)

n.a. no information available

3.6 Key Information on the Occurrence and Fate of priority Pharmaceuticals

3.6.1 Analgesics

Analgesics such as the priority pharmaceuticals aspirin (acetyl salicylic acid), ibuprofen, paracetamol (acetaminophen), diclofenac, naproxen, and codeine are drugs primarily used as pain-killers. Additionally most analgesics have anti-inflammatory and antipyretic properties. They are prescribed in high quantities in human medical care but most are sold in much higher amounts as so called over the counter drugs, without prescription. The analgesic paracetamol was sold in quantities of 128 t in 2004 in Switzerland, which makes it to the most popular drug in Switzerland whereas in Germany aspirin is the most sold drug (900t in 2001, cf. chapter 3.2). However, other sold analgesics such as diclofenac, ibuprofen, and naproxen have been recognized as being more relevant for the water cycle than those two.

Paracetamol is easily bio-degraded and removed during treatment processes. Investigations of sewage influents and effluents have shown that paracetamol is degraded to over 99 % during sewage treatment (Ternes 1998; Roberts and Thomas 2006).

Aspirin, a pro-drug, is easily degraded by deacetylation into its more active form salicylic acid and into two other metabolites namely ortho-hydroxyhippuric acid and the hydroxylated metabolite gentisic acid. (Ternes et al. 1998b) reported that salicylic acid and the two metabolites are efficiently removed by municipal STPs (81% (Ternes 1998)) and only salicylic acid was detected in very low concentrations in sewage effluents and surface water. Though higher concentration of salicylic acid was detected in studies in Greece and Spain (Farré et al. 2001; Heberer et al. 2001) whereat residues of salicylic acid can also derive from other sources such as from the use as keratolytic, dermatice and preservative of food.

Besides these two analgesics, diclofenac was identified as one of the most important PhAC present in the water cycle. Investigations about the fate of the drug have shown that

diclofenac is only partly removed during sewage treatment. A low removal rate of less than 20 % was reported by (Zwiener and Frimmel 2000), (Stumpf, Ternes et al. 1999), (Buser, Poiger et al. 1998), and (Plume, Martzinger et al. 2008). Although (Ternes, Hirsch et al. 1999) reported a moderate removal rate of 31-69 % for diclofenac in the STPs. Furthermore, it was reported that diclofenac undergoes photolytic degradation (Buser, Poiger et al. 1998a; Boreen, Arnold et al. 2003; Packer, Werner et al. 2003). Diclofenac concentrations of up to x were detected in surface waters and groundwater, respectively, which often exceeds the PNEC and is therefore a potential risk for the aquatic environment. It is shown that ozonation and membrane filtration during sewage treatment are efficient steps to eliminate diclofenac.

The analgesic ibuprofen is usually found in lower concentrations in sewage effluents than diclofenac, whereas in Spain ibuprofen was detected in concentration of up to 85 $\mu g \cdot L^{1-}$ in sewage effluent. Ibuprofen is degraded in the human body into its two metabolites hydroxyl and carboxy-ibuprofen and while (Buser, Poiger et al. 1999) observed an efficient elimination of all three compounds in municipal sewage plants, (Stumpf et al. 1998) observed no significant elimination between sewage influent and effluent concentration of the metabolite hydroxyl-ibuprofen. (Metcalfe, Koenig et al. 2003) and (Plume, Martzinger et al. 2008) reported an elimination of over 90 % and 99 %, respectively.

Other analgesic priority PhACs such as naproxen and codeine are sold in lower quantities than the mentioned analgesics but they were also detected in sewage and surface water samples (Ternes 1998; Stumpf, Ternes et al. 1999; Farré, Ferrer et al. 2001; Ternes 2001; Kolpin, Furlong et al. 2002; Andreozzi, Raffaele et al. 2003; BLAC 2003; Tixier, Singer et al. 2003; Metcalfe, Miao et al. 2004; Sedlak et al. 2005; Gomez et al. 2006). (Halling-Sörensen, Nors Nielsen et al. 1998) reported that naproxen and codeine phosphate are non-degradable compounds during sewage treatment. Several studies about the fate of naproxen during sewage treatment revealed that elimination rates are moderate (see chapter 3.4).

3.6.2 Antibiotics

Antibiotics are used in human medicine, veterinary medicine, farming and aquaculture for the prevention or treatment of diseases caused by microorganisms, such as bacteria or fungi. In livestock farming they are used to promote the growth of animals. Some antibiotics are also used in growing fruit and in bee keeping. In contrast to the properties and effects wanted from their therapeutic application, these same properties are often disadvantageous for target and non-target organisms, because they may induce resistance in bacterial strains causing a serious threat for public health as more and more infection cannot be treated with the presently used antidotes. Antibiotics can be divided according to their mode of action or chemical structure in commonly used subgroups such as ß-lactams (amoxicillin), fluroquinolones (ciprofloxacin, ofloxacin), tetracyclines (doxycycline), macrolides (erythromycin, clarithromycin), sulfonamides (sulfamethoxazole, trimethoprim) and others. Several studies have been carried out in Germany, Switzerland and USA to investigate the occurrence and fate of antibiotics in STPs (Hirsch, Ternes et al. 1999; Golet, Alder et al.

2002b; BLAC 2003; Göbel 2004a; Sedlak, Pinkston et al. 2005; Karthikeyan and Meyer 2006). They were detected down to the low $\mu g \cdot L^{1-}$-level in sewage water. In a study carried out in Switzerland a two times higher load of macrolide antibiotics in STPs during the winter season could be observed (McArdell, Molnar et al. 2003). Monthly sales data in Switzerland show that higher amounts of macrolide antibiotics were sold in January/February than in summer because they are mainly used to cure infections of the respiratory tract.

Out of the antibiotics considered in this study, amoxicillin, a widely used antibiotic to treat e.g. gastro-intestinal infections and respiratory diseases is the most used antibiotic in Germany and Switzerland with an annual consumption of 115 t and 11 t, respectively. Second popular antibiotic is sulfamethoxazole, mainly used to treat uric and respiratory diseases. It has an annual consumption of approximately 53.6 t in Germany and 1.8 t in Switzerland. The inactive metabolite of sulfamethoxazole, N4-acetylsulfamethoxazole (a conjugate) is likely to be cleaved during sewage treatment to yield the active parent compound (Göbel 2004a). This may increase the relevant environmental concentration of sulfamethoxazole for which reason N4-acetylsulfamethoxazole should not be neglected during risk assessment.

The third most used antibiotics in Germany are erythromycin and ciprofloxacin, followed by doxycycline and trimethoprim. Fewest used antibiotics are clarithromycin and ofloxacin. Some differences in the consumption patterns of antibiotics in Switzerland compared to Germany exist. A three times higher usage of clarithromycin and a ten fold lower usage of erythromycin can be noted. Beside the high consumption it was reported that amoxicillin is easily removed in biological STPs (Morse & Jackson 2004). Furthermore (Golet, Alder et al. 2002) reported a removal of 79-87 % of ciprofloxacin during sewage treatment. Other antibiotics such as sulfamethoxazole, trimethoprim, and erythromycin are more relevant for the water cycle, because they are only partially removed during sewage treatment and have been detected even in groundwater samples in Germany and Switzerland. Erythromycin is mostly not detected in its original form but as its antibacterially inactive degradation product with an apparent loss of water (Dehydro-Erythromycin or Erythromycin-H_2O)

Moreover the antibiotics erythromycin, sulfamethoxazole and clarithromycin affect the aquatic environment at very low concentrations of 0.02 $\mu g \cdot L^{-1}$, 0.1 $\mu g \cdot L^{-1}$, and 0.002 $\mu g \cdot L^{-1}$, respectively.

Studies have shown that treatment with activated carbon, chlorination and ozonation cause an effective elimination of these contaminants (Adams, Wang et al. 2002).

3.6.3 Antiepileptics

The anti-epileptic drug, carbamazepine, is ubiquitary in the aquatic environment. Its application to treat symptoms of not only epilepsy but also depressions explains the high consumption pattern which is comparable with the consumption quantities of the analgesic diclofenac. Investigations from different STPs have shown that it is not significantly removed (less than 10 %) during purification (see chapter 3.4). Furthermore field studies have shown that it is only low attenuated during bank filtration (Heberer, Fuhrmann et al. 2001; Jekel and Heberer 2005), so that carbamazepine can be described as highly persistent and mobile

drug. It has been detected in a number of groundwater samples at maximum concentrations of up to 1.1 $\mu g \cdot L^{-1}$ (Seiler, Zaugg et al. 1999; Sacher, Lange et al. 2001; Ternes 2001). In the literature it was also reported that carbamazepine has an additive effect in combination with other drugs as well as a toxic effect on the reproduction of the mammalian organism (Adams, Wang et al. 2002; BLAC 2003).

3.6.4 Lipid lowering Drugs

Clofibric acid, the active metabolite of the blood lipid regulators clofibrate, etofyllinclofibrate and etofibrate, was the first drug which was found in the aquatic environment in the 1970s in the U.S. (cf. chapter 2.3). Afterwards, a number of findings in STP effluents, surface water and groundwater have been reported for clofibric acid from Austria, Swiss, Brazil and Germany (Heberer et al. 1997; Heberer and Stan 1997; Ternes 1998; Stumpf, Ternes et al. 1999; Ahrer et al. 2001; Heberer, Fuhrmann et al. 2001; Öllers et al. 2001; Ternes 2001). Zwiener et al. (2000) carried out biodegradation studies using a pilot sewage plant and biofilm reactors and confirmed that clofibric acid is persistent under anoxic and oxic conditions. In laboratory experiments using soil columns clofibric acid leached almost tracer-like through the soil columns without sorption and retardation. Although clofibrate is taken off from the market, due to its adverse effects in the long time usage, it is still detectable in different water compartments even in the groundwater.

The most popular lipid regulator under the priority PhACs is bezafibrate, which is used in Germany in quantities of 33.5 t in 2001. It is better eliminable during sewage treatment than clofibric acid but was, however, detected in surface water and groundwater (Stumpf, Ternes et al. 1996; Ternes 1998; Zuccato et al. 2000; Ahrer, Scherwenk et al. 2001; Ternes 2001). The other lipid regulator gemfibrozil has also been detected up to low $\mu g \cdot L^{-}$1-level in STP effluents and surface water samples (Ternes 1998; Sacher et al. 2008).

3.6.5 Beta-blockers and Bronchodilators

There are more than 20 different beta blockers approved in the EU and North America (Ternes and Joss 2006), whereby ten of these account for approximately 98% of all beta blockers administrations. Beta blockers considered in this study are atenolol, metoprolol, and sotalol. Mostly used beta blocker in Germany with a quantity of 93 t in 2001 is metoprolol, followed by sotalol (26 t), and atenolol (13t). Data of sales quantities in Switzerland were only available for atenolol in 2005. Compared to Germany atenolol is sold twice as much in Switzerland. Atenolol with a low log K_{OW} is highly water soluble and has low sorption properties. Furthermore, studies about the removal of beta blockers show that atenolol is only little removed during sewage treatment (0-10 %) and metoprolol is partially removed (Hirsch, Ternes et al. 1996; Fent, Weston et al. 2006; MUNLV 2006). Data about ecotoxicology of beta blockers were not available. The bronchodilator salbutamol, also known as albuterol, is a pharmaceutical compound commonly used to relieve bronchial spasms associated with asthma. It is sold in quantities of 0.4 t in Germany in 2001. Hirsch et

al. (1996) reported that salbutamol is highly removed during sewage treatment. In Italy, in the River Po the compound was found up to 4.6 $ng \cdot L^{-1}$ (Castiglioni et al. 2004).

3.6.6 Radio Contrast Agents

In all countries with a developed medical care system, it can be expected that iodinated X-ray contrast media occur in appreciable quantities in STP effluents and hence lead to a contamination of receiving waters. Radio contrast agents are administered in high doses of up to 200 $g \cdot day^{-1}$, they are not metabolized in the human body and therefore excreted to over 95 % and they are biological persistent to a high extent. Furthermore loads of the X-ray contrast media are increased on weekdays, since X-ray examinations are performed in hospitals or radiological practices generally from Monday to Friday (Ternes and Hirsch 2000). The four X-ray contrast agents amidotrizoic acid, iopamidol, iopromide and iomeprol considered in this study had been found up to $\mu g \cdot L^{-1}$-level in groundwater samples (Putschew et al. 2000; Ternes and Hirsch 2000; Sacher, Lange et al. 2001).

3.6.7 Tranquillizers

The priority PhAC diazepam is used for the treatment of anxiety, epileptic fits and as a hypnotic. Because it induces physical and psychic addiction it is applied not longer than for four to six weeks, which is also confirmed by its low consumption rate of 1.1 t in Germany in 2001 and 0.04 t in Switzerland in 2000, respectively. (Thompson 2005)reported a removal of diazepam of 40-50 % after primary sedimentation in STPs and low sorption to secondary sludge, while (Van Der Hoeven 2004) determined an elimination rate of 93% for diazepam. However, diazepam occurred in low quantities ($ng \cdot L^{-1}$) in all sections of the environment even in drinking water in the UK and Italy (Waggott 1981; Zuccato, Calamari et al. 2000). Oxazepam, the active metabolite of diazepam with a similar application area, could be detected in low concentrations in surface water in Berlin (Heberer et al. 2002b).

3.6.8 Cytostatics

Cytostatic agents, such as the priority PhAC cyclophosphamide are used for cancer therapy. In 2001 cyclophosphamide was used in quantities of about 0.4 t in Germany which is compared to other drugs like antibiotics or analgesics rather low. Because of its carcinogenity, mutagenity and fetotoxic properties, cytostatics are an important group of drugs in terms of their risk potential for humans and the environment. Most of the active substances investigated proved to have a low biodegradability. They are expected to pass unchanged through municipal STPs, in so far as they are not eliminated due to adsorption onto sewage sludge (Aherne, Hardcastle et al. 1990; Kümmerer et al. 1997; Kümmerer 2001). Cyclophosphamide were detected in STP effluents and surface water in low $ng \cdot L^{-1}$ concentrations in Italy and Germany (Ternes 1998; Zuccato, Calamari et al. 2000; Thompson 2005).

Chapter 4
Study Sites

4.1 Berlin

4.1.1 Location

With a population of 3.41 million (2007) and an area of 891.67 km² (2007) Berlin is the most populous and largest city in Germany and the second populous city in the European Union.

4.1.2 Hydrological Settings

Surface Water

Berlin's urban environment is mainly shaped by the two main rivers Spree and Havel. The Spree enters Berlin in the south-east and flows westwards through the Warsaw Glacial Valley until it joins the Havel River, which enters Berlin in the north and flows from the north to the west. Beyond that there are smaller rivers and canals most of which flow into the main rivers Spree and Havel and serve as receiving water courses for the STP effluents. Figure 4 illustrates the main rivers Spree and Havel and their tributaries Fredersdorfer Mühlenfließ, Erpe, Wuhle, Panke, Nordgraben, Tegeler Fließ and Teltowkanal. The expanse of water of all watercourses in Berlin accounts for 6.7 % of its area (Berlin-Brandenburg 2008).

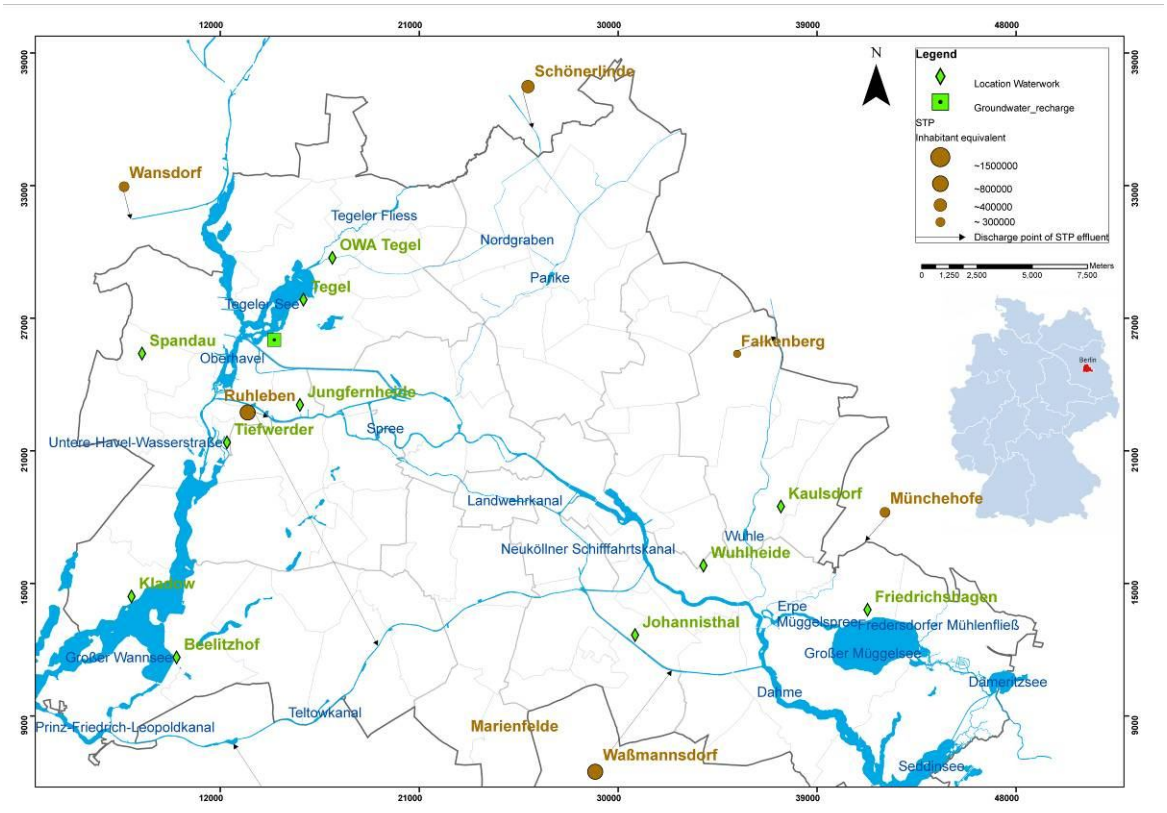


Figure 4: Map of Berlin with main watercourses, STPs and WWs (BWB)

For the evaluation of the occurrence of micro pollutants in the aquatic system of Berlin, it is important to have a look at the structure of Berlin's water system or respectively the entire north-east Germany lowland flow system. In contrast to other national flow systems it is characterised by little discharge, little discharge fluctuations and low water level variations (SenSUT 2001). In regard to the inflowing water volume Berlin is poor of water. An average water flow of 34.7 $m^3 \cdot s^{-1}$ (2001/2005) enters Berlin in the east via the River Spree, the River Dahme, the Oder-Spree-Canal and in the north via the River Havel. In comparison to the Rivers Rhein and Elbe with an average discharge volume of 2,280 $m^3 \cdot s^{1-}$ (1931-1995) and 714 $m^3 \cdot s^{1-}$ (1926-1995), respectively, the water volumes in Berlin are moderate. The Figure 5 compares discharge volumes of the rivers of Germany and discharge volumes of all Berlin STPs with each other.

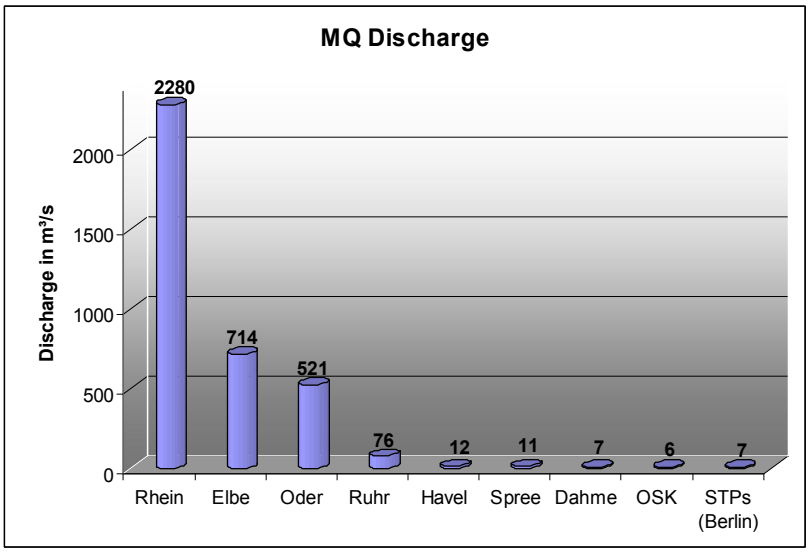


Figure 5: Long-time average discharge values in $m^3 \cdot s^{1-}$ for the Rivers Rhein (Rees, 1931-1995), Elbe (Neu Darchau, 1926-1995), Oder (Hohensaaten, 1991-1995), Ruhr (Mühlheim, 1991-2005,) Spree (Große Tränke, 1996-2005), Havel (Borgsdorf, 1977-1995), Dahme (Neue Mühle, 1996-2005) and the Oder-Spree-Canal (Wernsdorf, 1996-2005) as well as sum of discharge volumes of all STP in 2003 or 2005.

One reason for the low discharge volumes is, beside the relatively small catchment size of the Spree and the Havel, their location in the north-east lowlands, which are influenced by a dryer continental climate with lower precipitation values and an oceanic climate with hotter summers. Furthermore the heavy anthropogenic impacts and the land use of brown coal mining at the headwaters and middle reaches of the Spree influence the flow regime of the Spree. Since the 90s the brown coal mining in the Lausitz became economically unviable and is therefore being gradually reduced. This causes less discharge of groundwater into the Spree and therefore regressing water volumes which enter Berlin via the Spree. In the years from 1996 to 2000 the average discharge (MQ) at gauge Sophienwerder was 23 $m^3 \cdot s^{1-}$ which is 57% less compared to the MQ from the years 1986 to 1990 (SenSUT 2001).

Finally, Berlin's water system is characterised by low discharge volumes, a typical low hydraulic gradient of lowland rivers and therefore a low flow velocity. The anthropogenic impacts such as construction of canals, river regulation and construction of barriers and their year-around regulation for shipping additionally minimised the flow velocity and lead to anthropogenic affected backwater flow system. The flow velocity of the Spree in Berlin by average discharge conditions is approximately 0.09 $m \cdot s^{-1}$ (Riechel 2009).

In limnology these systems are regarded as a transition zone between rivers and lakes. Especially during the summer months which are affected by low water conditions, Berlin's water bodies are similar to stagnant waters. This makes them very susceptible for contamination by micro pollutants, especially with a look at the low proportion of surface water to treated sewage (see chapter 5.3).

Precipitation and Runoff Situation

Berlin's climate is classified as a transition between the continental and the oceanic climate. The annual average precipitation in Berlin is 568 mm which is rather dry compared to other regions in Germany (SenSUT 2003). Precipitation during the winter months, which is influenced by easterly continental and drier currents, is less than in the summer months. The summer months, during which up to 80mm additional rainfall occur are influenced by maritime westerly weather conditions (SenSUT 2001).

Rainwater runoff in Berlin is drained by two different systems. Within the city centre runoff is discharged by a combined sewer system (approximately a quarter of the total area connected to a sewer system), which directs the water volumes together with sewage water from households, trades and industry to the STPs. In the outskirts rainwater is discharged directly over a separate sewer system which has 730 outlets into the surface waters of Berlin. The amount of rainwater which is conveyed over the separate sewer system into surface water of Berlin is approximately 37.4 million $m^3 \cdot a^{-1}$ (SenSUT 2001). The amount of rainwater which is conveyed over the combined sewer system is around 19 million $m^3 \cdot a^{-1}$. This means that for example in the year 1999 of the total amount of rainfall of 480 million $m^3 \cdot a^{-1}$ only 10 % were conveyed over the two different sewage systems (Glugla 1999). The leftover (90 %) either evaporated or infiltrated replenishing groundwater.

During heavy rainfall events, it may happen that the combined sewer system is overloaded and pumping stations are not able to discharge the incoming water masses into the STPs as fast as they fill up the sewage system. Then untreated sewage water flows backwards out of one of the 190 outlets into Berlin's surface water in order to relieve the sewer system ((Riechel 2009)). Most outlets are located along the River Spree and the Canal Landwehrkanal. Overflow frequencies alternate between 1 and >30 times per year and are estimated to be in total approximately 7 million $m^3 \cdot a^{-1}$ (SenSUT 2001). This combined sewer overflow has to be managed because on the one hand it menaces aquatic organisms like fish due to oxygen deficiency and on the other hand micro pollutants are directly discharged in high concentration into the rivers and may exceed prescriptive limits of concentrations.

4.1.3 Drinking Water Supply

The water management in Berlin is a semi-closed water cycle. STPs discharge their treated sewage water into receiving surface waters, mainly into the rivers and canals Teltowkanal, Nordgraben, Erpe and Spree, whose waters sooner or later end up in the Spree and the Havel. Due to water extraction by WWs at wells which are located along the banks of lakes and rivers, surface water has the chance to infiltrate in the subsurface and to flow towards the abstraction wells. After the treatment of the extracted raw water enriched by bank filtrate in WWs, the pure water is supplied via the drinking water network. After the use in households, industry and trades the water returns to the STPs.

Drinking water in Berlin is extracted by eight WWs and originates from groundwater extraction, only. However the majority of the extracted water (~70 %) is not naturally replenished by rainfall but by bank filtrate and from artificial groundwater enrichment (GWA) (Möller and Burgschweiger 2008).

The annual extraction of raw water in Berlin from 1991 to 2006 decreased considerably. The amount of sold drinking water declined from 281 million m³ in 1991 to 202 million m³ in 2006 (Möller and Burgschweiger 2008). This is with the exception of the very hot and dry year 2003, when an increase in drinking water consumption occurred. The Statistic Office of Berlin estimated daily water consumption in households of around 112 litres per inhabitant in 2007, which is a decrease of 26 litres from 1991 to 2007. Table 11 illustrates raw water extraction of all WWs in 2001, 2003 and 2005 and the respective amounts of bank filtration.

Bank Filtration

Bank filtration describes the process of infiltration of surface water into the groundwater aquifer. Bank filtration occurs when the water table of the surface water is higher than the groundwater table. This happens either due to natural conditions or, artificially, due to the abstraction of groundwater from wells located near the bank of surface water.

Drinking Water Management using bank filtration in Berlin has several advantages. Firstly bank filtration is a sustainable system, because the natural water supply is secured in the long term. Secondly merely minimal treatment steps of raw water (aeration and filtration with sand filter) in Berlin are necessary, because natural cleaning along the flow path ensures a good water quality. The quality of the bank filtrate depends on length, duration (retention time), level of organics, redox conditions, and quality of the flow path. Generally positive effects of bank filtration are the elimination of particulate substances, bacteria, viruses, vermin and biodegradable substances, as well as the diminishment of different nutrients, micropollutants, absorbable substances and organic substances due to filtration, sorption, degradation, precipitation and mixing processes.

Regarding the contamination of groundwater by pharmaceutical active compounds, high bank filtration rates in abstraction wells may lead to the occurrence of PhACs in drinking

water if the neighbouring surface water is ubiquitously contaminated and the PhAC is highly persistent during bank filtration.

Table 11: Raw water extraction and bank filtration ratios of Berlin's WWs (BWB, Möller and Burgschweiger 2008).

Waterwork	Bank Filtration in %[1]	Neighbouring water body	Raw water extraction in M $m^3 \cdot a^{-1}$		
			2001	2003	2005
WW Beelitzhof	**67-74**	**Lake Wannsee/Havel**	**31.59**	**37.78**	**33.39**
WW Friedrichshagen	**82-83**	**Lake Müggelsee/ Dahme/Lake Seddinsee**	**38.32**	**44.03**	**49.20**
WW Kaulsdorf	0	-	5.59	6.35	6.59
WW Kladow	~ 68	Havel	4.64	5.04	4.66
WW Spandau	~ 79		29.42	31.87	25.56
WW Stolpe	~ 71	Havel	20.83	22.30	23.79
WW Tegel	**80-82**	**Lake Tegel**	**42.30**	**52.38**	**42.55**
WW Tiefwerder	~ 61	Havel	18.47	16.95	17.50
WW Wuhlheide	~ 29	Spree	9.80	9.62	8.68
WW Johannisthal	~ 62	Teltowkanal/Britzer Verbindungskanal	7.23	(10.00)	(8.64)
WW Jungfernheide	~ 95	Spree	16.23	(6.98)	(5.41)
Sum			**224.42**	**243.3**	**225.97**

[1] with groundwater enrichment

The main WWs with the highest raw water extractions are the WW Friedrichshagen, the WW Beelitzhof and the WW Tegel. At all three sites the rate of bank filtration in the extracted water is relatively high. Therefore a potential risk for drinking water contamination by PhACs exists if neighbouring surface water is contaminated.

The Lake Tegel, which is surrounded by eight well transects of the WW Tegel of which three are influenced by artificial groundwater enrichment, is fed by water from the Tegeler Fließ and the Nordgraben. The Nordgraben contains a considerable amount of treated sewage water from the STP Schönerlinde, which is located in the North of Berlin.

The Lake Wannsee, a bulge of the River Havel is surrounded by the abstraction wells of the WW Beelitzhof. In the south, the Lake Wannsee is fed by water from the Friedrich Leopold Canal, which contains a considerable amount of treated sewage water originating from the Teltowkanal, into which three out of six STPs discharge their treated sewage water.

The majority of groundwater samples included in this study belongs to these two bank filtration sites of the Lake Tegel and the Lake Wannsee.

In comparison to the WW Tegel and the WW Beelitzhof the neighbouring waters of the WW Friedrichshagen are not heavily affected by the discharge of treated sewage water.

Since 2002 the WWs Johannisthal and Jungfernheide extract their water for groundwater protection only.

4.1.4 Sewage Disposal

The inhabitants of Berlin use around 112 litres of drinking water per person in households. This means that 3.4 million people produce around 380 800 m³ of sewage a day. Together with sewage from public institutions, industries and trade and rainwater runoff large quantities of sewage have to be piped away and treated by currently six local STPs, every day (cf. Figure 4). All STPs in Berlin are equipped with mechanical treatment steps and biological treatment steps of nitrification and denitrification and biological phosphate removal. An overview about the amount of treated sewage of each STP in 2000, 2003, and 2005 is given in Table 12.

Table 12 Overview of discharge volumes, receiving surface waters, connected inhabitants, and population equivalents of each STP of Berlin

STPs	Connected Population (calculated)[1]	Population Equivalent (BSB 60)[2]		Recipient	Treated sewage water in M $m^3 \cdot a^{-1}$, [3]		
	2003	2001	2004		2000	2003	2005
Falkenberg	-	646,900	-	Wuhle (Spree)	34,449,211	2,656,450	-
Münchehofe	82,315	235,700	241,274	Erpe (Spree)	15,814,601	14,787,359	13,325,926
Ruhleben	1,225,606	1,025,400	835,334	Spree (Oct-March) Teltowkanal (Apr-Sept)	77,400,400	77,588,96	81,548,456
Schönerlinde	600,914	228,400	661,784	Nordgraben (Lake Tegeler See) Panke (Spree)	24,714,088	32,209,632	35,631,867
Stansdorf	383,340	401,300	346,421	Teltowkanal	19,200,619	22,425,867	18,785,860
Wansdorf	108,077	199,200	264,592	Havelkanal	n.a.	13,681,209	13,491,453
Waßmannsdorf	942,111	1,097,800	1,378,280	Teltowkanal, BÜL(Nuthe)	55,788,300	73,144,405	70,729,947
Sum	**3,342363**					**236,493,889**	**233,513,50**

1 (Adam 2005) / 2/3 BWB

The STP Ruhleben and the STP Waßmannsdorf have treated the largest amounts of sewage water between 2002 and 2004. The STP Falkenberg, which is located in the north-east of Berlin and had been discharging its water into the River Wuhle, was closed at the beginning of 2003. Its sewage was partitioned between the STP Waßmannsdorf and Schönerlinde, whereupon the amounts of treated sewage in the Teltowkanal and Nordgraben increased in 2003. Sewage water from approximately 1 million inhabitants is treated in the STPs Ruhleben and Waßmannsdorf. Depending on the season the STP Ruhleben discharges its effluents either into the Spree (October to March) or via a pipe into the Teltowkanal (April to September) in order to guarantee an adequate water quality in the Havel during the summer

months. Therefore a higher burden of treated sewage water occurs in the Teltowkanal in the winter time.

In 2003 the local sewage plants treated some 236 million m³ of sewage water, which is 650,000 m³ per day. This quantity is equivalent to around 7.5 $m^3 \cdot s^{-1}$ or one third of the Berlin Spree river run-off, given medium water flow.

4.1.5 Data Availability

In the study implemented data of Berlin belong to four long term and four short term studies, carried out from 1996 to 2006. All studies analysed the occurrence of at least one priority PhAC in either STP effluents and/or surface water and/or groundwater. Figure 6 demonstrates the monitoring periods undertaken for the study on a timeline with the names in the boxes representing the references or the project name.

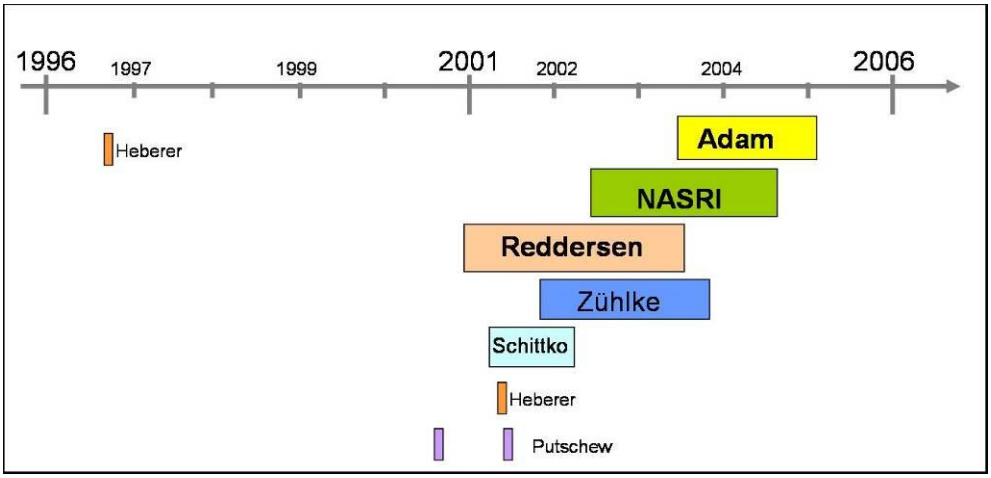


Figure 6: Timetable of monitoring periods in Berlin implemented in the study

Projects considered in this study:

During the project realised by (Adam 2005) surface water samples were taken between August 2003 and February 2005. The aim of the study was the determination of the concentrations of PhACs in inflowing water bodies of Berlin and the analysis of the impact of the five municipal STPs located on the banks of Berlin's surface water.

A second study, with a huge volume of data, belongs to the NASRI "Natural and artificial system for recharge and infiltration" project, which was managed at the KWB (2002-2005). The main objective was the development of a comprehensive process understanding to ensure the long term sustainability of bank filtration and artificial recharge keeping in mind future requirements and threats.

Furthermore, data of concentrations of PhACs measured in surface water (15 different locations), WWs and STPs were recorded over a period of 2 years during the doctoral thesis of Reddersen (2004) and were considered in this study.

Additionally, Zühlke's doctoral thesis was considered, too. He studied the behaviour of phenazone, carbamazepine and estrogens during different water treatment systems from November 2001 to January 2003. The aim of his study was the identification of degradation processes of the PhACs during the treatment steps (Zühlke 2004).

Finally some data from (Heberer, Schmidt-Bäumler et al.)(1998), (Heberer et al. 2001), (Schittko et al. 2004), and (Putschew and Jekel 2001) were considered.

Because monitoring sites differ in number of samples, in analysed water compartments and in analysed compounds, the number of samples for each priority compound in different water compartments varies substantially. So it happens that for example Zühlke sampled 118 times STP effluents in his study period but analysed only one compound considered in this study (compare Table 13).

Table 13: Number of samples taken in Berlin and number of analysed priority compounds (bold), classified by water compartment for each monitoring campaign.

Campaign	STP effluents	Surface Water	Groundwater	Priority Compounds
Adam	/	117	/	**21**
NASRI	/	158	965	**16**
Reddersen	33	162	/	**8**
Zühlke	127	52	65	**1**
Schittko	/	11	55	**2**
Putschew	1	5	3	**2**
Heberer	2	27	8	**5**
Sum	163 **(9)**	532 **(21)**	1096 **(16)**	

Most groundwater samples belong to the NASRI-project and were obtained on two important bank filtration sites of Berlin, located at the Lake Tegel and the Lake Wannsee.

The project of (Adam 2005) has contributed a bright range of priority pharmaceuticals measured on 7 different surface water locations. Additionally many surface water samples belong to the study of (Reddersen 2004).

The amount of data for the evaluation of the occurrence of pharmaceuticals in Berlin is quite large. Even so, by comparing the occurrence of pharmaceutical concentrations in the different water compartments obtained by different monitoring campaigns one has to be aware that different sample methods and different analytical methods lead to different analytical results. A list of sample locations, sample methods, analytical methods and detection limits of each compound for each monitoring period is given in the annex.

4.1.6 Sample Locations

All together 152 different locations were sampled in Berlin, 97 groundwater sample points, 49 surface water points and STP effluents of 6 STPs (see Figure 7).

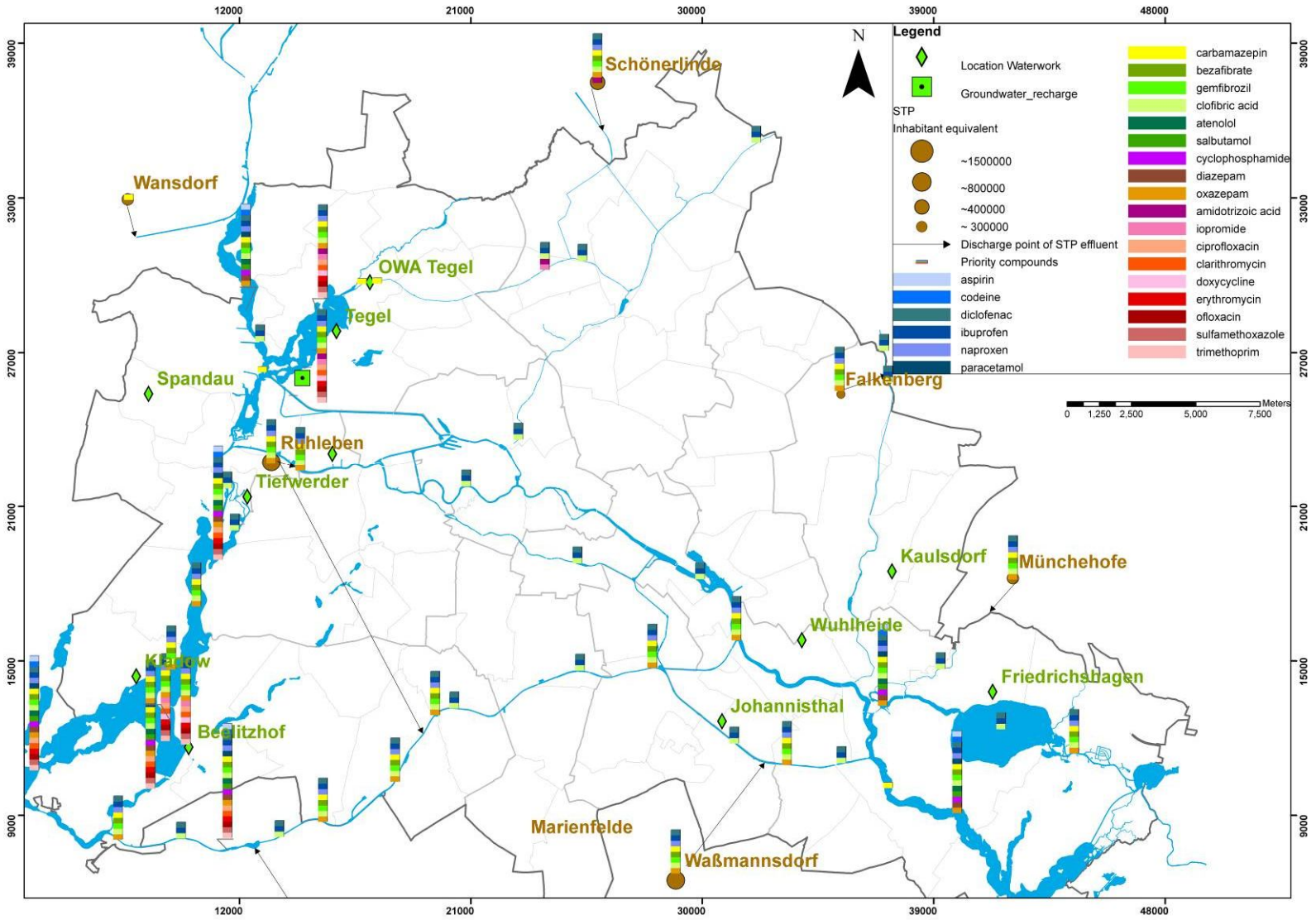


Figure 7: Sample Locations and analysed compounds in Berlin. (Out of 97 groundwater samples, only one on each bank filtration site is illustrated; data source see chapter 4.1.5)

4.2 Zurich

4.2.1 Location

Switzerland is divided in 26 cantons. The Canton Zurich is located in the Midlands of Switzerland, in the north of the country and has a population of 1.32 million people (2008). That makes it the most populous canton in Switzerland. Its area of 1792 km² is affected by the capital Zurich and its agglomeration. Approximately a quarter of the whole population of the Canton lives in the capital.

4.2.2 Hydrological Settings

Surface Water

The main watercourse in the Canton is the Lake Zürichsee, which is located in the south and divides the Canton in two parts. It has a water volume of 3364 million m³ on average and an average hydraulic residence time of 440 days (Q average = 89.2 $m^3 \cdot s^{-1}$). Furthermore Lake Greifensee in the Glatt Valley and Lake Pfäffikersee are located in the Canton. Their average water volumes are 148.5 million m³ and 57.1 million m³, respectively. Smaller watercourses, with a volume of more than 500,000 m³ are Lake Türlersee, Lake Hüttnersee, Lake Katzensee and Lake Lützelsee (AWEL, 1998).

The most important river is the Limmat, which leaves the Lake Zürichsee in the town Zurich and combines in the Canton Aargau with the River Reuss, Aare and later the Rhein (Q average = 96 m³·s-1 (1938-1996). The River Glatt, whose entire stream course is located in the Canton Zurich, is the outflow of Lake Greifensee and flows near Glattfelden with an average discharge of 8.56 $m^3 \cdot s^{-1}$ into the Rhein. Another mountain river is the River Töss. It has its source at the Zürcher Oberland and flows into the River Rhein, near Tössegg. At its last kilometres River Thur flows through the Canton Zurich, as well. River Sihl has its source in the Canton Schwyz, flows through the Valley Zürcher Sihltal until it joins the Limmat. In the southwest the River Reuss represents, in a small part, the border between the Canton Zurich and the Canton Aargau. Smaller rivers and streams which were tested on PhACs in the Canton Zurich and which also serve as recipient from STP are River Reppisch, Eulach, Furtbach, Aa, Jonen, Aabach, and Jona (see Figure 8).

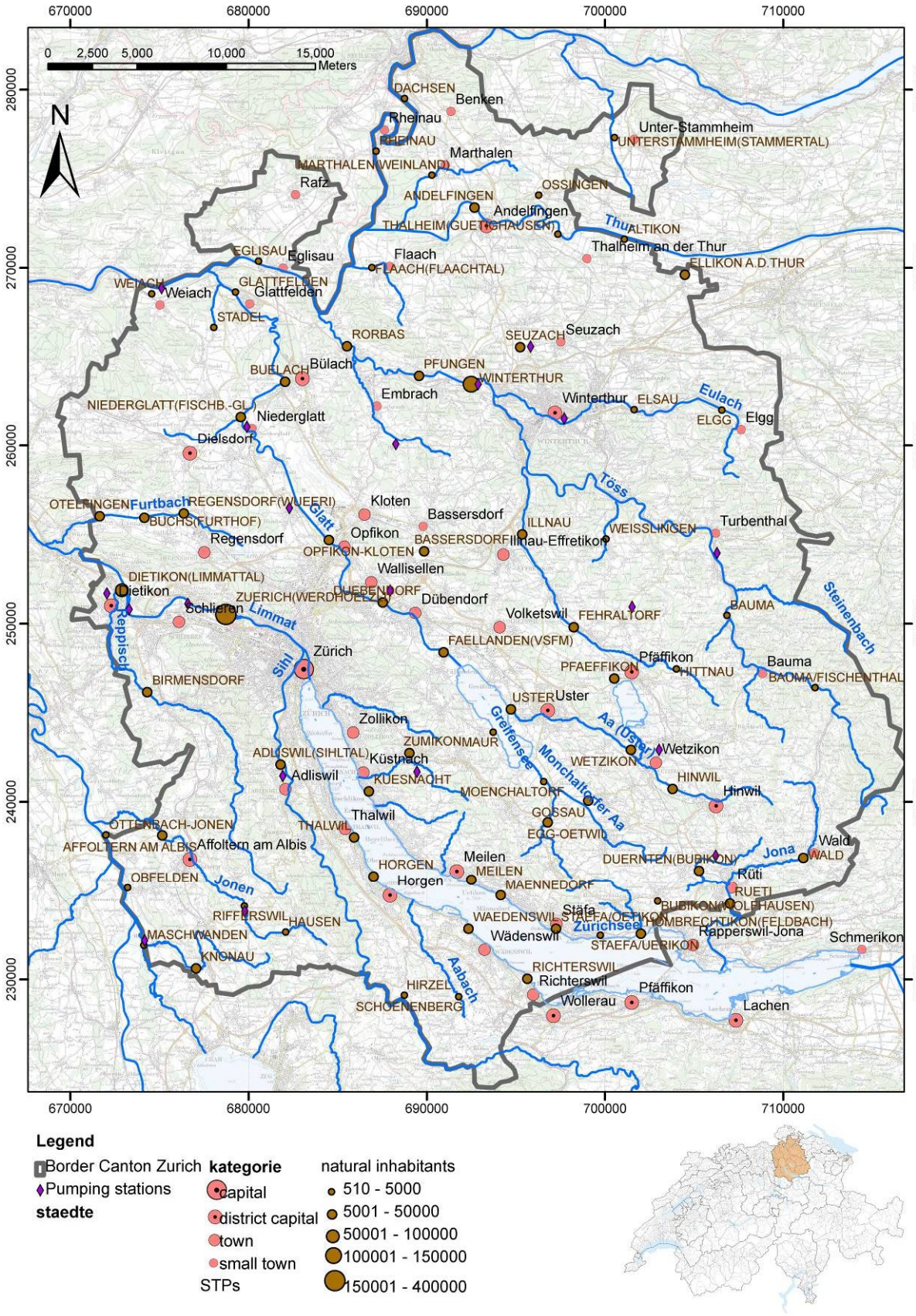


Figure 8: Map of the Canton Zurich with main water bodies (data provided by Eawag)

The average discharge volumes of main rivers located in the Canton Zurich are presented in Figure 9.

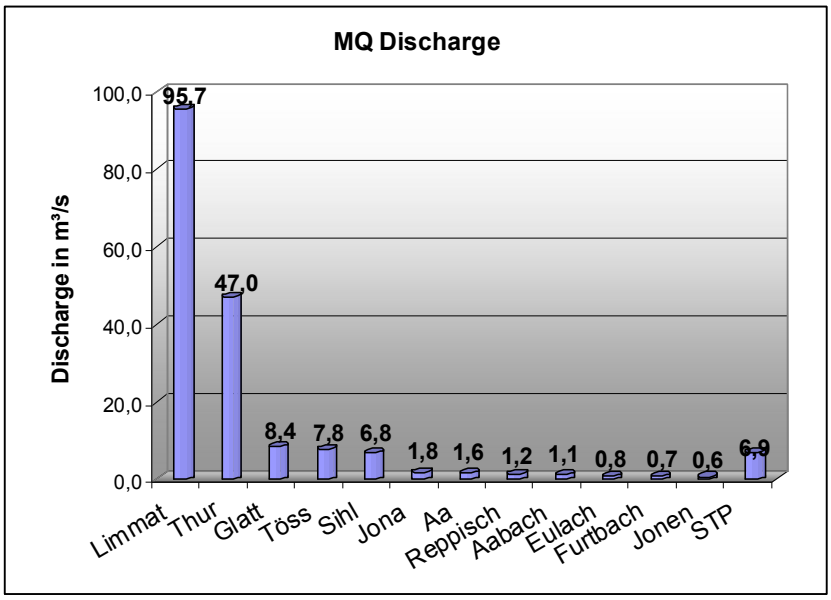


Figure 9: Discharge volumes of rivers located in the Canton Zurich. (Amt für Wasser, Energie und Luft 1998)

Compared to Berlin, higher water volumes flow through the Canton Zurich. However, there are also a number of rivers with low discharge volumes. Consequently, if high amounts of treated sewage water are discharged into the water bodies, the potential risk of contamination by PhACs increases (see chapter 5.2.2).

Precipitation

As the Canton Zurich is located in the Midlands of Switzerland, weather conditions are often affected by oceanic winds. In the Midlands, annual precipitation range from 1000 mm to 1500 mm. Annual average precipitation within the Canton Zurich is about 1201 mm (based on data belonging to 24 stations located in the Canton in the years from 1998 to 2007). Rainwater is distributed over the whole year, but more rainfall occurs in the summer months due to convective precipitation. Compared to Berlin (568mm), these average rain volumes are twice as high.

4.2.3 Drinking Water Supply

Drinking water for the 1.3 million inhabitants living in the Canton Zurich is extracted from 45 % of lake water, 15% of spring water and 40% of groundwater. On the contrary, in the regions Furttal, Glatttal, Knonaueramt, Limmattal, Obertal, Unterland, Weinland and Winterthur, all located in the Canton Zurich, the drinking water consists almost entirely of groundwater and spring water. In the remaining regions, it is again the treated lake water, which contributes to cover the drinking water needs, mainly extracted from Lake Zürichsee (see Figure 10).

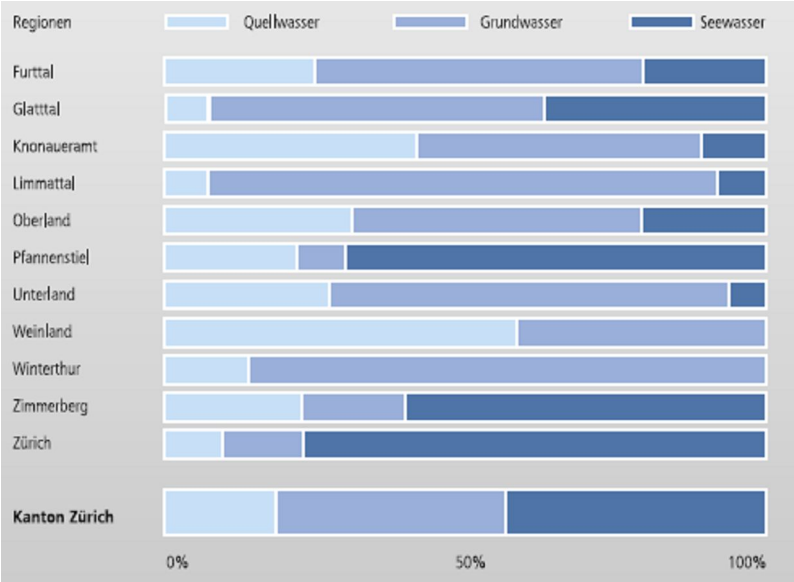


Figure 10: Proportion of spring water, groundwater and lake water in the drinking water production of the regions belonging to the Canton Zurich (Wasserqualitᵃt der Seen, Fliessgewässer und des Grundwassers im Kanton Zürich - Statusbericht 2006)

Around 250 million litres of drinking water are delivered every day to the population of the Canton Zurich. Since 1980, a decrease in the average daily water consumption in Switzerland and especially in the Canton Zurich and surrounding townships can be observed. Due to arrangements in creating lower water usage in industries and trades, along with the diminishing water losses and a propensity to save water in households, the average daily treated volume per inhabitant of 500 litres in 1981 in Switzerland was reduced to 404 litres in 2006, and thereof 305 litres in the Canton Zurich, respectively. In the last two decades drinking water consumption in households minimised of about 20 litres and average today is 160 litres per inhabitant a day, which is about 40 to 50 litres more than in Berlin.

4.2.4 Sewage Disposal

In 2007, approximately 240 million m³ of sewage water was purified in the 103 public STPs in the Canton Zurich. Additional to these public STPs, another 119 smaller private STPs are operated in the Canton Zurich. Only 72 out of the 103 public STPs dispose water of more than 500 inhabitants (see Figure 8).

One percent of the sewage water enters the rivers or streams after the mechanical treatment step but about two to four percent directly enter the natural water system by overflow channels during heavy rainfalls. About 99 % of the STPs consist of a mechanical and biological treatment and around 60 % have additionally phosphate precipitation, complete nitrification and denitrification (2008).

The biggest STP of the Canton Zurich, which treats around 70 to 90 million m³ sewage water every year, is the STP Werthölzli. This STP purifies sewage water originating from inhabitants living in the town Zurich or in one of the surrounding townships. It is located northward of Lake Zurich and discharges its water into the River Limmat after a four-stage treatment (mechanical, biological, precipitation and filtration). With a connected population of

around 400,000 people and a population equivalent of 450,000 people it is comparable to the Berlin STP Wansdorf (Abwasser_Broschuere, 2009).

The Canton's second biggest STP is located at the River Toss. With a little more than 100,000 connected people the STP Winterthur is ranked third, followed by STP Dübendorf, STP Kloten-Opfikon, STP Niederglatt, and STP Uster. Each of them has natural inhabitants of around 30,000 people.

A treatment volume of 240 million m³ per year in Switzerland can be regarded as equivalent to the volumes treated in the Berlin's six STPs. Seeing that in comparison to the number of inhabitants living in Switzerland, twice as much treated sewage waters arises in Switzerland than it does Berlin. This is caused due to the higher drinking water consumption in Switzerland and due to higher rain water amounts treated in the Swiss STPs.

By comparing Berlin's and the Canton Zurich's susceptibility to surface water contamination by PhACs, it is obvious that levels of concentrations have to be higher in Berlin's surface water than they are in the Canton Zurich (assuming that consumption rates are more or less the same). Firstly, concentrations of PhACs are more diluted in sewage, due to higher drinking water consumption and secondly, higher natural water volumes lead to a higher dilution of treated sewage. Furthermore, the loads of PhACs originating from households in the Canton Zurich do not concentrated in only a comparatively few number of STPs (cf. Berlins six STPs) and the discharge of treated sewage water does not only occur into four main rivers, as it can be found in Berlin, so that a better overall distribution of the loads of PhACs and therefore a lower concentrations of PhACs in the Canton Zurich are likely to occur.

4.2.5 Data Availability

Several studies about the behaviour and occurrence of PhACs in STPs, surface water and groundwater were investigated in Switzerland. For the evaluation of the occurrence of PhACs 14 monitoring campaigns were considered, mostly short term studies realised in the Canton Zurich in the time from 1996 to 2008 (see Figure 11).

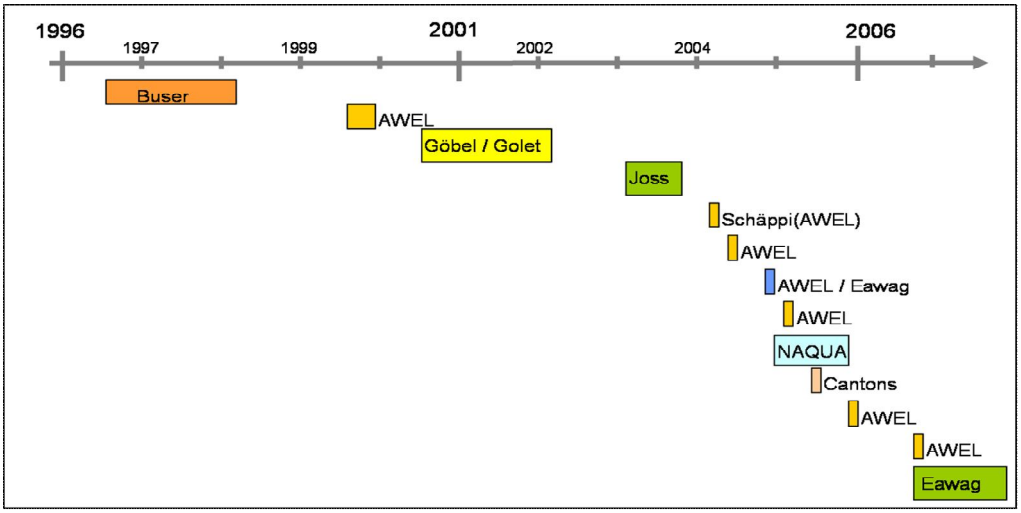


Figure 11: Timetable of monitoring campaigns in Zurich implemented in the study.

Projects considered in this study:

During the Project MicroPoll operated at the aquatic research institute Eawag from 2006 to 2008, an additional treatment step was installed at the STP Regensdorf. For the evaluation of the efficiency of further elimination of PhACs, when adding a further treatment step, samples from STP effluents and river waters upstream and downstream of the STP (before starting the additional treatment step) were taken and analysed for several PhACs (Hollender et al. 2009; Ort 2009). Data were provided by Eawag (Abbeglen, Escher et al. 2009)

In 1999, 2004, 2005 and 2006 the agency of waste, water, energy and air (AWEL) of the Canton Zurich initiated several studies about the determination of the contamination by PhACs of several rivers, in groundwater and STP effluents. Data were provided by Eawag (AWEL 2005; AWEL 2007) (http://www.wasser.zh.ch/internet/bd/awel/wa/de/mikroverunr.html.html).

In 2005 the Cantons St. Gallen, Appenzell Ausserhoden, Thurgau and Glarus evaluated the occurrence of hormones and PhACs in stream waters including Lake Zürichsee, River Jona and River Thur. All three sample locations are located on the border of the Canton Zurich and are therefore included in this study. Data were provided by Eawag (St.Gallen 2006).

Within the national monitoring net NAQUA a pilot study about the occurrence of PhACs in groundwater was carried out in 2004 to 2005. Thereby locations with potential contamination due to the infiltration of contaminated surface water were selected and measured for several compounds (Hanke, Singer et al. 2007). Data were provided by Eawag.

The institute Eawag in cooperation with the AWEL started a monitoring program in October 2004 to determine the impact of STP effluents in the Limmat valley. Within two month samples of the biggest STP Werthölzli, as well as Limmat water and groundwater of two WWs at the Limmat Valley were taken. Analysed compounds were radio contrast agents, antibiotics and corrosive agents (Blüm, McArdell et al. 2005).

Within an internship proceeded in January and February 2004, (Schäppi et al. 2004) analysed 10 bigger STPs, river water and raw water of the WW Lengg located around the Lake Zürichsee for several PhACs.

In 2003 the removal of seven pharmaceuticals and fragrances in the biological STP named Kloten-Opfikon was studied. Data were provided by Eawag (Göbel et al. 2005; Joss et al. 2005).

During two dissertations carried out at the Eawag in 2000 to 2003 some more extensive studies about the occurrence of antibiotics (macrolides and fluorochinole) in the Glatt Valley were undertaken. Therefore nine STPs, which discharge their water directly or indirectly in the river Glatt were analysed. Besides, river water from the

River Glatt at three different points was measured (Golet 2002a; Golet, Alder et al. 2002b; McArdell, Molnar et al. 2003; Göbel 2004a).

The last study, which was taken into account, was carried out by Buser from 1996 to 1998 (Buser, Poiger et al. 1998a; Buser et al. 1998b; Buser, Poiger et al. 1999). He analysed water samples of lakes, rivers and STPs of Switzerland and waters from the North Sea for the priority compounds ibuprofen, diclofenac and clofibric acid.

The following Table 14 lists the numbers of samples for each water compartment taken by the different monitoring campaigns.

Table 14: Number of samples and different locations of each monitoring campaign carried out in the Canton Zurich classified by water compartment.

CAMPAIGN	STP EFFLUENTS	SURFACE WATER	GROUNDWATER	PRIORITY COMPOUNDS
Buser	5	31	-	3
AWEL 1999	33	-	-	5
Göbel	38	18	-	2
Golet	43	15	-	2
Göbel / Golet	-	9	-	4
Joss	12	-	-	5
Schäppi	12	1	1	24
AWEL_03.2004	-	-	4	3
AWEL / Eawag	9	13	9	9
AWEL_11.2004	3	17	-	26
NAQUA	-	-	44	28
Cantons	-	3	-	16
AWEL_2005	5	-	-	21
AWEL	-	3		20
Eawag MicroPoll	25	27	-	23
Sum	185 (25)	137 (23)	58 (25)	

Compared to the available amount of data in Berlin, fewer samples were obtained for groundwater and surface water in the Canton Zurich. But in contrast a wider range of priority pharmaceuticals was analysed in the Canton Zurich. A list of sample methods, analytical methods and detection limits for each compound of each monitoring campaign is given in the annex.

4.2.6 Sample Locations

All together 84 different locations were sampled in the Canton Zurich, 26 groundwater sample points, 33 surface water points and STP effluents of 25 STPs.

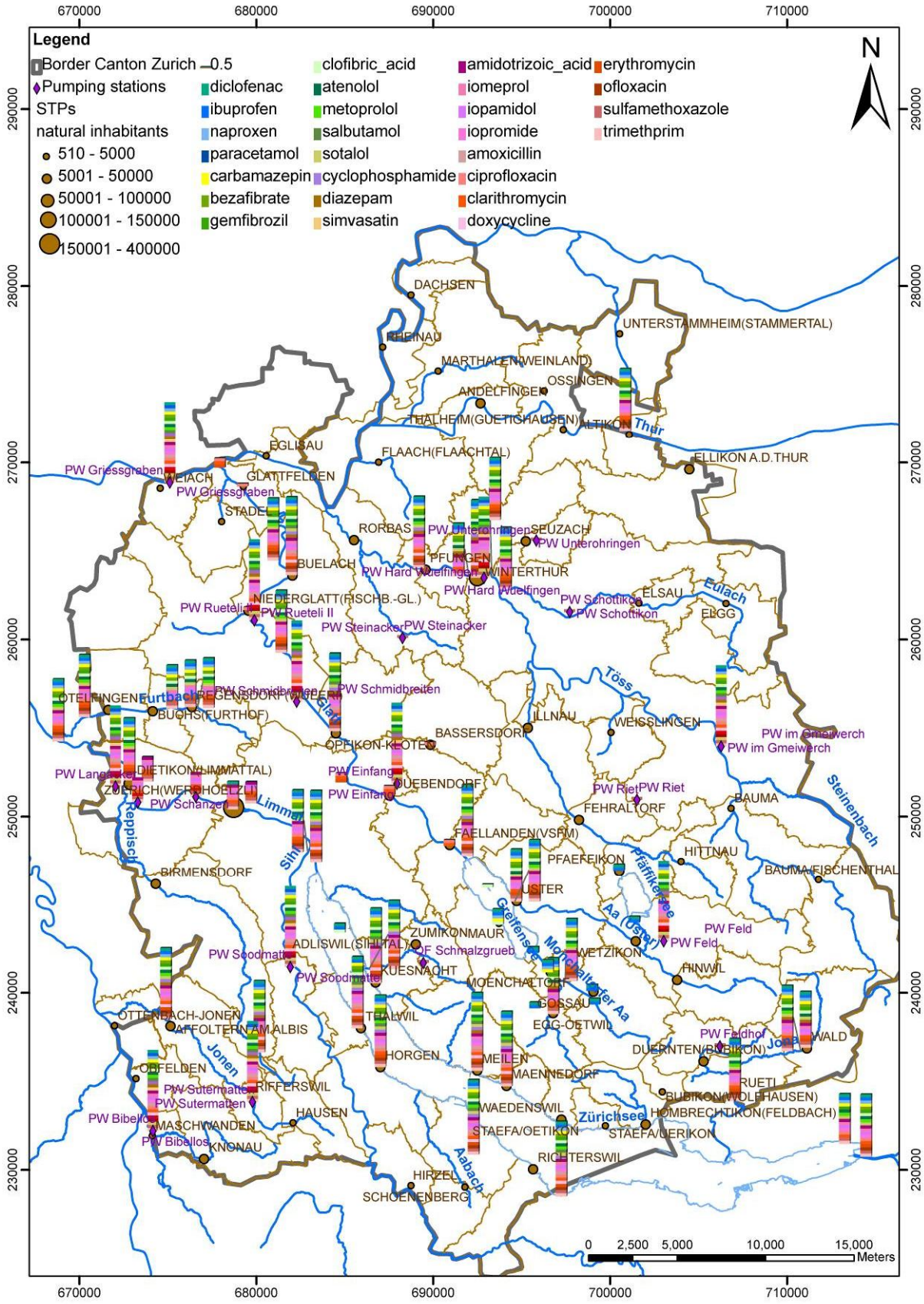


Figure 12: Sample Locations and analysed compounds in the Canton Zurich (six groundwater sample locations are not illustrated because no data about the locations of the water work were available; data source see chapter 4.2.5)

Chapter 5

Calculation of the Proportion of treated Sewage in Surface Water

As previously mentioned, the main path of human pharmaceuticals entering the aquatic environment is the discharge of treated sewage into receiving water bodies. Surface water sites with a high input of STP effluents and low dilution of the effluents by the natural water flow are therefore susceptible to a high contamination of organic micropollutants and constitute a potential risk for the aquatic environment.

The purpose of the study was to obtain a benchmark of concentrations of PhACs in different water compartments. Especially surface water concentrations were examined based on studies in Berlin and the Canton Zurich. A differentiation of the Berlin data was made according to the proportion of treated sewage in surface water in order to allow for further classification of surface waters in the benchmarking. This chapter describes how proportions of treated sewage at different surface water locations in Berlin were calculated. The information was used to study the correlation of measured concentrations of PhACs versus the rate of treated sewage at the Berlin sample points. Based on the correlations the classification of surface waters was carried out (see chapter 7). Due to a lack of detailed data (especially on water flows at specific times), a comparable calculation for the Canton Zurich could not be carried out.

5.1 Model Description

The proportions of treated sewage in surface water samples were estimated via two steps. The first step was the calculation of the discharge in specific river sections. That was necessary since simultaneous flow measurements were not available for all sample points during the sample time from June 2000 to December 2004. An average monthly discharge value for each of the 26 river sections (Q_{Ri}) was calculated via mass balance of incoming and outgoing water volumes. The calculations were based on a substance flow model available from former studies (Kraume and Broll 2007; Knodel 2008)

$$Q_{Ri} = Q_{Ri-1} + Q_{STP} + Q_P - Q_{WW} \qquad \text{Eq. 5}$$

Q_{ri-1} is the incoming flow of water from the river section located upstream of the river section Q_{ri} of interest [$m^3 \cdot d^{-1}$]

Q_{STP} is the incoming flow of STP effluent entering the river section [$m^3 \cdot d^{-1}$]

Q_P is the incoming flow of rainwater entering the river section [$m^3 \cdot d^{-1}$]

Q_{WW} is the outgoing flow of water extracted by the WWs due to bank filtration, and therefore removed from the river section [$m^3 \cdot d^{-1}$]

Water which enters or leaves the river section via exchange with groundwater, evaporation, combined sewer overflows, and water inflow or extraction from industry was neglected.

In a second step the proportion of treated sewage water (P_{Ri}) at the specific river sections in % was estimated with following equation:

$$P_{Ri} = \frac{1 \times Q_{STP} + p_{Ri-1} \times Q_{Ri-1}}{Q_{Ri}} \times 100 \qquad \text{Eq. 6}$$

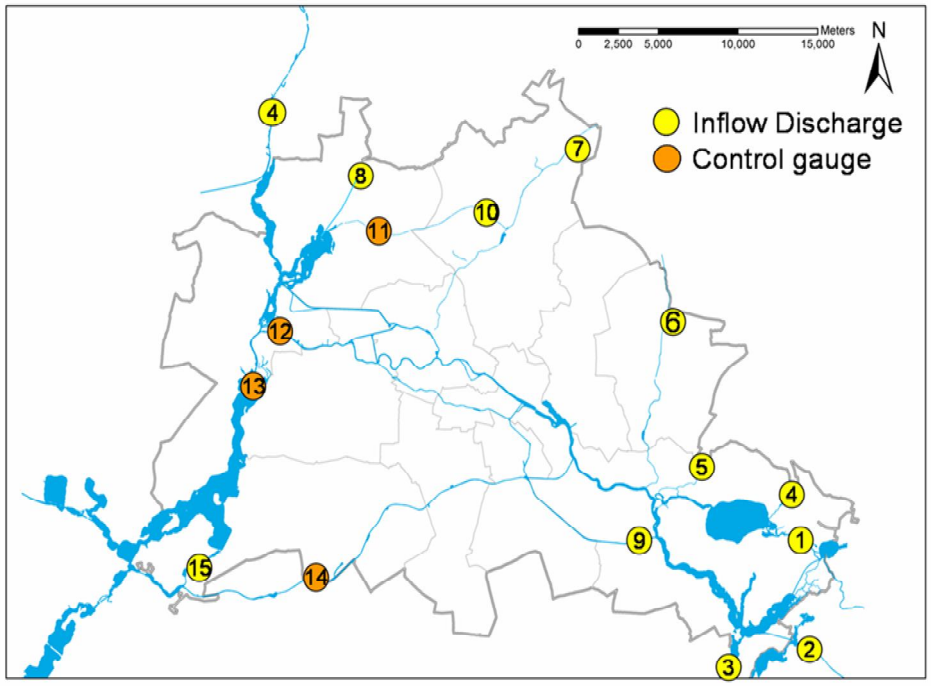
$_{pRi-1}$ *is the proportion of treated sewage water in the river section located upstream of the sample point ($100/P_{Ri-1}$) [-]*

Both calculation steps were implemented in the open source software R (x).

5.2 Input and Reference Data

a) Average monthly river discharges

Discharge values from gauges of the Spree, the Dahme, the Oder-Spree-Canal, the Havel, the Wuhle, the Panke, the Erpe, the Fredersdorfer Fließ and the Tegeler Fließ were available from the Berlin Senate of Environment. They were used as input data to the model either as inflow volumes to the water system (see Figure 13) or in case of flow-splitting to define the resulting flow proportions (gauge 9, 10, 15) Furthermore, discharge values of the Teltowkanal, the Spree, the Nordgraben and the Havel were available. These values served as reference data for validation of the calculated flows at four control points.



1)Rahnsdorf
2)Wernsdorf
3)Neue Mühle
4)Hegemeisterweg
5)Ravensteiner Mühle
6)Hornsfelder Brücke
7)Röntgental
8)St. Joseph Steg
9)Grünau
10)Pasewalker Brücke
11)Eisenbahnbrücke
12)Sophienwerder
13)Tiefwerder
14)Lichterfelde
15)Alsenbrücke

Figure 13: Location of river gauges used as boundary condition and reference points for the model

b) Discharge volumes of STP effluents

Data of average monthly discharge volumes Q_{STP} in $m^3 \cdot month^{1-}$ of all STPs in Berlin were available from BWB.

c) Abstraction of surface water by bank filtration

The water volumes which were extracted from surface water due to bank filtration were estimated via the ratio of bank filtration of each WW (cf. Table 16) multiplied by the respective monthly volume of extracted raw water. Data of raw water extraction were provided by BWB.

Table 15: Bank filtration ratios of Berlin's WWs without gw enrichment as used for model input

Waterwork	Proportion of bank filtration in %[2]
Beelitzhof	67
Friedrichshagen	83[1]
Kaulsdorf	0
Kladow	68
Spandau	30
Stolpe	14
Tegel	80
Tiefwerder	61
Wuhlheide	29
Johannisthal	62
Jungfernheide	52

[1] SenSUT 1992 Bank filtration and artificial groundwater enrichment

[2] Schuhmacher & Skripalle 1999 (Data generated by the model BIBER)

d) Rain water runoff

Rain water volumes, which enter 19 river sections via the separate sewer system (see Figure 14) have been calculated based on average monthly precipitation heights (P) from 1996 to 2005, the expanse (A) of connected surface types such as streets, sealed building area, undeveloped sealed area and the average runoff coefficient (Ψ) of each surface type. Runoff coefficients and surface areas were taken from (SenSUT 2001). Information about precipitation was provided by BWB.

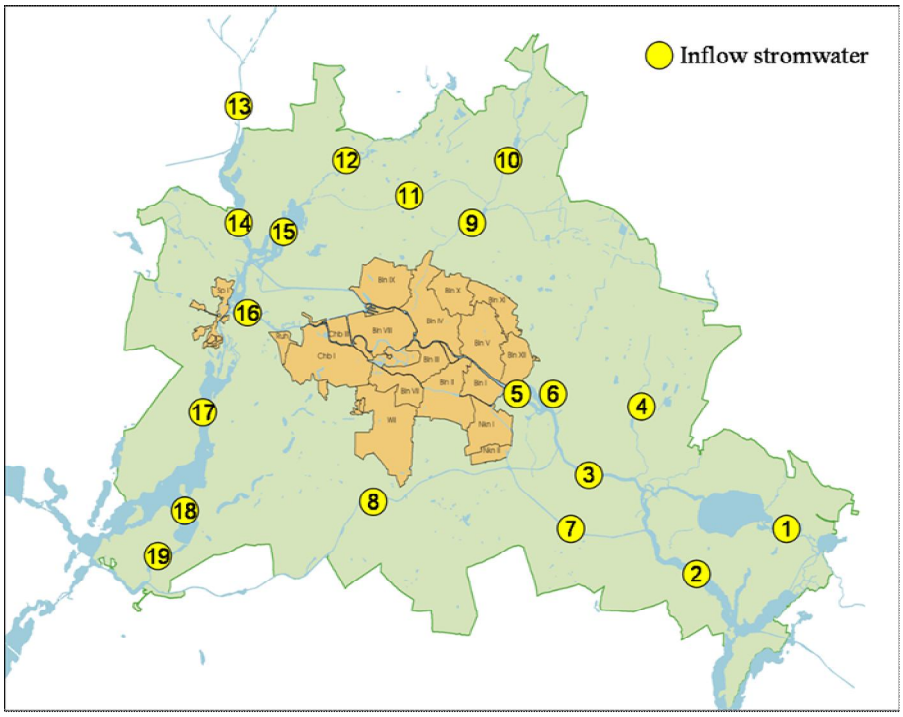


Figure 14: Schematic presentation of storm water inflow points (modified from Riechel 2009)

The average monthly storm water runoff (S_{ri}) was calculated for each river section using the following equation:

$$S_{ri}[m^3/a] = A \times \psi \times P \qquad \text{Eq. 7}$$

A area of surface type i in m²

Ψ runoff coefficient of surface type i [-]

P average precipitation in m·month^{-1}

5.3 Validation of Flow Calculations

5.3.1 Discharge Values

Monthly discharge values of 26 different river sections for the time from 2000-2004 have been calculated.

For the validation of the model results, calculated discharges were compared with measurements at the four reference points. Results are shown in Figure 15.

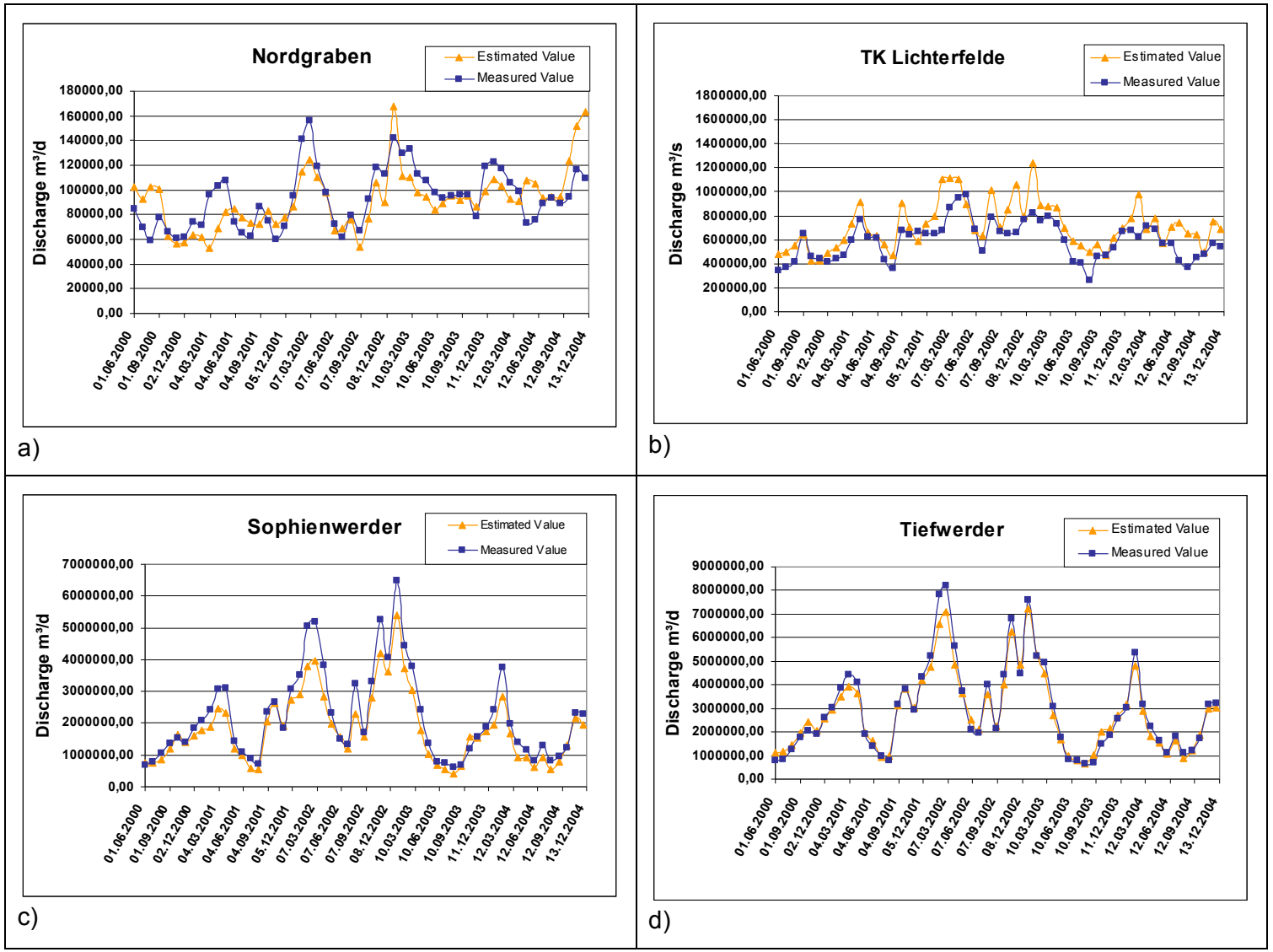


Figure 15: Comparison of calculated versus measured monthly discharges of the Berlin water system at four reference points

Figure 15 shows that the estimated discharge values at the Gauge Sophienwerder (c) located in the River Spree and at the Gauge Tiefwerder (d) located in the River Havel agree well with the measured discharges. However, in some time periods (especially in spring) the calculation leads to underestimates. This may be caused due to neglecting of groundwater inflow and overflows of the combined sewer system in the model.

Higher discrepancies of measured versus estimated discharges values occur at the River Nordgraben (a) and the Teltowkanal (b). This can be explained by uncertainties in the hydrological situation of these streams which could not be gathered by the monthly flow data considered in this study. Overall, the estimated flow values show sufficient accuracy to be used for the calculation of the proportions of treated sewage in the river sections.

5.4 Proportions of treated Sewage

The following Figures 16 and 17 show the calculated minimum, maximum and average proportions of treated sewage in Berlin's river network for the period from June 2000 to December 2004. Due to the varying discharge points of the STP Ruhleben in the summer (Teltowkanal) and the winter (Spree) two scenarios are illustrated. The proportions shown for the River Wuhle consider the time from June 2000 to February 2003 only, because after the 25th of February 2003 the STP Falkenberg was closed and the sewage was redistributed to the STP Waßmannsdorf and the STP Schönerlinde.

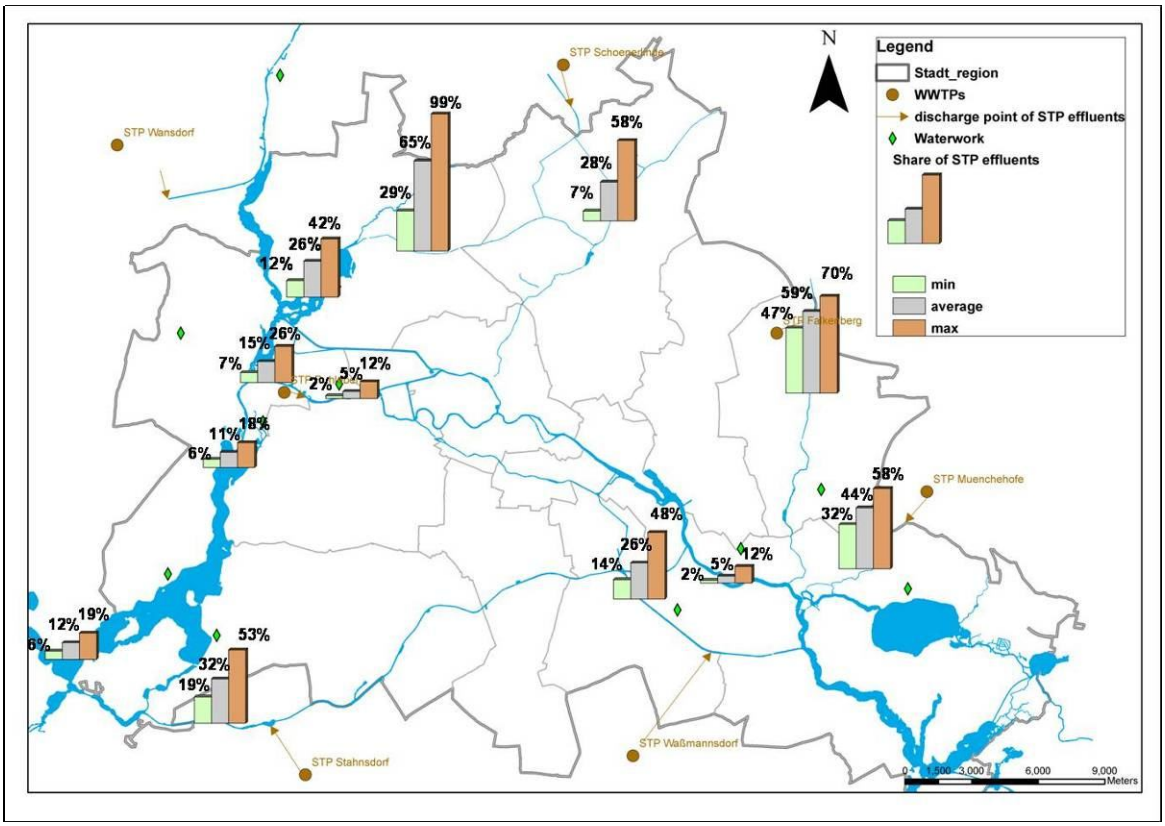


Figure 16: Minimum, maximum and average proportion of treated sewage in different sections of the Berlin river system (winter scenario)

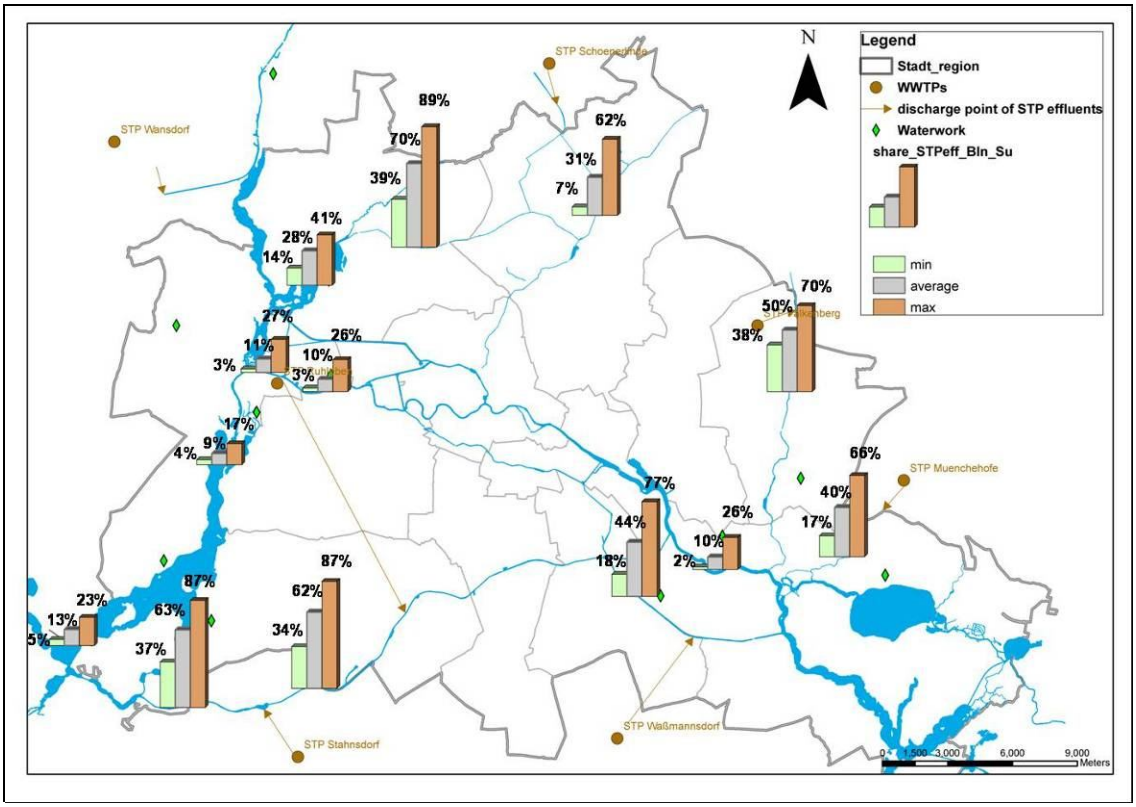


Figure 17: Minimum, maximum and average proportion of treated sewage in different sections of the Berlin river system (summer scenario)

Highest proportions of treated sewage of up to 99% and 87%, respectively were estimated in the Nordgraben, located in the North of Berlin and the Teltowkanal, located in the South. The Teltowkanal is influenced by the effluents of two STPs in the winter and three STPs in the summer. The Nordgraben receives the effluents of the STP Schönerlinde and has a rather low natural discharge value of ~1 m³s (1999-2004, gauge Neu Tegel) on average.

Furthermore, tributaries of the Spree such as the River Erpe and Wuhle carried high loads of treated sewage, whereas since 2003, after the closure of the STP Falkenberg, the River Wuhle is free of treated sewage. The main water courses Spree and Havel show average proportions of treated sewage between 9 % and 15 %.

These results are included in the following chapters, where detected concentrations of priority PhACs at different river sections are correlated with the proportion of treated sewage.

Actually, pharmaceuticals mainly originate from households and hospitals, whereas sewage from industry usually does not contain pharmaceuticals. Consequently, when estimating pharmaceutical concentrations, sewage from industry should not be taken into account. In this study a distinction between sewage from household, hospitals and industry could not be done due to missing data on industry shares. However, since there are only few industry sites located in Berlin, which are more or less equally distributed over the city that does not impact the correlation between the proportion of treated sewage and the measured concentrations of priority PhACs. When comparing the correlations in chapter 6.1.2 with other sites this has to be taken into account.

Chapter 6
Occurrence of priority Pharmaceuticals

In this chapter the levels of the detected concentrations of priority PhACs in Berlin and Switzerland in the different water compartments are illustrated via box plot diagrams. The box plots demonstrate maximum and minimum concentration, median concentration and 10^{th}, 25^{th}, 75^{th}, and 90^{th} percentiles (see Figure 18). Furthermore correlations between detected surface water concentrations of different drugs and the estimated proportions of treated sewage in the samples are demonstrated.

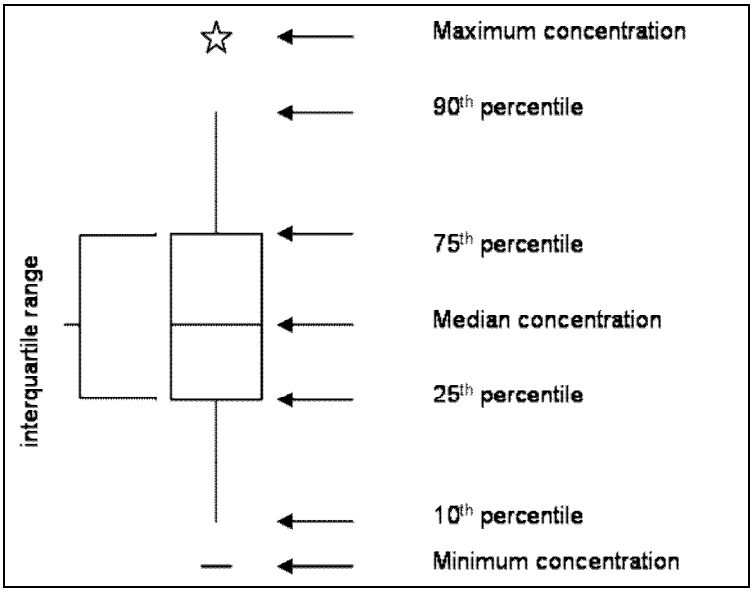


Figure 18: Box plot and its display

6.1 Berlin

Table 16 shows all priority compounds which were measured in Berlin either in STP effluents, in surface water or in groundwater. Additionally the numbers of samples for each priority PhAC with concentrations above the detection limit are given.

Table 16: Numbers of samples of measured priority PhACs in the different water compartments in Berlin and the numbers of samples with concentrations above the detection limit.

Compound	Number of Samples of **STP effluents**	Number of Samples of STP effluents with Concentrations **>LOD**	Number of Samples of **Surface Water**	Number of Samples of Surface Water with Concentrations **> LOD**	Number of Samples of **Groundwater**	Number of Samples of Groundwater with Concentrations **> LOD**
Acetyl salicylic acid	n.m.	n.m.	117	n.d.	n.m	n.m.
Amidotrizoic acid	1	1	6	6	7	7
Atenolol	n.m.	n.m.	117	n.d.	n.m.	n.m.
Bezafibrate	28	26	305	207	695	23
Carbamazepine	161	161	464	462	1008	764
Ciprofloxacin	n.m.	n.m.	10+?	n.d.	?	n.d.
Clarithromycin	n.m.	n.m.	48	48	379	33
Clofibric acid	35	35	373	345	695	471
Codeine	n.m.	n.m.	117	n.d.	n.m.	n.m.
Cyclophosphamide	n.m.	n.m.	117	n.d.	n.m.	n.m.
Diazepam	n.m.	n.m.	117	n.d.	n.m.	n.m.
Diclofenac	35	35	373	334	696	436
Doxycycline	n.m.	n.m.	?	n.d.	?	n.d.
Erythromycin	n.m.	n.m.	48	48	375	212
Gemfibrozil	33	24	279	96	?(NASRI)	n.d.
Ibuprofen	35	30	305	260	?	n.d.
Iopromide	1	1	71	71	254	109
Naproxen	33	33	279	180	?(NASRI)	n.d.
Ofloxacin	n.m.	n.m.	10	n.d.	n.m.	n.m.
Oxazepam	33	19	279	54	?(NASRI)	n.d.
Paracetamol	n.m.	n.m.	117	n.d.	n.m.	n.m.
Salbutamol	n.m.	n.m.	117	n.d.	n.m.	n.m.
Sulfamethoxazole	2	2	47	47	376	284
Trimethoprim	n.m.	n.m.	48	48	379	4

n.d. not detected

n.m. not measured

?(NASRI) compound was measured but no further information about numbers of samples were available

6.1.1 Sewage Treatment Plant Effluents

The occurrence of priority PhACs in STP effluents were studied during the dissertations of Reddersen (2004) and Zühlke (2004), whereby Reddersen analysed more priority PhACs than Zühlke, who measured only one for this study relevant compound, the antiepileptic drug carbamazepine. Additionally a study carried out by (Heberer, Schmidt-Bäumler et al. 1998) includes the sampling of two STPs located in Berlin.

From the nine different priority PhACs measured in Berlin's STP effluents all have been detected.

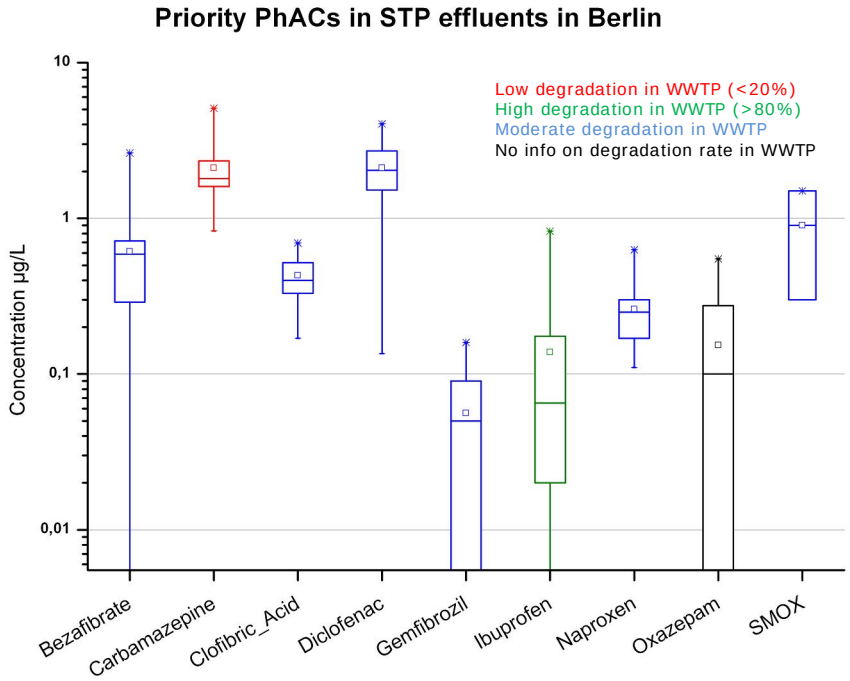


Figure 19: Measured priority PhACs in Berlin's STP effluents (data source see chapter 4.1)

Highest concentrations in STP effluents in Berlin have been detected for the analgesic diclofenac and the antiepileptic drug carbamazepine. Both drugs were detected in all STP effluent samples considered in this study. Their median concentrations are about 2 $\mu g \cdot L^{-1}$and 1.8 $\mu g \cdot L^{-1}$, respectively. Carbamazepine and diclofenac are sold in quantities of around 85 t in Germany in 2001, which is not the highest reported consumption rate in Germany, but their moderate (diclofenac) and low (carbamazepine) elimination rates during sewage treatment lead to high concentrations in the STP effluents. In contrast ibuprofen, which is sold in more than four-times higher amounts than diclofenac and carbamazepine, was detected in rather low concentrations (median of 65 $ng \cdot L^{-1}$). That's because it is very good removed during sewage treatment.

The lipid lowering drugs bezafibrate and the metabolite clofibric acid are detectable in all STP effluent samples in concentrations up to 2.6 $\mu g \cdot L^{-1}$. Their median concentrations are 0.59 $\mu g \cdot L^{-1}$ and 0.4 $\mu g \cdot L^{-1}$, respectively. In contrast the detected concentrations of gemfibrozil, the other lipid lowering drug, are clearly lower than those of bezafibrate and clofibric acid (maximum concentration of 0.16 $\mu g \cdot L^{-1}$. Bezafibrate is the most sold drug out of these three (33 t per year in 2001), but has a rather good elimination rate, whereas clofibric acid in regards to its low consumption is not that good eliminated during sewage treatment.

The analgesic naproxen has been detected in all samples with a median concentration of 0.25 $\mu g \cdot L^{-1}$. The sedative drug oxazepam was measured in more than the half of the samples with concentrations up to 550 $ng \cdot L^{1-}$.

Analyses of the antibiotic sulfamethoxazole was conducted in just one study via grab samples of two STPs of Berlin, so that insufficiently data are available to give reliable statement about the occurrence of sulfamethoxazole in STP effluents of Berlin.

6.1.2 Surface water

Surface water samples in Berlin were taken frequently during the NASRI project of Lake Tegel, Lake Wannsee and the River Nordgraben as well as from Reddersen, who sampled 15 different locations distributed over the whole city area. During another study carried out by Adam in 2003 to 2004 surface water locations involving incoming and out flowing water courses of Berlin were analysed.

In the consideration of contamination of surface water by PhACs only surface waters which are influenced by the discharge of STP were taken into account, that means that locations located upstream of a STP, where no PhACs were detectable are not considered in the following statistic.

All together 14 priority PhACs, out of 24 measured, were detected in Berlin's surface waters. The 10 drugs which were not detected are the analgesics acetyl salicylic acid, codeine, paracetamol, the beta blocker atenolol, the bronchodilator salbutamol, the tranquilizer diazepam, the cytostatic cyclophosphamide, and the antibiotics ciprofloxacin, doxycycline, and ofloxacin.

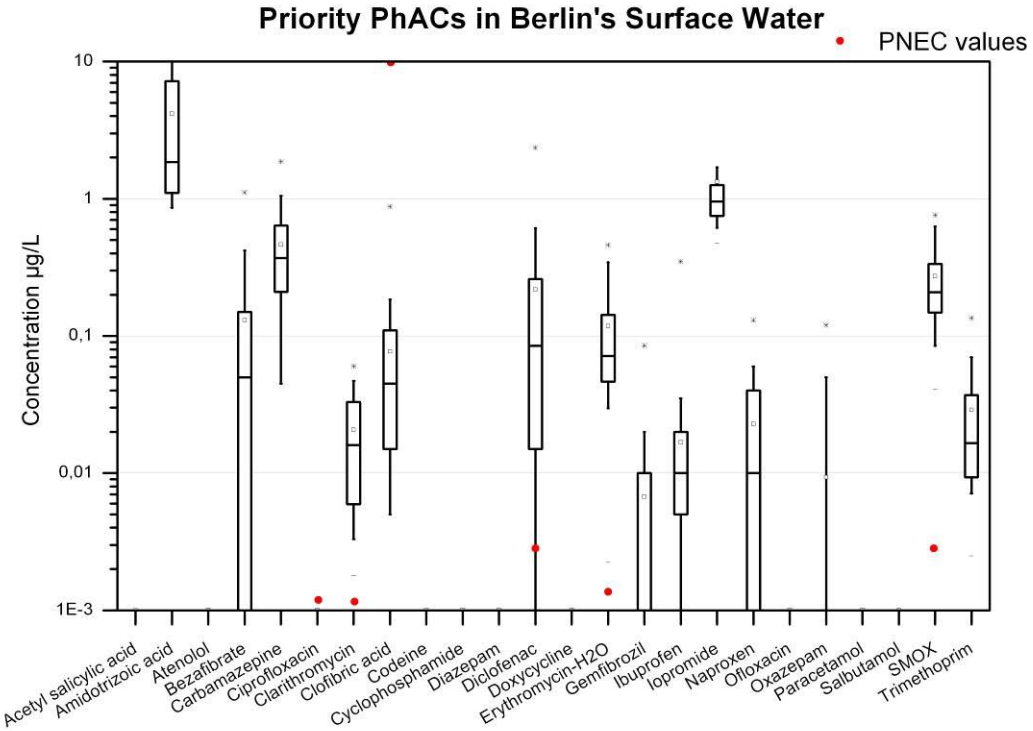


Figure 20: Measured priority PhACs in Berlin's surface water (data source chapter 4.1). PNEC-values (red dots) taken from (Adams, Wang et al. 2002) and (LANUV 2007), cf. chapter 3.5.

A similar situation as in STP effluents is visible for the concentrations of diclofenac and carbamazepine in surface water samples. Both drugs were found in highest concentrations

(diclofenac 2.36 µg·L^{-1} and carbamazepine 1.87 µg·L^{-1}) in the Teltowkanal which contains high loads of treated sewage water (cf. chapter 5). A look at the median concentration of both drugs shows that the concentration ranges are rather high which is caused by considering samples which contain either high or low proportions of treated sewage water. Compared to median concentrations of STP effluents, surface water concentration of diclofenac and carbamazepine are approximately ten times lower.

Besides those two, the analysed radio contrast agents iopromide was detectable in a high median concentration of 0.95 µg·L^{-1}. As mentioned in chapter 3.2.1 usually radio contrast agents are detected in highest concentration due to their high application amount and due to its non degradability during sewage treatment and its high water solubility.

The antibiotic sulfamethoxazole, for which only a few data of STP effluents samples were available, was detected in all 47 surface water samples. Out of the 21 analysed priority PhACs its median concentration of 0.21 µg·L^{-1} in surface water is the third highest.

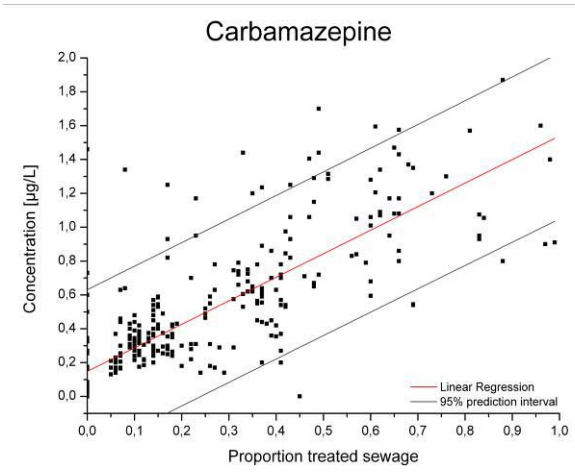
Furthermore the antibiotics clarithromycin, erythromycin and trimethoprim were detected in all 48 surface water samples with median concentrations of 16 ng·L^{-1}, 72 ng·L^{-1} and 17 ng·L^{-1}, respectively.

Bezafibrate, naproxen, and ibuprofen were found in median concentration of 50 ng·L^{-1}, 10 ng·L^{-1}, and 10 ng·L^{-1}. Gemfibrozil and oxazepam have been detected only in a few samples.

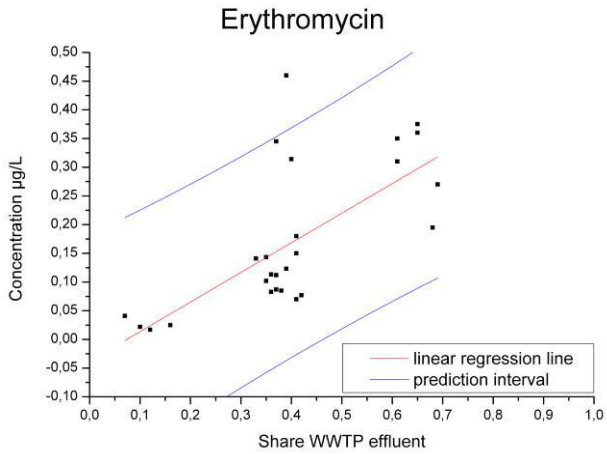
The concentrations of the analgesic diclofenac and the antibiotics clarithromycin, sulfamethoxazole, and erythromycin often exceed the PNEC. These compounds may have toxicological effects on aquatic organisms.

Correlation – Proportion of treated sewage water vs. priority PhAC concentration

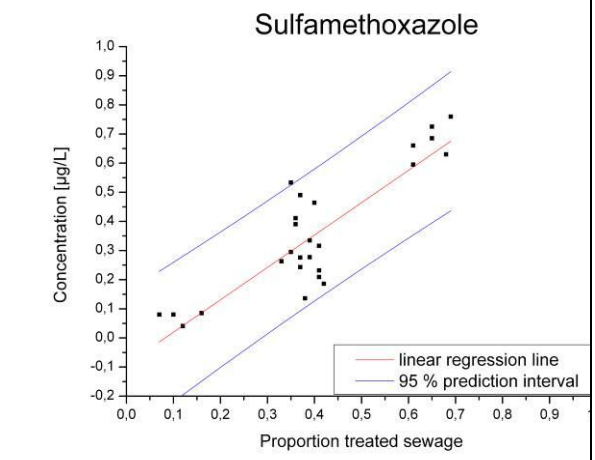
In this section the correlations of estimated proportions of treated sewage via the detected concentrations of some PhACs at different river sections in Berlin are demonstrated. Due to the fact, that the variables are not equally distributed a rank correlation according to Spearman was conducted. Generally it is to say that some compound concentrations correlate significantly (checking with significance test) with the estimated proportion of treated sewage and some do not. Thus a clear disjunction of all priority PhACs and their concentration ranges dependent on low, medium and high proportion of treated sewage could not be done. Examples for compounds with a significant correlation [a) Spearman correlation coefficient >0.75], a moderate correlation [b) Spearman correlation coefficient 0.45 > x< 0.75], and a low correlation [c) Spearman correlation coefficient < 0.45] are given below.



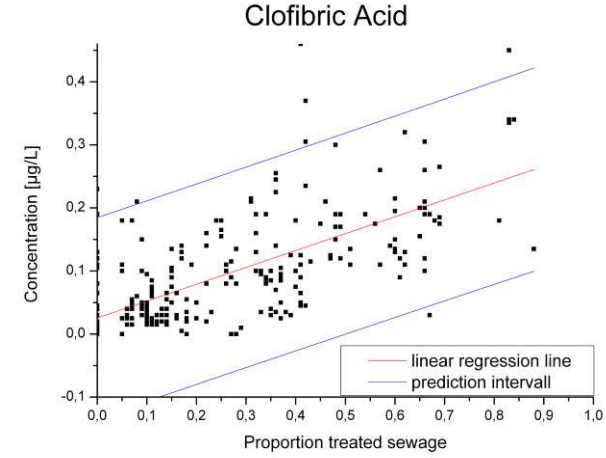
a) Spearman correlation coefficient 0.837



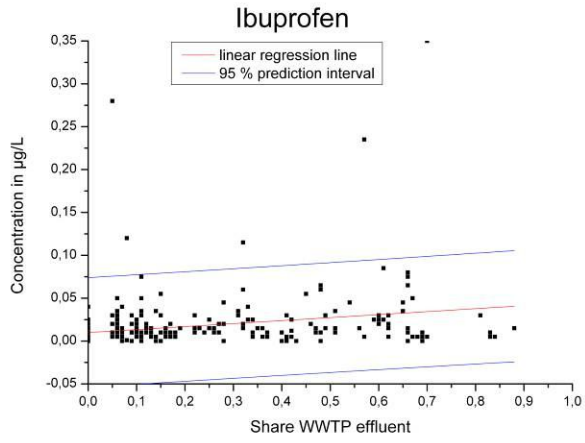
Spearman correlation coefficient 0.864



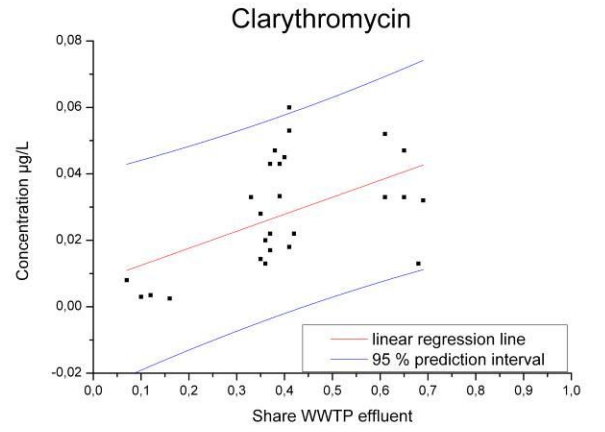
b) Spearman correlation coefficient 0.605



Spearman correlation coefficient 0.749



c) Spearman correlation coefficient 0.422



Spearman correlation coefficient 0.531

Figure 21 Correlation of concentrations of priority PhACs in surface water against proportion of treated sewage (data source see chapter 4.1)

For the overall benchmarking in chapter 7 we decided to show levels of concentration of priority PhACs in surface water with either a proportion of treated sewage above 30% or less than 30 %. Usually, and it can also be observed in the data above, are more sample locations available for which the proportion of sewage is under 30%. The classification was made in order to show water practitioners who are able to differentiate between a low and a high proportion of sewage in receiving surface waters, which concentrations of priority PhACs can be expected.

6.1.3 Groundwater

All together 1096 groundwater samples, belonging mainly to the NASRI project, were considered in this study. Most samples were taken at the banks of Lake Tegel and Lake Wannsee. About 65 samples were taken at the WW Stolpe, which is located in the North of Berlin. The results take into account different ratios of bank filtrates (from <20% to > 90%).

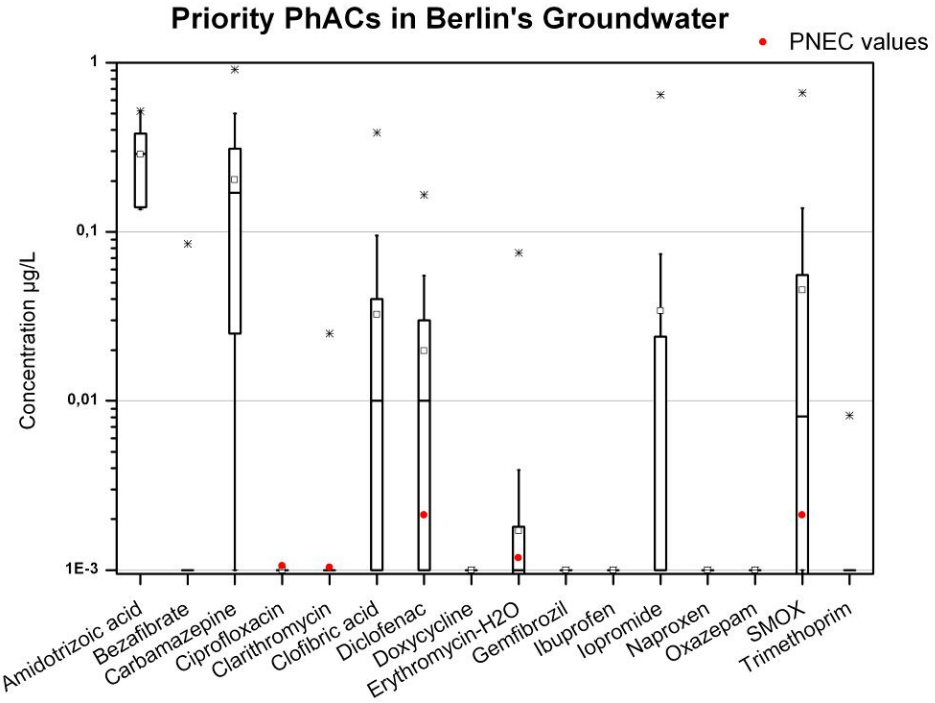


Figure 22: Measured priority PhACs in Berlin's groundwater (data source chapter 4.1). PNEC-values (red dots) taken from (Adams, Wang et al. 2002) and (LANUV 2007), cf. chapter 3.5.

The most persistent analysed priority PhACs which could be detected in the groundwater in Berlin are the antiepileptic drug carbamazepine, the metabolite of a lipid lowering drug clofibric acid, the analgesic diclofenac, the radio contrast agents iopromide and amidotrizoic acid, and the antibiotic drug sulfamethoxazole. Only in single measurements the lipid lowering drug bezafibrate and the antibiotics clarithromycin, erythromycin and trimethoprim were detectable. Most of the detections were positive at monitoring wells which are located close to the Lake Wannsee and Lake Tegel. Besides sulfamethoxazole, no compounds could be detected in bank filtrate (≥ 1 month) and the abstraction wells (Heberer et al. 2008)

6.2 Zurich

Following table show all priority compounds which were measured in Zurich in the different water compartments STP effluents, surface water or groundwater. Furthermore, are given the numbers of samples for each priority PhAC with concentrations above the detection limit.

Table 17: Numbers of samples of measured priority PhACs in the different water compartments in the Canton Zurich and the numbers of samples with concentrations above the detection limit (data source see chapter 4.2)

Compound	Number of Samples of **STP effluents**	Number of Samples of STP effluents with Concentrations **>LOD**	Number of Samples of **Surface Water**	Number of Samples of Surface Water with Concentrations **> LOD**	Number of Samples of **Groundwater**	Number of Samples of Groundwater with Concentrations **> LOD**
Amidotrizoic acid	39	17	40	14	36	15
Amoxicillin	25	3	n.m	n.m	23	n.d.
Atenolol	34	34	34	25	23	n.d.
Bezafibrate	34	23	34	4	23	n.d.
Carbamazepine	78	78	34	27	23	2
Ciprofloxacin	67	57	48	22	22	n.d.
Clarithromycin	85	84	75	63	32	n.d.
Clofibric acid	53	25	31	n.d.	23	n.d.
Cyclophosphamide	15	n.d.	6	n.d.	23	n.d.
Diazepam	7	n.d.	8	n.d.	22	n.d.
Diclofenac	78	78	68	51	23	n.d.
Doxycycline	13	n.d.	6	n.d.	n.m.	n.m.
Erythromycin	79	53	63	27	31	n.d.
Gemfibrozil	30	4	27	n.d.	23	n.d.
Ibuprofen	72	51	44	11	23	n.d.
Iomeprol	43	7	45	3	32	n.d.
Iopamidol	44	27	44	13	36	4
Iopromide	55	42	46	23	32	n.d.
Metoprolol	25	23	25	13	23	n.d.
Naproxen	61	58	33	15	22	n.d.
Ofloxacin	25	7	20	0	23	n.d.
Salbutamol	15	n.d.	n.m	n.m	23	n.d.
Simvastatin ß-hydroxy-acid	n.m.	n.m.	n.m	n.m	22	n.d.
Sotalol	35	35	34	26	23	n.d.
Sulfamethoxazole	47	45	47	19	58	27
Trimethoprim	44	42	47	22	32	0

n.m. not measured

n.d. not detected

6.2.1 Sewage Treatment Plant Effluents

During October 1997 to September 2008 a number of 24 STPs were tested for several PhACs in the Canton Zurich. Aside from four of the tested STP, all receive sewage water from more than 10000 inhabitants. Out of the 25 priority PhACs analysed in STP effluents the tranquilizer diazepam, the bronchodilator salbutamol, and the cytostatic drug cyclophosphamide were not detected.

Following Figure 24 presents the concentration ranges of the priority compounds detected in STP effluents in the Canton Zurich.

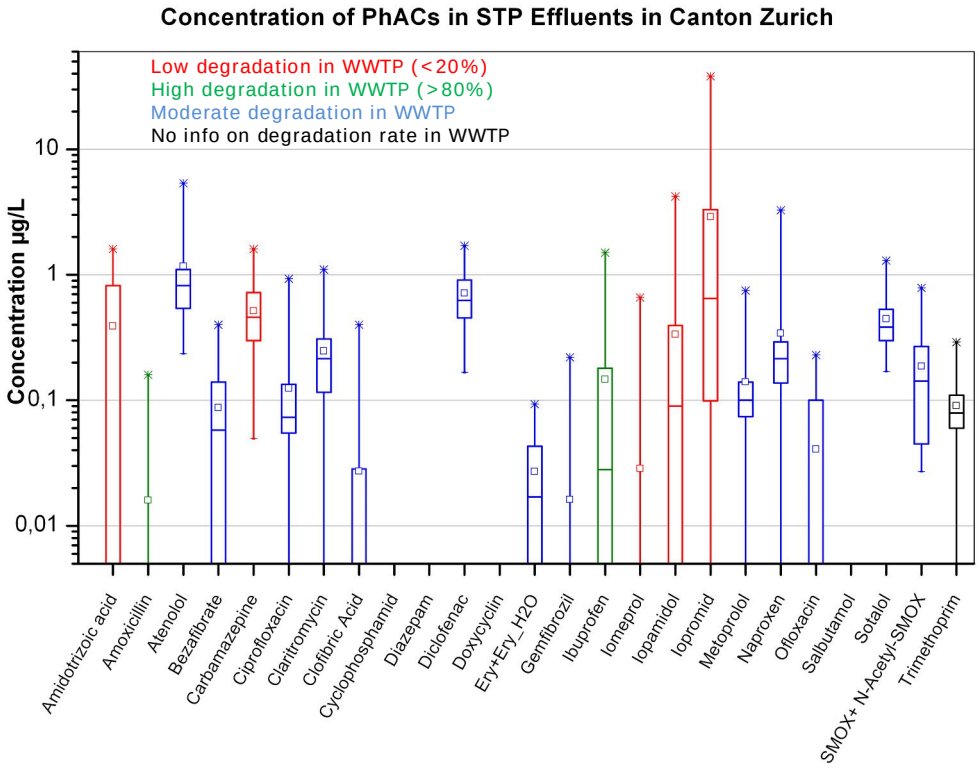


Figure 23 Measured priority PhACs in STP effluents of the Canton Zurich (data source chapter 4.2)

The most frequently detected compounds with a detection rate over 90 % are the analgesics diclofenac and naproxen, the antibiotics clarithromycin, sulfamethoxazole (and its metabolite) and trimethoprim, as well as the antiepileptic carbamazepine, the beta-blockers atenolol, metoprolol and sotalol.

The highest median concentrations of over 0.5 $\mu g \cdot L^{-1}$ was found for the beta blocker atenolol, the analgesic diclofenac and the radio contrast agent iopromide. Whereas a maximum concentration of 38 $\mu g \cdot L^{-1}$ was found for iopromide. Atenolol is sold in two times higher amounts in Switzerland than in Germany but a comparison of their concentrations detected in STP effluents of both sites cannot be done, because the compound was not analysed in Berlins STP effluents. However, in surface water samples of Berlin atenolol was not detected.

Median concentrations < 0.5 µg·L^{-1} but ≥ 0.1 µg·L^{-1} were detected for carbamazepine, sotalol, clarithromycin and naproxen as well as for sulfamethoxazole and metoprolol.

Following with low median concentration rates of under < 0.1 µg·L^{-1} are iopamidol, trimethoprim, ciprofloxacin, bezafibrate, ibuprofen, and erythromycin (plus its metabolite).

The lipid lowering drugs clofibric acid and gemfibrozil are rarely detected in the STP effluents in the Canton Zurich.

Comparing priority compounds measured at both sites, median concentration in Zurich are generally lower than in Berlin. Except for naproxen, which median concentration is on both sites similar (~0.2 µg·L^{-1}).

The median concentrations of carbamazepine, diclofenac and ibuprofen are three, three and two times lower, respectively. Significant differences exist for the concentrations of bezafibrate which are ten times higher findable in STP effluents of Berlin.

6.2.2 Surface water

Surface water samples in the Canton Zurich were taken from 30 different locations belonging to 17 rivers. They were sampled between June 1996 and January 2008.

Out of 23 measured compounds 17 were detected in surface waters of the Canton Zurich. Not detectable were the tranquilizer diazepam, the cytostatic cyclophosphamide, the antibiotic doxycycline and ofloxacin, and the lipid lowering drugs clofibric acid and gemfibrozil.

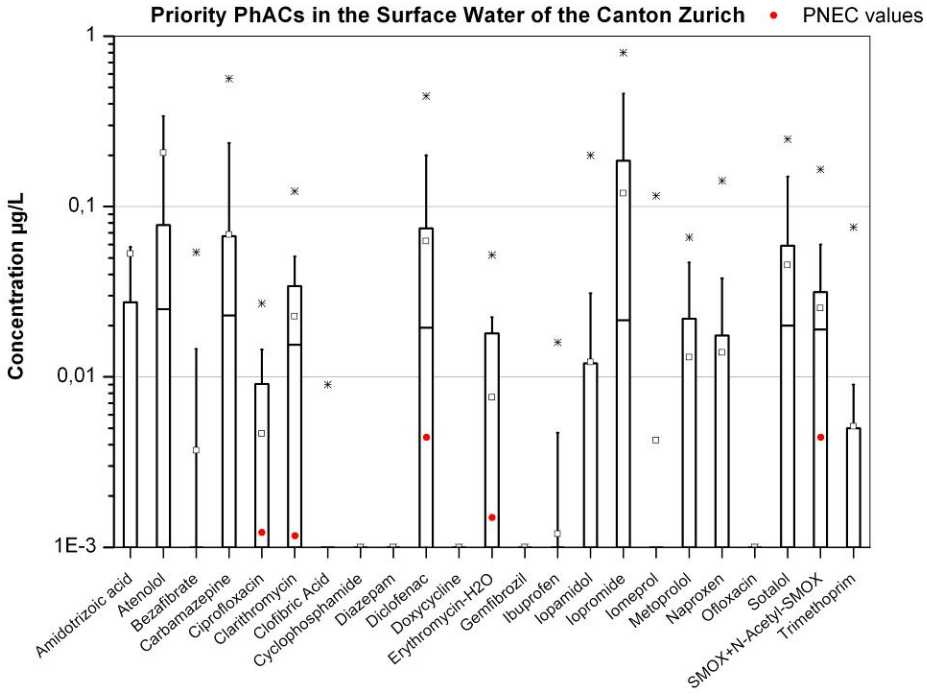


Figure 24: Measured priority PhACs in the surface water of the Canton Zurich (data source chapter 4.2). PNEC-values (red dots) taken from (Adams, Wang et al. 2002) and (LANUV 2007), see chapter 3.5.

Compounds which were highly detected in STP effluents are also present in the surface water. The analgesic diclofenac, the antibiotics clarithromycin and sulfamethoxazole, the antiepileptic carbamazepine, the beta-blocker atenolol and sotalol and at last the radio contrast agent iopromide were measured with detection rates of over 60 %.

The compounds atenolol, diclofenac and iopromide, carbamazepine and sotalol have been detected with median concentrations of about 0.02 $\mu g \cdot L^{-1}$ which are more than twenty times lower compared to STP effluent median concentrations.

The antibiotics sulfamethoxazole and clarithromycin are measured in median concentrations of 0.02 and 0.015, respectively which is in the same order as the compound mentioned above.

Highest values of the radio contrast agents amidotrizoic acid (1.3 $\mu g \cdot L^{-1}$) and iopromide (0.8 $\mu g \cdot L^{-1}$), as well as of atenolol (2.5 $\mu g \cdot L^{-1}$), carbamazepine (0.56 $\mu g \cdot L^{-1}$) and of diclofenac. (0.44 $\mu g \cdot L^{-1}$) were detected in rivers with low discharge volumes and high amounts of treated sewage water.

Aside of one exception all median concentration of at both sites analysed compounds are up to a factor of ten (carbamazepine and sulfamethoxazole) smaller in Switzerland than in Berlin. The median concentration of the antibiotic clarithromycin in Berlin of 17.5 $ng \cdot L^{-1}$ is a little lower than the median concentration of 25 $ng \cdot L^{-1}$ in Zurich.

6.2.3 Groundwater

Just a few groundwater samples in the Canton Zurich were available. Three projects carried out from 2004 to 2005 contribute to altogether 58 samples. Out of 25 priority compounds 4 were found in ground waters of the Canton Zurich.

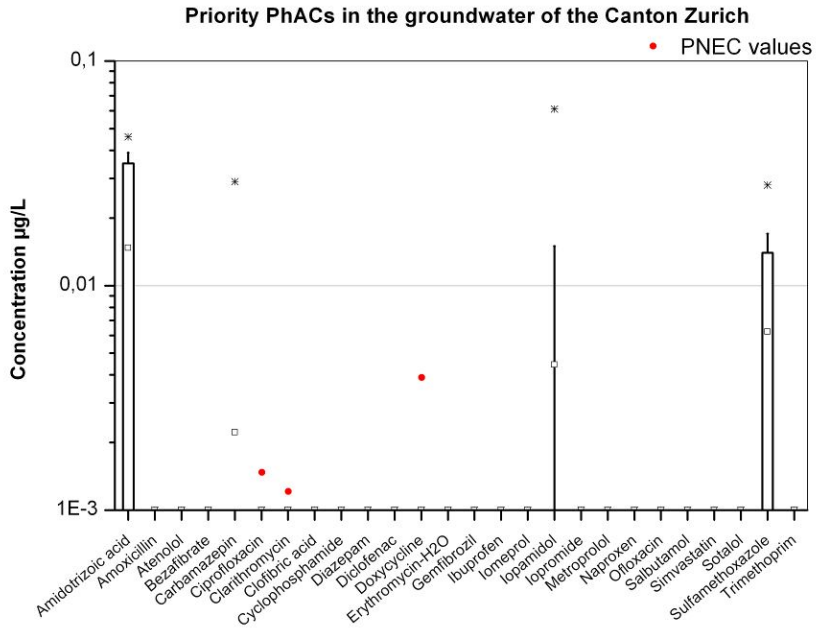


Figure 25: Measured priority PhACs in the groundwater of the Canton Zurich (data source see chapter 4.2)

The radio contrast agents amidotrizoic acid and iopamidol, the antiepileptic agent carbamazepine and the antibiotic sulfamethoxazole were detected in groundwater samples. Sulfamethoxazole was the most detected compound, out of 57 samples 50% were measured above the detection limit. Highest concentration of 0.028 $\mu g \cdot L^{-1}$ for sulfamethoxazole was measured. As you can see on the map, the whole stream, from its source to the inflow of river Rhein, receive the effluents of 11 STPs. Out of 36 samples amidotrizoic acid was detected 15 times. The detection rates of iopamidol and carbamazepine were rather low with 11% and 9 %, respectively. The highest concentrations of amidotrizoic acid and iopamidol occurred at nearby pumping stations. Like sulfamethoxazole, carbamazepine was measured with the highest concentration at the same pumping station.

6.3 Comparison

The analysis about the occurrence of priority PhACs in Berlin and Switzerland have shown that a huge amount of relevant PhACs can be detected in STP effluents and in surface water at both study sites. Furthermore it is observable that the levels of concentration of most priority PhACs in STP effluents and surface water of Switzerland are a range lower than in Berlin. This is caused due to several differences at both study sites. For example could be outlined that firstly the dilution of PhACs in the STP due to e.g. a higher water consumption or/and higher precipitation can be a reason for lower concentrations in STP effluents. Furthermore was shown that the natural discharges in receiving surface water bodies play an important role for the dilution of STP effluents and at the same time for the detection of priority PhACs in surface waters. These are only two factors out of a complex interaction of several factors such as consumption patterns, treatment efficiency (HRT, SRT, sludge age), discharging volumes of sewage, natural parameters (temperature, sunlight) etc. which lead to differences in the occurrence of PhACs in environmental compartments.

Even if only two study sites were analysed, the detected concentrations help to get a reliable estimation about which levels of concentrations of priority PhACs can be expected at other comparable study sites. An overview about the levels of concentration based on data of both study sites is given in the following chapter.

Chapter 7
Benchmarking of priority Pharmaceuticals

7.1 Occurrence of priority Pharmaceuticals in the urban Water Sector

Based on the measurements collected in Berlin and the Canton Zurich, a benchmarking synthesis on the levels of PhACs in the water compartments is proposed in this chapter. In order to make the visual tools easy to read and to understand, the same sorting for the PhACs is used in the different graphs, according the 75%-fractile concentrations that were measured in the STP effluents.

Table 18 serves as initial support. It presents the alphabetical list of considered priority PhACs with the corresponding ranking (position) on the graphs as well as the number of measurements that were actually taken into account for each of the water compartments. The levels of concentrations of priority PhACs in STP effluents (Berlin and the Canton Zurich), in surface water (Berlin and the Canton Zurich), in surface water with a proportion of less than 30% of treated sewage (for Berlin only) and in surface water with a proportion of more than 30% of sewage (for Berlin only) are presented in the following graphs.

Water practitioners who are interested in the occurrence of one specific PhAC can firstly use Table 18 to quickly know where the compound is located on the x-axis of the graphs and secondly can better appreciate the statistical weight of the illustrated values.

Table 18: Alphabetical list of considered priority PhACs implemented in the benchmarking with corresponding ranking (position) on the graphs and number of measurements for each water compartment (STP effluents, Surface Water (SW), SW with a proportion of <30% sewage, and SW with a proportion of>30% sewage).

PhACs	Ranking according to 75%-fractile	Number of measurements			
		STP effluents	SW	SW <30%	SW >30%
Acetyl salicylic	-[1]	0	117	0	0
Amidotrizoic acid	22	40	46	0	4
Amoxicillin	5	25	0	0	0
Atenolol	23	34	45	0	0
Bezafibrate	21	62	350	178	73
Carbamazepine	25	239	515	211	114
Ciprofloxacin	11	67	48	0	0
Clarithromycin	17	85	140	4	22
Clofibric Acid	18	88	417	211	100
Codeine	-[1]	0	117	0	0
Cyclophosphamide	1	15	6	0	0
Diazepam	4	7	8	0	0
Diclofenac	24	113	441	211	100
Doxycycline	3	13	6	0	0
Erythromycin (+Ery._H20)	8	82	118	47	30
Gemfibrozil	7	63	306	187	75
Ibuprofen	13	105	360	200	84
Iomeprol	6	43	45	0	0
Iopamidol	19	44	44	0	0
Iopromide	26	56	117	0	22
Metoprolol	12	25	36	0	0
Naproxen	16	94	323	187	75
Ofloxacin	9	25	20	0	0
Oxazepam	14	33	279	187	75
Paracetamol	-[1]	0	117	0	0
Salbutamol	2	15	0	0	0
Sotalol	20	35	45	0	0
Sulfamethoxazole (+N-Acetyl-SMOX)	15	71	130	17	28
Trimethoprim	10	44	106	4	22

[1] not included in the graphs (compounds were measured in Berlin's surface water but were not detected)

7.1.1 Occurrence in STP Effluents

The benchmarking overview which presents the concentrations in STP effluents (Figure 26) is plotted according to the increasing 75%-fractile concentrations. As previously mentioned, this sorting of PhACs will be kept as reference for other graphs. With a quick look, the water practitioner can have an idea of which PhACs are more likely to be found in high concentrations. Moreover, a colour code is also implemented in order to inform on the compound's degradation rate (when available) in conventional STPs. Thus, when atenolol and carbamazepine show low removal rates (<20%) in STP, it is no surprise to have them appeared along with the compounds with the highest levels.

7.1.2 Occurrence in Surface Water

For surface water, a similar pattern - with lower concentration ranges than for STP effluents (due to dilution) - is visualized (see Figure 27) although some discrepancies could be observed: amidotrizoic acid has a large 10-90%-fractile concentration range due to few but high measurements in Berlin and concentration levels of sulfamethoxazole (SMOX) and its metabolite N-acetyl sulfamethoxazole seem less affected by the dilution effect than other PhACs are.

By differentiating the surface water samples according to their proportion of treated sewage, a significant number of surface water measurements were neglected since the calculation of the proportion of sewage at some sample locations in Berlin was not possible or no comparable data were available for the Canton Zurich. Thus, only 63% of the surface water samples could be specified and categorized whether they contain more or less than 30% of treated sewage and they are then taken into account in the Figures 28 and 29. As expected, the surface water samples with <30% of treated sewage show lower concentrations of the 3rd-quartile levels below 0.4 g. L-1.

If the water practitioners have a hint on the proportion of treated sewage in their surface water samples, it is recommended to directly refer to the figures and in order to make the comparison. Indeed, when looking separately at the levels of PhACs in Berlin’s and the Canton Zurich’s surface waters, it has been clearly shown that the local hydrological realities play an important role, especially the dilution of STP effluents, which explains among other things the different concentration ranges detectable in Berlin and the Canton Zurich.

However, if no potential information on the proportion of treated sewage is available, the water practitioner could use the general overview of concentrations in surface water (Figure 27) which has been drawn based on more measurements (and involves more relevant priority PhACs).

7.1.3 Occurrence in Groundwater

No general overview on the levels of PhACs in groundwater in Berlin and the Canton Zurich was performed as large disparities were observed within the two case studies. This is linked to the differences in the concentration ranges already observed in surface

waters which have an impact on the potential contamination of groundwater via bank filtration. Due to this site specificity, we recommend to any water practitioners that are interested in comparing PhACs levels in groundwater samples to have a look at Figure 22 (Berlin) or Figure 25 (Zurich) depending on the hydrogeological similarities of the considered sites.

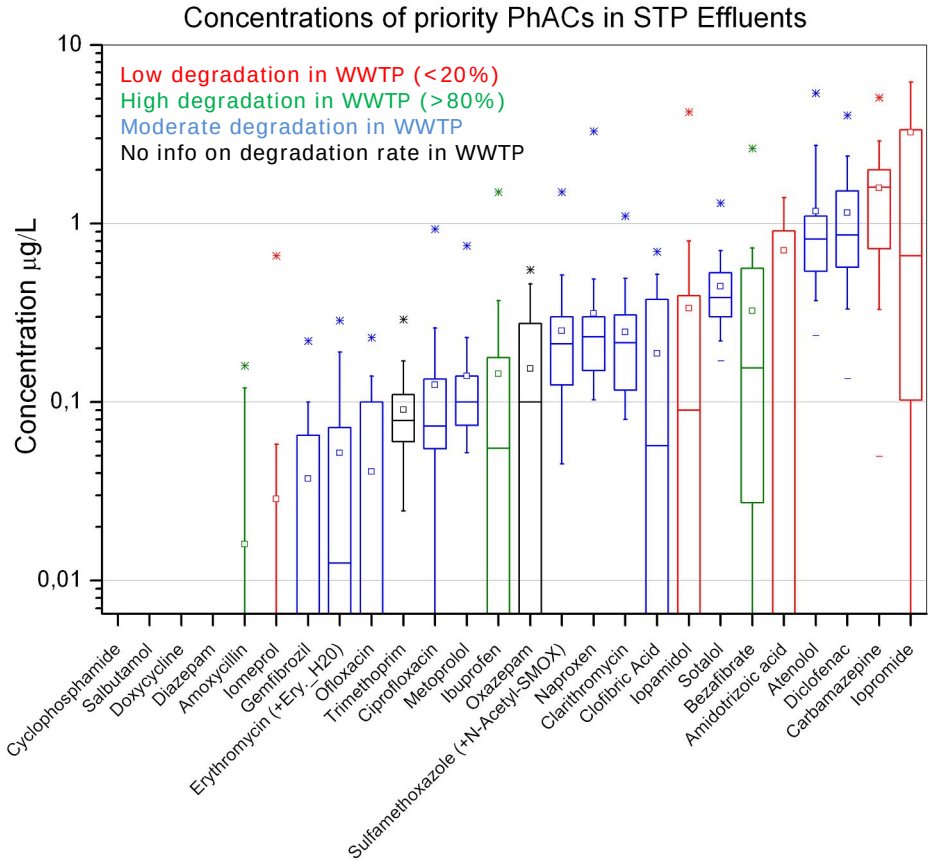


Figure 26 Benchmark of concentrations of priority PhACs in STP effluents (data source see chapters 4.1 and 4.2)

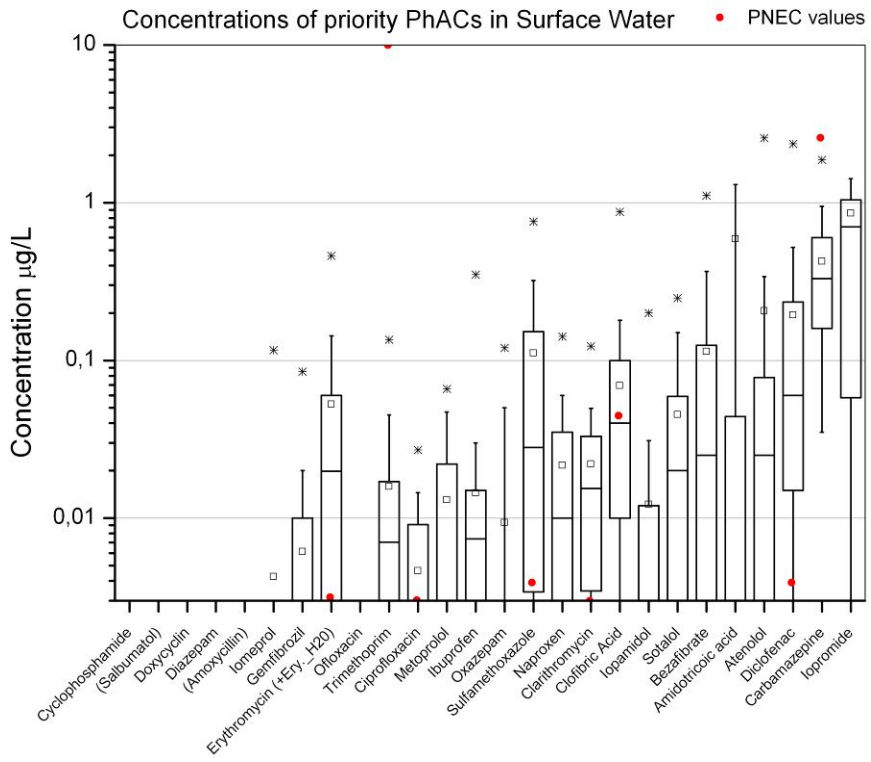


Figure 27: Benchmark of concentrations of priority PhACs in surface water (compounds in brackets were not measured in this water compartment; data source chapters 4.1 and 4.2)

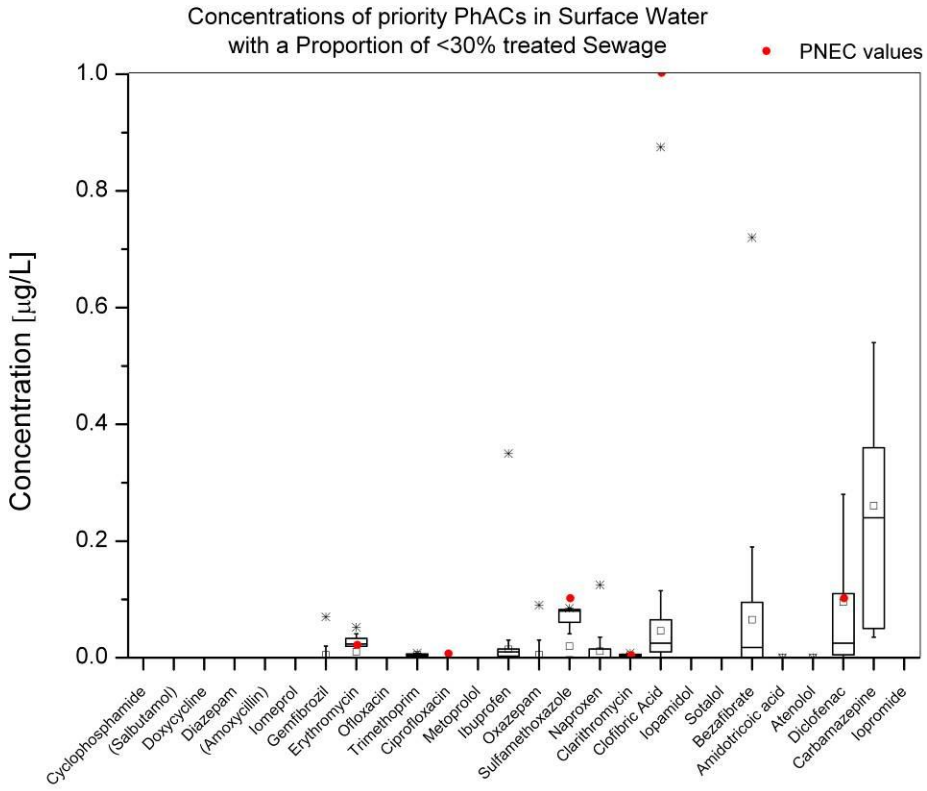


Figure 28: Benchmark of concentrations of priority PhACs in Surface Waters with a proportion of <30% treated sewage (compounds in brackets were not measured; ; data source see chapters 4.1 and 4.2).

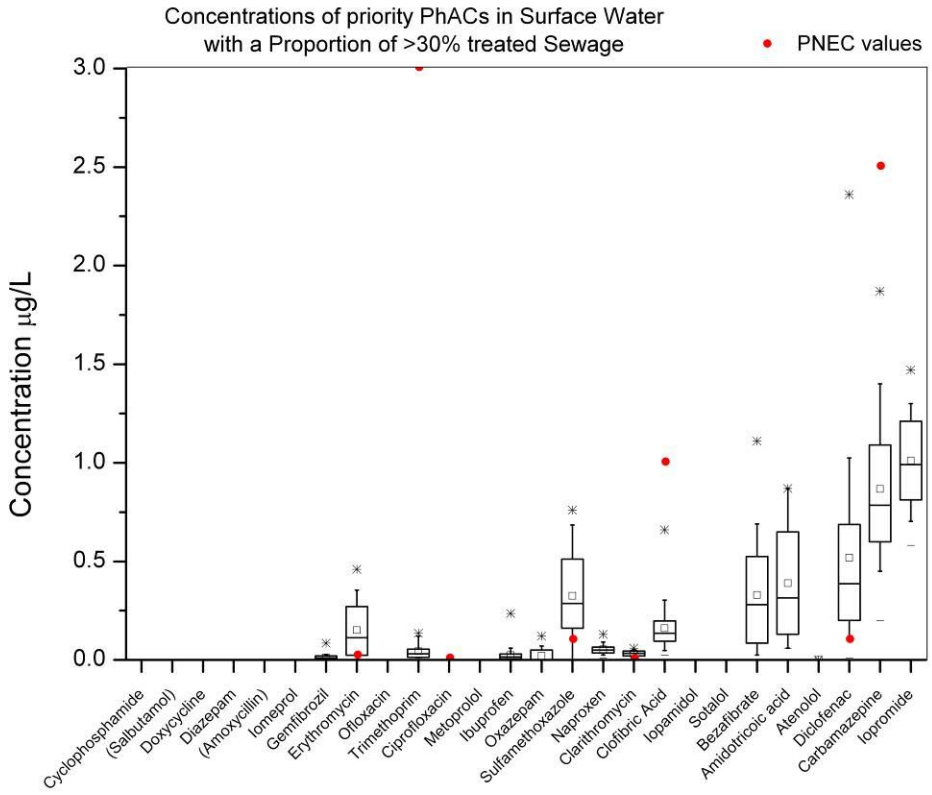


Figure 29: Benchmark of concentrations of priority PhACs in Surface Waters with a proportion of >30% treated sewage (compounds in brackets were not detected; ; data source see chapters 4.1 and 4.2).

Bibliography

Abbeglen, C., et al. (2009). "Ozonung von gereinigtem Abwasser. Schlussbericht Pilotversuch Regensdorf."

Adam, M. (2005). Vorkommen und ökotoxikologische Bewertung von Pharmakarückständen im Gewässersystem Berlins

Berlin, Senate for urban development VIII E 2.

Adams, C., et al. (2002). "Removal of antibiotics from surface and distilled water in conventional water treatment processes." Journal of Environmental Engineering 128(3): 253-260.

Ahel, M. and Jelicic, I. (2001). Phenazone analgesics in soil and groundwater below a municipal solid waste landfill. ACS Symposium Series. 791: 100-115.

Aherne, G. W., et al. (1990). "Cytotoxic drugs and the aquatic environment: Estimation of bleomycin in river and water samples." Journal of Pharmacy and Pharmacology 42(10): 741-742.

Ahrer, W., et al. (2001). "Determination of drug residues in water by the combination of liquid chromatography or capillary electrophoresis with electrospray mass spectrometry." Journal of Chromatography A 910(1): 69-78.

Alder, A. C., et al. (1997). "The fate of organic pollutants in wastewater and sludge treatment: Significant processes and impact of compound properties." Chimia 51(12): 922-928.

Alvarez, D. A. (1999). Development of an integrative sampling device for hydrophilic organic contaminants in aquatic environments. Columbia, University of Missouri-Columbia. Ph. D.

Andreozzi, R., et al. (2003). "Pharmaceuticals in STP effluents and their solar photodegradation in aquatic environment." Chemosphere 50(10): 1319-1330.

AWEL (2005). "Arzneimittelrückstände und homonell wirksame Stoffe in Fliessgewässern sowie Kläranlagenabläufen."

AWEL (2007). "Risikobeurteilung von Arzneimitteln und endokrin wirksamen Substanzen in Oberflächengewässern des Kantons Zürich."

Berlin-Brandenburg, A. f. S. (2008). Die kleine Berlin Statistik. Berlin-Brandenburg.

BLAC (2003). Arzneimittel in der Umwelt - Auswertung der Untersuchungen. Hanmburg, Agency of environment and health (sanitation and environment): 175.

Blüm, W., et al. (2005). Organische Spurenstoffe in Grundwasser des Limattales- Ergebnisse der Untersuchungskampagne 2004. Zürich, Baudirektion Kanton Zürich.

Boreen, A. L., et al. (2003). "Photodegradation of pharmaceuticals in the aquatic environment: A review." Aquatic Sciences 65(4): 320-341.

Buser, H. R., et al. (1998b). "Occurrence of the pharmaceutical drug clofibric acid and the herbicide mecoprop in various Swiss Lakes and in the North Sea." Environmental Science and Technology 32(1): 188-192.

Buser, H. R., et al. (1998a). "Occurrence and fate of the pharmaceutical drug diclofenac in surface waters: Rapid photodegradation in a lake." Environmental Science and Technology 32(22): 3449-3456.

Buser, H. R., et al. (1999). "Occurrence and environmental behavior of the chiral pharmaceutical drug ibuprofen in surface waters and in wastewater." Environmental Science and Technology 33(15): 2529-2535.

Carballa, M., et al. (2004). "Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant." Water Research 38(12): 2918-2926.

Castiglioni, S., et al. (2006). "Removal of pharmaceuticals in sewage treatment plants in Italy." Environmental Science and Technology 40(1): 357-363.

Castiglioni, S., et al. (2004). "Methodological approaches for studying pharmaceuticals in the environment by comparing predicted and measured concentrations in River Po, Italy." Regulatory Toxicology and Pharmacology 39(1): 25-32.

Clara, M., et al. (2005). "The solids retention time - A suitable design parameter to evaluate the capacity of wastewater treatment plants to remove micropollutants." Water Research 39(1): 97-106.

Clara, M., et al. (2004). "Carbamazepine as a possible anthropogenic marker in the aquatic environment: Investigations on the behaviour of Carbamazepine in wastewater treatment and during groundwater infiltration." Water Research 38(4): 947-954.

Cleuvers, M. (2003). "Aquatic ecotoxicity of pharmaceuticals including the assessment of combination effects." Toxicology Letters 142(3): 185-194.

Daughton, C. G. and Ternes, T. A. (1999). "Pharmaceuticals and personal care products in the environment: Agents of subtle change?" Environmental Health Perspectives 107(SUPPL. 6): 907-938.

de Voogt, P., et al. (2009). "Development of a common priority list of pharmaceuticals relevant for the water cycle." Water science and technology : a journal of the International Association on Water Pollution Research 59(1): 39-46.

Drewes, J. E., et al. (2003). "Fate of pharmaceuticals during ground water recharge." Ground Water Monitoring and Remediation 23(3): 64-72.

DWA (2001). ATV-DVWK-M 775 Abwasser aus Krankenhäusern und anderen medizinischen Einrichtungen.

EU (1994). EU Directive 91/689/EWG on Hazardous Waste 94/904/EWG.

Farré, M., et al. (2001). "Determination of drugs in surface water and wastewater samples by liquid chromatography-mass spectrometry: Methods and preliminary results including toxicity studies with Vibrio fischeri." Journal of Chromatography A 938(1-2): 187-197.

Fent, K., et al. (2006). "Ecotoxicology of human pharmaceuticals." Aquatic Toxicology 76(2): 122-159.

Ferrari, B., et al. (2003). "Erratum: Ecotoxicological impact of pharmaceuticals found in treated wastewaters: Study of carbamazepine, clofibric acid, and diclofenac (Ecotoxicology and Environmental Safety (2003) 55 (359-370))." Ecotoxicology and Environmental Safety 56(3): 450.

Garrison, A. W., et al. (1976). GC/MS analysis of organic compounds in domestic wastewaters. Identification and analysis of organic pollutants in water. L. H. Keith, Ann Arbor Science Publisher: 517-556.

Giger, W. (2005). "Antibiotikarückstände in Abwasser und Gewässern." gwa 1: 17-23.

Glugla (1999). "Langjährige Abflußbildung und Wasserhaushalt im urbanen Gebiet Berlin." Wasserwirtschaft 89(1).

Göbel (2004a). Occurrence and Fate of Sulfonamide and Macrolide Antimicrobials in Wastewater Treatment. Swiss Federal Institute of Technology Zurich. Zurich, University of Bonn. Doctor of Science: 172.

Göbel, A., et al. (2004b). "Trace determination of macrolide and sulfonamide antimicrobials, a human sulfonamide metabolite, and trimethoprim in wastewater using liquid chromatography coupled to electrospray tandem mass spectrometry." Analytical Chemistry 76(16): 4756-4764.

Göbel, A., et al. (2005). "Occurrence and sorption behavior of sulfonamides, macrolides, and trimethoprim in activated sludge treatment." Environmental Science and Technology 39(11): 3981-3989.

Golet, E. M. (2002a). Environmental Exposure Assessment of Fluoroquinolone Antibacterial Agents in Sewage, River Water and Soil. Swiss Federal Institute of Technology Zurich. Zurich, University of Girona. Doctor of natural Science: 188.

Golet, E. M., et al. (2002b). "Environmental exposure and risk assessment of fluoroquinolone antibacterial agents in wastewater and river water of the Glatt Valley watershed, Switzerland." Environmental Science and Technology 36(17): 3645-3651.

Gomez, M. J., et al. (2006). "Determination of pharmaceuticals of various therapeutic classes by solid-phase extraction and liquid chromatography-tandem mass spectrometry analysis in hospital effluent wastewaters." Journal of Chromatography A 1114(2): 224-233.

Gros, M., et al. (2007). "Wastewater treatment plants as a pathway for aquatic contamination by pharmaceuticals in the ebro river basin (northeast Spain)." Environmental Toxicology and Chemistry 26(8): 1553-1562.

Halling-Sörensen, B., et al. (1998). "Occurrence, fate and effects of pharmaceutical substances in the environment- A review." Chemosphere 36(2): 357-393.

Hanisch, B., et al. (2002). Ökotoxikologische Bewertung von Humanarzneimitteln in aquatischen Ökosystemen. E. a. o. t. Brandenburg. Potsdam

Frankfurt (Oder), Ecology and environmental analysis.

Hanke, I., et al. (2007). "Arzneimittel und Pestizide im Grundwasser." Eawag GWA 3/2007.

Heberer (2004). Meeting Record "Relevanz der getrennten Erfassung vo Pharmaka im Krankenhausabwasser", Kompetenz Zentrum Wasser Berlin.

Heberer, T. (2002a). "Tracking persistent pharmaceutical residues from municipal sewage to drinking water." Journal of Hydrology 266(3-4): 175-189.

Heberer, T. (2002c). "Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: A review of recent research data." Toxicology Letters 131(1-2): 5-17.

Heberer, T., et al. (1997). "Detection of drugs and drug metabolites in groundwater samples of a drinking water treatment plant." Fresenius Environ. Bull. 6: 438-443.

Heberer, T., et al. (2001). Occurrence of pharmaceutical residues in sewage, river, ground and drinking water in Greece and Germany. Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues. C. G. Daughton and T. Jones-Lepp. Washington DC, American Chemical Society. Symposium Series 791: 70-83.

Heberer, T., et al. (2008). "Behaviour and redox sensitivity of antimicrobial residues during bank filtration." Chemosphere 73(4): 451-460.

Heberer, T., et al. (2002b). From municipal sewage to drinking water: Fate and removal of pharmaceutical residues in the aquatic environment in urban areas. Water Science and Technology. 46: 81-88.

Heberer, T., et al. (1998). "Occurrence and distribution of organic contaminants in the aquatic system in Berlin. Part I: Drug residues and other polar contaminants in Berlin surface and groundwater." Acta Hydrochimica et Hydrobiologica 26(5): 272-278.

Heberer, T. and Stan, H.-J. (1997). "Determination of clofibric acid and N-(phenylsulfonyl)-sarcosine in sewage, river and drinking water." International journal of environmental analytical chemistry 67: 113-124.

Heberer, T., et al. (2001). "Occurrence and fate of pharmaceuticals during bank filtration-Preliminary results from investigations in Germany and United States." Pharmaceuticals and Endocrine Disrupting Chemicals: Emerging Contaminants in Drinking Water 120: 4-17.

Hignite, C. and Azarnoff, D. L. (1977). "Drugs and drug metabolites as environmental contaminants: chlorophenoxyisobutyrate and salicylic acid in sewage water effluent." Life Sciences 20(2): 337-341.

Hirsch, R., et al. (1999). "Occurrence of antibiotics in the aquatic environment." Science of the Total Environment 225(1-2): 109-118.

Hirsch, R., et al. (1996). "Nachweis von Betablockern und Bronchospasmolytika in der aquatischen Umwelt." Vom Wasser 87: 263-274.

Hirsch, R., et al. (2000). "A sensitive method for the determination of iodine containing diagnostic agents in aqueous matrices using LC-electrospray-tandem-MS detection." Fresenius' Journal of Analytical Chemistry 366(8): 835-841.

Hollender, J. (2005). "Polar organic micropollutants in the water cycle."

Hollender, J. (2007). "Mikroverunreinigungen - Vorkommen in Gewässern der Schweiz und Bewertung."

Hollender, J., et al. (2009). "Elimination of Organic Micropollutants in a Municipal Wastewater Treatment Plant Upgraded with a Full-Scale Post-Ozonation Followed by Sand Filtration." Environmental Science and Technology 42(No20): 7862-7869

Holm, J. V. (1995). "Response to comment on "occurrence and distribution of pharmaceutical organic compounds in the groundwater downgradient of a landfill (Grindsted, Denmark)" [6]." Environmental Science and Technology 29(12): 3074.

HSDB (2001). Hazardous Substances Data Bank. P. b. U. S. N. L. o. Medicine, Provided by: Canadian Centre of Occupational Health and Safety.

Isidori, M., et al. (2005). "Toxic and genotoxic evaluation of six antibiotics on non-target organisms." Science of the Total Environment 346(1-3): 87-98.

Jekel, M. and Heberer, T. (2005). Occurrence and fate of drug residues and related polar contaminants during bank filtration and artificial recharge. Natural and Artificial Systems for Recharge and Infiltration “NASRI”. Berlin, KWB.

Jones, O. A. H., et al. (2007). "The occurrence and removal of selected pharmaceutical compounds in a sewage treatment works utilising activated sludge treatment." Environmental Pollution 145(3): 738-744.

Joss, A., et al. (2005). "Removal of pharmaceuticals and fragrances in biological wastewater treatment." Water Research 39(14): 3139-3152.

Joss, A., et al. (2005). "Removal of pharmaceuticals and fragrances in biological wastewater treatment." Water Research 39(14): 3139-3152.

Karthikeyan, K. G. and Meyer, M. T. (2006). "Occurrence of antibiotics in wastewater treatment facilities in Wisconsin, USA." Science of the Total Environment 361(1-3): 196-207.

Kaufman, D. W., et al. (2002). "Recent patterns of medication use in the ambulatory adult population of the United States: The Slone survey." Journal of the American Medical Association 287(3): 337-344.

Khan, S. J., et al. (2004). Removal of hormones and pharmaceuticals in the advanced water recycling demonstration plant in Queensland, Australia. Water Science and Technology. 50: 15-22.

Kingston, J. K., et al. (2000). "Development of a novel passive sampling system for the time-averaged measurement of a range of organic pollutants in aquatic environments." Journal of Environmental Monitoring 2(5): 487-495.

Knodel, J. (2008). "Simulation von Röntgenkontrastmitteln im Wasserkreislauf von Berlin. ." Praktikumsarbeit. 1.3.2008.

Kolpin, D. W., et al. (2002). "Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999-2000: A national reconnaissance." Environmental Science and Technology 36(6): 1202-1211.

Kraume, I. and Broll, J. (2007). "Wasserkreislaufsimulation für Nährstoffe Pt und NH4-N+NO3-N. ." BWB-interner Arbeitsbericht. 11/2007.

Kümmerer, K. (2001). Pharmaceuticals in the Environment- Sources, fate, Effects and Risk. Berlin, Heidelberg, New York, Springer.

Kümmerer, K. (2004). Pharmaceuticals in the environment- Sources, fate, Effects and Risks. Berlin, Heidelberg, New York, Springer.

Kümmerer, K., Ed. (2008). Pharmaceuticals in the Environment-Sources, Fate, Effects and Risk. Berlin, Heidelberg, New York, Springer.

Kümmerer, K., et al. (1997). "Biodegradability of the anti-tumour agent ifosfamide and its occurrence in hospital effluents and communal sewage." Water Research 31(11): 2705-2710.

Landsdorp, D., et al. (1990). "Pharmacokinetics of rectal diclofenac and its hydroxy metabolites in man." International Journal of Clinical Pharmacology Therapy and Toxicology 28(7): 298-302.

LANUV (2007). Eintrag von Arzneimitteln und deren Verhalten und Verbleib in der Umwelt-Fachbericht 2. Recklinghausen, LANUV- State office of environment, nature, and consumer protection North Rhine-Westphalia

MUNLV- Agency for environment, conservation, agriculture and consumer protection: 358.

Liebig (2005). Untersuchungen zu Umweltrisikoabschätzungen von Humanpharmaka und Inhaltsstoffen von Körperpflegeprodukten vor dem Hintergrund europäischer Bewertungskonzepte. Frankfurt, Johann Wolfgang Goethe-Universität: 220.

Lienert, J., et al. (2007). Reducing micropollutants with source control: Substance flow analysis of 212 pharmaceuticals in faeces and urine. Water Science and Technology. 56: 87-96.

Lienert, J., et al. (2007). "Screening method for ecotoxicological hazard assessment of 42 pharmaceuticals considering human metabolism and excretory routes." Environmental Science and Technology 41(12): 4471-4478.

Lienert, J., et al. (2007). "Supporting Information "Screening Method for Ecotoxicological Hazard Assessment of 42 Pharmaceuticals considering Human Metabolism and Excretory Routes"." Environmental Science Technology.

Lindqvist, N., et al. (2005). "Occurrence of acidic pharmaceuticals in raw and treated sewages and in receiving waters." Water Research 39(11): 2219-2228.

Martinez, V., et al. (2000). "Determination of the pK(a) values of ß-blockers by automated potentiometric titrations." Journal of Pharmaceutical and Biomedical Analysis 23(2-3): 459-468.

Massmann, G., et al. (2009). "Hydrodynamic or hydrochemical aspects of anthropogenic and naturally induced bank filtration - examples from Berlin/Brandenburg." Hydrodynamische und hydrochemische Aspekte der anthropogen und natÃ¼rlich induzierten Uferfiltration am Beispiel von Berlin/Brandenburg: 1-15.

Mazzella, N., et al. (2007). "Determination of kinetic and equilibrium regimes in the operation of polar organic chemical integrative samplers. Application to the passive sampling of the polar herbicides in aquatic environments." Journal of Chromatography A 1154(1-2): 42-51.

McArdell, C. S., et al. (2003). "Occurrence and Fate of Macrolide Antibiotics in Wastewater Treatment Plants and in the Glatt Valley Watershed, Switzerland." Environmental Science and Technology 37(24): 5479-5486.

Metcalfe, C. D., et al. (2003). "Occurrence of neutral and acidic drugs in the effluents of canadian sewage treatment plants." Environmental Toxicology and Chemistry 22(12): 2872-2880.

Metcalfe, C. D., et al. (2004). Pharmaceuticals in the canadian environment. In Pharmaceuticals in the environment - Sources, fate,effects and risks. K. Kümmerer. Berlin, Heidelberg, Springer: 67-90.

Mills, G. A., et al. (2007). "Trends in monitoring pharmaceuticals and personal-care products in the aquatic environment by use of passive sampling devices." Analytical and Bioanalytical Chemistry 387(4): 1153-1157.

Morse, A. and Jackson, A. (2004). "Fate of amoxicillin in two water reclamation systems." Water, Air, and Soil Pollution 157(1-4): 117-132.

Möller, K. and Burgschweiger, J. (2008). Wasserversorgungskonzept für Berlin und für das von den BWB versorgte Umland (Entwicklung bis 2040), BWB.

MUNLV (2006). Abschlußbericht zum Forschungsvorhaben Untersuchungen zum Eintrag und zur Elimination von gefährlichen Stoffen in kommunalen Kläranlagen, Teil 2, Ministerium für Umwelt und Naturschutz, Landwirtschaft und Verbraucherschutz des Landes Nordrhein-Westfalen.

n.a. (2008). Umweltbericht Kanton Zürich, Baudirektion im Auftrag des Regierungsrates des Kantons Zürich. 5: 144.

NASRI-project (2005). Final Report.

Nikolaou, A., et al. (2007). "Occurrence patterns of pharmaceuticals in water and wastewater environments." Analytical and Bioanalytical Chemistry 387(4): 1225-1234.

Norpoth, K., et al. (1973). "Studies on the problem of solubility and stability of steroid ovulation inhibitors in water, waste water and activated sludge." Untersuchungen zur Frage der LÃ¶slichkeit und StabilitÃ¤t ovulationshemmender Steroide in Wasser, AbwÃ¤ssern und Belebtschlamm. 156(6): 500-511.

Oaks, J. L., et al. (2004). "Diclofenac residues as the cause of vulture population decline in Pakistan." Nature 427(6975): 630-633.

Öllers, S., et al. (2001). "Simultaneous quantification of neutral and acidic pharmaceuticals and pesticides at the low-ng/l level in surface and waste water." Journal of Chromatography A 911(2): 225-234.

Ort, C. (2009). "Model-Based Evaluation of Reduction Strategies for Micropollutants

from Wastewater Treatment Plants in Complex River Networks." Environmental Science and Technology.

Ort, C., et al. (2004). Modeling stochastic load variations in sewer systems. In Urban drainage Modeling Conference, Dresden.

Ort, C. and Gujer, W. (2005). Sampling for representative micropullutant loads in sewer systems. ICUD, 10th International Conference on Urban Drainage, Copenhagen, Denmark.

Ort, C., et al. (2005). Modelling stochastic load variations in sewer systems. Water Science and Technology. 52: 113-122.

Pacini, N., et al. (1997). "Water-quality surveillance of Swiss rivers." Chimia 51(12): 929-934.

Packer, J. L., et al. (2003). "Photochemical fate of pharmaceuticals in the environment: Naproxen, diclofenac, clofibric acid, and ibuprofen." Aquatic Sciences 65(4): 342-351.

Plume, S., et al. (2008). Trace pollutants in combined sewer overflows. Berlin, Kompetenzzentrum Wasser Berlin gGmbH (KWB).

Putschew, A. and Jekel, M. (2001). "Iodinated X-ray contrast media in the anthropogenic influenced water cycle." Vom Wasser 97: 103-114.

Putschew, A., et al. (2000). "Occurrence of triiodinated X-ray contrast agents in the aquatic environment." Science of the Total Environment 255(1-3): 129-134.

Queiroz, R. H. C., et al. (2008). "Quantification of carbamazepine, carbamazepine-10,11-epoxide, phenytoin and phenobarbital in plasma samples by stir bar-sorptive extraction and liquid chromatography." Journal of Pharmaceutical and Biomedical Analysis 48(2): 428-434.

Reddersen, K. (2004). Das Verhalten von Arzneimittelrückständen im Wasserkreislauf von Berlin. Fakultät III - Prozesswissenschaften. Berlin, Technical University Berlin. Dr. rer. nat: 327.

Reddersen, K. and Heberer, T. (2003). "Multi-compound methods for the detection of pharmaceutical residues in various waters applying solid phase extraction (SPE) and gas chromatography with mass spectrometric (GC-MS) detection." Journal of Separation Science 26(15-16): 1443-1450.

Reddersen, K., et al. (2002). "Identification and significance of phenazone drugs and their metabolites in ground- and drinking water." Chemosphere 49(6): 539-544.

Richardson, M. L. and Bowron, J. M. (1985). "The Fate of Pharmaceutical Chemicals in the Aquatic Environment." Journal Pharm. Pharmacol. 37: 1-12.

Riechel, M. (2009). Auswirkungen von Mischwassereinleitungen auf die Berliner Stadtspree. Fakultät III Prozesswissenschaften Berlin Center for Competence of Water. Berlin, TU-Berlin. Diploma: 129.

Roberts, P. H. and Thomas, K. V. (2006). "The occurrence of selected pharmaceuticals in wastewater effluent and surface waters of the lower Tyne catchment." Science of the Total Environment 356(1-3): 143-153.

Rönnefahrt (2005). Verbrauchsmengen in der Bewertung des Umweltrisikos von Humanarzneimitteln,. Arzneimittel in der Umwelt- Zu Risiken und Nebenwirkungen fragen Sie das Umweltbundesamt. Umweltbundesamt. Dessau. UBA texte 29/05.

Roth, H. and Fenner, H. (2000). Arzneistoffe. Stuttgart, Deutscher Apotheker Verlag.

Routledge, E. J., et al. (1998). "Identification of estrogenic chemicals in STW effluent. 2. In vivo responses in trout and roach." Environmental Science and Technology 32(11): 1559-1565.

Sacher, F., et al. (2008). "Pharmaceutical residues in the river Rhine - Results of a one-decade monitoring programme." Journal of Environmental Monitoring 10(5): 664-670.

Sacher, F., et al. (2001). "Pharmaceuticals in groundwaters: Analytical methods and results of a monitoring program in Baden-Württemberg, Germany." Journal of Chromatography A 938(1-2): 199-210.

Schäppi, B., et al. (2004). Untersuchung der organischen Spurenstoffe in den Zuflüssen und Kläranlagenabläufen im Einzugsgebiet des Zurichsees. Zürich, Wasserversorgung Zürich.

Schittko, S., et al. (2004). Bank filtration: A suitable process for the removal of iodinated x-ray contrast media? Water Science and Technology. 50: 261-268.

Schuster (2005). "Möglichkeiten der getrennten Erfassung von Arzneimitteln in Krankenhäusern zur Entlastung des Abwassers am Beispiel der iodorganischen Röntgenkontrastmittel und der Zytostatika."

Schwaiger, J., et al. (2004). "Toxic effects of the non-steroidal anti-inflammatory drug diclofenac. Part I: Histopathological alterations and bioaccumulation in rainbow trout." Aquatic Toxicology 68(2): 141-150.

Sedlak, D. L., et al. (2005). Occurrence survey of pharmaceutically active compounds. Denver, Awwa Research Foundation.

Seiler, R. L., et al. (1999). "Caffeine and pharmaceuticals as indicators of waste water contamination in wells." Ground Water 37(3): 405-410.

SenSUT (2001). "Abwasserbeseitigungsplan Berlin."

SenSUT (2003). "Digitaler Umweltatlas Berlin.".

Söderström, H., et al. (2009). "Strategies for monitoring the emerging polar organic contaminants in water with emphasis on integrative passive sampling." Journal of Chromatography A 1216(3): 623-630.

St.Gallen, A. f. U. d. K. (2006). "Hormone und Arzneimittel in Gewässern der Ostschweiz."

Stan, H. J. and Linkerhägner, M. (1992). "Identifizierung von 2-(4-Chlorphenoxy)-2-methyl-propionsäure im

Grundwasser mittels Kapillar-Gaschromatographie mit Atomemissionsdetektion und

Massenspektrometrie." Vom Wasser 79: 75-88.

Steger-Hartmann, T., et al. (1999). "Environmental risk assessment for the widely used iodinated X-ray contrast agent iopromide (ultravist)." Ecotoxicology and Environmental Safety 42(3): 274-281.

Steger-Hartmann, T., et al. (1998). "Umweltverhalten und ökotoxikologische Bewertung von iodhaltigen Röntgenkontrastmitteln." Vom Wasser 91: 185-194.

Strenn, B., et al. (2004). Carbamazepine, diclofenac, ibuprofen and bezafibrate - investigations on the behaviour of selected pharmaceuticals during wastewater treatment. Water Science and Technology. 50: 269-276.

Stuer-Lauridsen, F., et al. (2000). "Environmental risk assessment of human pharmaceuticals in Denmark after normal therapeutic use." Chemosphere 40(7): 783-793.

Stumpf, M., et al. (1998). "Isolierung von Ibuprofen-Metaboliten und deren Bedeutung als Kontaminanten in der aquatischen Umwelt. [Isolation of ibuprofen-metabolites and their importance as pollutants of the aquatic environment]." Vom Wasser 91(291-303).

Stumpf, M., et al. (1996). "Nachweis von Arzneimittelrückständen in den Kläranlagen und Fliessgewässern." Vom Wasser 86: 291-303.

Stumpf, M., et al. (1999). "Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil." Science of the Total Environment 225(1-2): 135-141.

Tabak, H. H. and Bunch, R. L. (1970). "Steroid hormones as water pollutants. ." Developments in Industrial Microbiology. Washington: 367-376.

Tauxe-Wuersch, A., et al. (2005). "Occurrence of several acidic drugs in sewage treatment plants in Switzerland and risk assessment." Water Research 39(9): 1761-1772.

Ternes, T., et al. (1999). Nachweis und Screening von Arzneimittelrückständen, Diagnostika und Antiseptika in der aquatischen Umwelt. . Abschlußbericht zum Forschungsvorhaben 02WU9567/3 des BMBF, ESWE-Institut für Wasserforschung und Wassertechnologie GmbH: 234.

Ternes, T. and Joss, A., Eds. (2006). Human Pharmaceuticals, Hormones and Fragrances. Analytical Methods.

Ternes, T. and Joss, A., Eds. (2006). Human Pharmaceuticals, Hormones and Fragrances. Consumption and Occurrence.

Ternes, T., et al. (2005). "Removal of pharmaceuticals and personal care products: results of the POSEIDON project." WEFTEC 2005 227-243.

Ternes, T. A. (1998). Arzneimittel in Kläranlagen und Gewässern-Materialien Nr. 88. ATV-Fachgespräch "Krankenhausabwässer", München, Bayrisches Landesamt für Wasserwirtschaft.

Ternes, T. A. (1998). "Occurrence of drugs in German sewage treatment plants and rivers." Water Research 32(11): 3245-3260.

Ternes, T. A. (2001). Pharmaceuticals and metabolites as contaminants of the aquatic environment. . Pharmaceuticals and Personal Care Products in teh Environment: Scientific and Regular Issues. C. G. Daughton and T. L. Jones-Lepp. Washington DC, American Chemical Society. ACS Symposium Series 791: 39-54.

Ternes, T. A., et al. (2005). "Determination of pharmaceuticals, iodinated contrast media and musk fragrances in sludge by LC tandem MS and GC/MS." Journal of Chromatography A 1067(1-2): 213-223.

Ternes, T. A. and Hirsch, R. (2000). "Occurrence and behavior of X-ray contrast media in sewage facilities and the aquatic environment." Environmental Science and Technology 34(13): 2741-2748.

Ternes, T. A., et al. (1998). "Methods for the determination of neutral drugs as well as betablockers and Î²2-sympathomimetics in aqueous matrices using GC/MS and LC/MS/MS." Fresenius' Journal of Analytical Chemistry 362(3): 329-340.

Ternes, T. A. and Joss, A. (2006). Human Pharmaceuticals, Hormones and Fragrances. The challenge of micropollutants in urban water management, IWA.

Ternes, T. A., et al. (1998b). "Simultaneous determination of antiseptics and acidic drugs in sewage and river water." Vom Wasser 90: 295-309.

Thomas, P. M. and Foster, G. D. (2004). "Determination of nonsteroidal anti-inflammatory drugs, caffeine, and triclosan in wastewater by gas chromatography-mass spectrometry." Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering 39(8): 1969-1978.

Thompson, A. (2005). Human pharmaceuticals in the aquatic environment a review. Department of Water Science, Cranfield University

Dr: 296.

Tixier, C., et al. (2003). "Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters." Environmental Science and Technology 37(6): 1061-1068.

Togola, A. and Budzinski, H. (2007). "Development of polar organic integrative samplers for analysis of pharmaceuticals in aquatic systems." Analytical Chemistry 79(17): 6734-6741.

Triebskorn, R., et al. (2004). "Toxic effects of the non-steroidal anti-inflammatory drug diclofenac: Part II. Cytological effects in liver, kidney, gills and intestine of rainbow trout (Oncorhynchus mykiss)." Aquatic Toxicology 68(2): 151-166.

Van Der Hoeven, N. (2004). "Current issues in statistics and models for ecotoxicological risk assessment." Acta Biotheoretica 52(3): 201-217.

Vieno, N. M., et al. (2005). "Seasonal variation in the occurrence of pharmaceuticals in effluents from a sewage treatment plant and in the recipient water." Environmental Science and Technology 39(21): 8220-8226.

Waggott, A. (1981). Trace organic substances in the river Lee (Great Britan). Chemistry in Water Reuse. W. J. Cooper. USA. 2: 55-59.

Webb, S. F. (2001). A data based perspective on the environmental risk assessment of human pharmaceuticals II: aquatic risk characterisation. Pharmaceuticals in the Environment. Sources, Fate, Effects and Risks. K. Kümmerer. Berlin, Springer-Verlag: 319-343.

Weissbrodt, D., et al. (2009). "Mass flows of x-ray contrast media and cytostatics in hospital wastewater." Environmental Science and Technology 43(13): 4810-4817.

Yamamoto, H., et al. (2005). "Fate and partitioning of selected pharmaceuticals in aquatic environment." Environmental sciences : an international journal of environmental physiology and toxicology. 12(6): 347-358.

Zimmer, A., et al. (2000). "Rücklauf von Altarzneimitteln in hessischen Apotheken." Pharmazeutische Zeitung.

Zimmer, A., et al. (1992). "Rücklauf von Altarzneimitteln." Pharmazeutische Zeitung: 20-29.

Zuccato, E., et al. (2000). "Presence of therapeutic drugs in the environment." Lancet 355(9217): 1789-1790.

Zühlke, S. (2004). Verhalten von Phenazonderivaten, Carbamazepin und estrogenen Steroiden während verschiedener Verfahren der Wasseraufbereitung. Fakultät III – Prozesswissenschaften. Berlin, Technical University Berlin. Dr. rer. net: 295.

Zwiener, C. and Frimmel, F. H. (2000). "Oxidative treatment of pharmaceuticals in water." Water Research 34(6): 1881-1885.

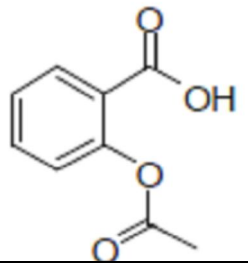
Zwiener, C., et al. (2000). "Biodegradation of pharmaceutical residues investigated by SPE-GC/ITD-MS and on-line derivatization." HRC Journal of High Resolution Chromatography 23(7-8): 474-478.

Appendix A

Fact-Sheets of Priority Pharmaceuticals

In the following tables a compendium about physico-chemical parameters, degradation and ecotoxicity as well as sales data for each priority PhAC are presented. Thereby excretion rates and degradation rates are given as average values of the data found in the literature (see chapter 3.3 and 3.4). The ecotoxicity of each compound is described in its current PNEC value and its corresponding toxicological test organism and the resulting test concentration (compare chapter 3.5). For more information about ecotoxicological tests and different test organisms for each compound the reader is referred to (LANUV 2007), (Fent, Weston et al. 2006), and (Hanisch et al. 2002).

A.1 Acetyl salicylic acid (Aspirin)

Data on priority PhAC	
Class of PhAC	Analgesic, Antiphlogistic
CAS-no.	50-78-2
Molecular formula	C9-H8-O4
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	180.15
Water solubility (mg/l)	4.6 at 25°C[1,2]
Vapour pressure (mm Hg)	2.52*E-5 at 25°C[1,2]
$\log K_{ow}$	1.19[1,2] 1.12[3]
Henry's constant K_H (atm*m^3/mol)	1.3*E-9[1,2]
$\log K_{oc}$	0,84[1]
Dissociation constant K_a [pK_a]	3.49 at 25°C[1,2]
Degradation	
Excretion as parent compound (%)	6.5 ± 2.1
Excretion as metabolite (%)	91 ± 8.5
Elimination Rate in conventional STPs (%)	81[6]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	40
EC_0 bacteria (µg·L^{-1})	8000
Sales/ Production volumes	
Consumption (t/a)	902 (Germany, 2001)[4] 47 (Switzerland, 2004)[5]

1 Hanisch et al. 2002

2 http://chem.sis.nlm.nih.gov/chemidplus/

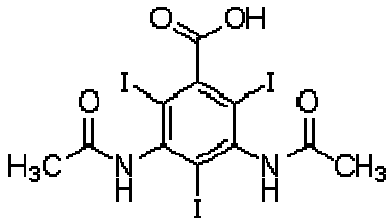
3 Hirsch et al 2002

4 BLAC 2003

5 Lienert et al. 2007

6 Ternes 1998

A.2 Amidotrizoic Acid (Diatrizoate)

Data on priority PhAC	
Class of PhAC	Contrast media
CAS-no.	117-96-4
Molecular formula	C11-H9-I3-N2-O4
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	613.9
Water solubility (mg/l)	8.9 at 25 °C[1]
Vapour pressure (mm Hg)	3.8E-15 at 25°C[1]
$\log K_{ow}$	1.37[1]
Henry's constant K_H (atm*m^3/mol)	2.8E-18 at 25 °C[1]
Dissociation constant K_a [pK_a]	1 (for the carboxylic acid of diatrizoate)[1]
Degradation	
Excretion as parent compound (%)	100[4]
Excretion as metabolite (%)	-
Elimination Rate in conventional STPs (%)	20 ± 28.3
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	1000000
All test organisms (µg·L^{-1})	10000000
Sales/ Production volumes	
Consumption (t/a)	60.7 (Germany, 2001)[2] 0.487 (Switzerland, 2003)[3]

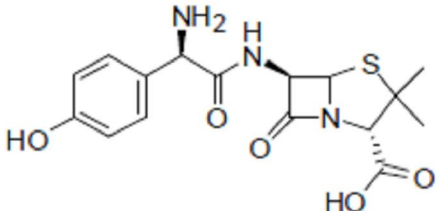
1 http://toxnet.nlm.nih.gov

2 BLAC 2003

3 Blüm at al. 2005

4 LANUV 2007

A.3 Amoxicillin

Data on priority PhAC	
Class of PhAC	Antibiotic (anti bacterial agent)
CAS-no.	26787-78-0
Molecular formula	C16-H19-N3-O5-S
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	365.4
Water solubility (mg/l)	3430[1]
Vapour pressure (mm Hg)	4.69E-17[1]
$\log K_{ow}$	0.87[1]
Henry's constant K_H (atm*m^3/mol)	2.49E-21[1]
$\log K_{oc}$	n.a.
Dissociation constant K_a [pK_a]	n.a.
Degradation	
Excretion as parent compound (%)	80 ± 7
Excretion as metabolite (%)	16 ± 1.4
Elimination Rate in conventional STPs (%)	high[5]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test	n.a.
Sales/ Production volumes	
Consumption in (t/a)	333.2 (France)[3] 115 (Germany, 2001)[2] 11 (Switzerland, 1999)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

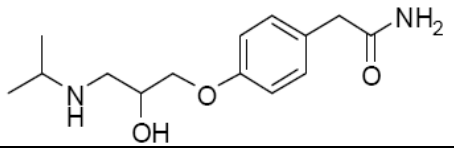
2 BLAC 2003

3 (Webb 2001)

4 ISM Health

5 Morse & Jackson 2004

A.4 Atenolol

Data on priority PhAC	
Class of PhAC	Beta-Blocker
CAS-no.	29122-68-7
Molecular formula	C14-H22-N2-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	266.3
Water solubility (mg/l)	1.33E+04 at 25 °C[1]
Vapour pressure (mm Hg)	2.92E-10 at 25°C[1]
$\log K_{ow}$	0.16[1] 0.23[3] -0.03[8]
Henry's constant K_H (atm*m^3/mol)	1.37E-18 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant K_a [pK_a]	9.5[7]
Degradation	
Excretion as parent compound (%)	83[5] >90[3]
Excretion as metabolite (%)	5[5]
Elimination Rate in conventional STPs (%)	34.5 ± 38.1
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	18.336 (France)[4] 13.6 (Germany, 2001)[2] 3 (Switzerland, 2005)[6]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 LANUV 2007

4 (Webb 2001)

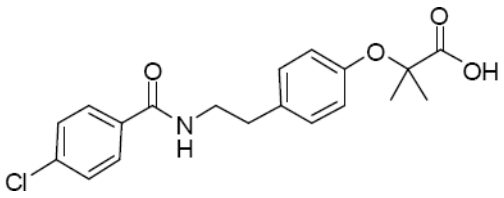
5 Lienert et al. 2007

6 Hollender 2007

7 (Martinez et al. 2000)

8 (Yamamoto et al. 2005)

A.5 Bezafibrate

Data on priority PhAC	
Class of PhAC	Lipid lowering drug
CAS-no.	41859-67-0
Molecular formula	C19-H20-Cl-N-O4
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	361.8
Water solubility (mg/l)	insoluble [1] 1.55E-03 (predicted)[4]
Vapour pressure (Pa)	1.4E-11[1]
logK_{ow}	4.2 [1,2]
Henry's constant K_H (atm*m^3/mol)	3.8E-11[1]
log K_{OC}	n.a.
Dissociation constant K_a [pK_a]	13.9[6]
Degradation	
Excretion as parent compound (%)	47 ± 6.1
Excretion as metabolite (%)	32.5 ± 14.8
Elimination Rate in conventional STPs (%)	60 ± 23.8
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	6
LC_{50} fish (µg·L^{-1})	6000
Sales/ Production volumes	
Consumption (t/a)	34.5 (France, 1998)[5] 33.5 (Germany, 2001)[3] 1.6 (Switzerland, 2000)[5]

1 Hanisch et al. 2002

2 http://chem.sis.nlm.nih.gov/chemidplus/

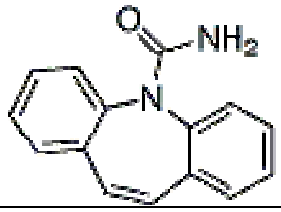
3 BLAC 2003

4 http://www.drugbank.ca/drugs/

5 Ternes & Joss 2006

6 Adam 2005

A.6 Carbamazepine

Data on priority PhAC	
Class of PhAC	Antiepileptic drug
CAS-no.	298-46-4
Molecular formula	C15-H12-N2-O
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	236.3
Water solubility (mg/l)	17.7 at 25 °C[1]
Vapour pressure (mm Hg)	1.84E-07at 25 °C[1]
$\log K_{ow}$	2.45[1]
Henry's constant K_H (atm*m^3/mol)	1.08E-10 at 25 °C[1]
log K_{OC}	n.a.
Dissociation constant K_a [pK_a]	13.4[4]
Degradation	
Excretion as parent compound (%)	7.4 ± 6.25
Excretion as metabolite (%)	51.5 ± 29.8
Elimination Rate in conventional STPs (%)	5.2 ± 6.4
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	2.5
NOEC daphnia (µg·L^{-1})	25
Sales/ Production volumes	
Consumption (t/a)	35.2 (France 1998)[3] 87.6 (Germany, 2001)[2] 4.1 (Switzerland, 2000)[3]

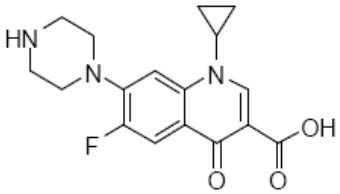
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 Ternes & Joss 2006

4 (Queiroz et al. 2008)

A.7 Ciprofloxacin

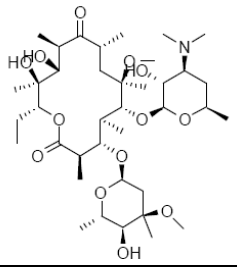
Data on priority PhAC	
Class of PhAC	Antibiotic
CAS-no.	85721-33-1
Molecular formula	C17-H18-F-N3-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	331.3
Water solubility (mg/l)	3.00E+04 at 20 °C[1]
Vapour pressure (mm Hg)	1.65E-12 at 25°C[1]
$\log K_{ow}$	0.28[1]
Henry's constant K_H (atm*m^3/mol)	5.09E-19 at 25°C[1]
$\log K_{oc}$	3.07 (K_D=416.9)[3]
Dissociation constant K_a [pK_a]	6.09[1]
Degradation	
Excretion as parent compound (%)	72.5 ± 13.4
Excretion as metabolite (%)	17.9 ± 1.3
Elimination Rate in conventional STPs (%)	68.5 ± 2.1
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	0.005
EC_{50} bacteria (µg·L^{-1})	5
Sales/ Production volumes	
Consumption (t/a)	17.9 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 (Hanisch, Abbas et al. 2002)

A.8 Clarithromycin

Data on priority PhAC	
Class of PhAC	Antibiotic (macrolide)
CAS-no.	81103-11-9
Molecular formula	C38-H69-N-O13
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	748.0
Water solubility (mg/l)	0.342 at 25°C[2]
Vapour pressure (mm Hg)	8.60E-27 at 25 °C[2]
$\log K_{ow}$	2.6[1] 3.16[2]
Henry's constant K_H (atm*m^3/mol)	1.73E-29 at 25°C[2]
$\log K_{oc}$	n.a.
Dissociation constant K_a [pK_a]	8.99 at 25°C[2]
Degradation	
Excretion as parent compound (%)	>60[6] 50[7]
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	45.3 ± 39.9
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	0.002
EC_{50} algae (µg·L^{-1})	2
Sales/ Production volumes	
Consumption (t/a)	15.104 (France)[4] 7.2 (Germany, 2001)[3] 1.4 (Switzerland, 2005)[5]

1 Hanisch et al. 2002

2 http://chem.sis.nlm.nih.gov/chemidplus/

3 BLAC 2003

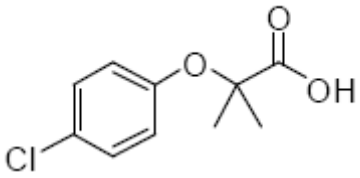
4 (Webb 2001)

5 Hollender 2007

6 Hirsch et al.19999

7 Roth & Fenner 2000

A.9 Clofibric acid (Metabolite of clofibrate, etofibrate, and etofyllinclofibrate)

Data on priority PhAC	
Class of PhAC	Lipid lowering drug
CAS-no.	882-09-7
Molecular formula	C10H11ClO3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	214.6
Water solubility (mg/l)	583 at 25°C[1]
Vapour pressure (mm Hg)	1.13E-04 at 25°C[1]
$\log K_{ow}$	2.57[1]
Henry's constant K_H (atm*m^3/mol)	2.19E-08 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant K_a [pK_a]	n.a.
Degradation	
Excretion as parent compound (%)	3 ± 4.2
Excretion as metabolite (%)	>90[3] 85[4]
Elimination Rate in conventional STPs (%)	42 ± 26
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	1
NOEC daphnia (µg·L^{-1})	10 (for clofibrate)
Sales/ Production volumes	
Consumption (t/a)	0,002 (Germany, 2001)[2] 1.8 (Germany, 1998)[2]

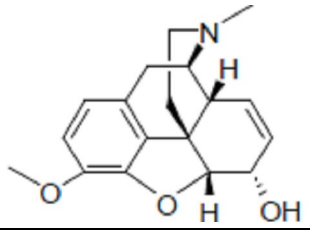
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 Ternes & Joss 2006

4 Lienert et al. 2007

A.10 Codeine

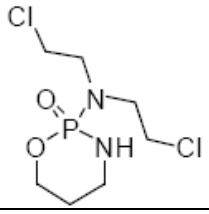
Data on priority PhAC	
Class of PhAC	Analgesic
CAS-no.	67-57-3
Molecular formula	$C_{18}H_{21}NO_3$
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	299.4
Water solubility (mg/l)	9000 at 20°C[1]
Vapour pressure (mm Hg)	4.15E-09 at 25°C[1]
$\log K_{ow}$	1.19[1] 1.14[3]
Henry's constant K_H (atm*m^3/mol)	7.58E-14 at 25°C[1]
$\log K_{oc}$	
Dissociation constant K_a [pK_a]	8.21 at 25°C[1] 10.6[3]
Degradation	
Excretion as parent compound (%)	n.a.
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	n.a.
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	9.7 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

A.11 Cyclophosphamide

Data on priority PhAC	
Class of PhAC	Anticancer
CAS-no.	50-18-0
Molecular formula	C7-H15-Cl2-N2-O2-P
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	261.1
Water solubility (mg/l)	4.00E+04 at 20 °C[1]
Vapour pressure (mm Hg)	4.45E-05 at 25°C[1]
$\log K_{ow}$	0.63[1,3]
Henry's constant K_H (atm*m^3/mol)	1.40E-11 at 25°C[1]
$\log K_{oc}$	1.72[6]
Dissociation constant K_a [pK_a]	n.a.
Degradation	
Excretion as parent compound (%)	23.8±1.8
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	<1[5]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	19680
NOEC fish (µg·L^{-1})	>984000
Sales/ Production volumes	
Consumption (t/a)	0.39 (Germany, 2001)[2] 0.033 (Switzerland, 2004)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

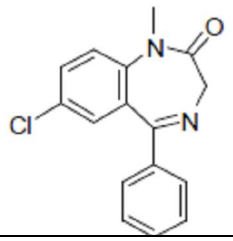
3 http://toxnet.nlm.nih.gov

4 Lienert et al. 2007

5 Halling Sörensen et al. 1998

6 (Hanisch, Abbas et al. 2002)

A.12 Diazepam

Data on priority PhAC	
Class of PhAC	Anticonvulsant, Sedative
CAS-no.	439-14-5
Molecular formula	C16-H13-Cl-N2-O
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	284.7
Water solubility (mg/l)	50 at 25 °C[1] 3000 at 25°C[3]
Vapour pressure (mm Hg)	2.78E-08 at 25°C[1]
$\log K_{ow}$	2.82[1] 2.99[3]
Henry's constant K_H (atm*m^3/mol)	3.64E-09 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant K_a [pK_a]	3.4[1,3]
Degradation	
Excretion as parent compound (%)	8[6]
Excretion as metabolite (%)	82[6]
Elimination Rate in conventional STPs (%)	no significant removal[2,5]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	0.4 (France, 1998)[4] 1.1 (Germany, 2001)[2] 0.04 (Switzerland, 2000)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

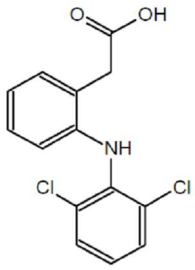
3 http://toxnet.nlm.nih.gov

4 Ternes & Joss 2006

5 Ternes et al. 2005

6 Lienert et al. 2007

A.13 Diclofenac

Data on priority PhAC	
Class of PhAC	Analgesic, Antiphlogistic
CAS-no. Diclofenac	15307-86-5
CAS-no. Diclofenac-Na	15307-79-6
Molecular formula	C14-H11-Cl2-NO2
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol) Diclofenac	296.15
Water solubility (mg/l)	2.37 at 25 °C[1,3]
Vapour pressure (mm Hg)	6.14E-8 at 25 °C[1,3]
$\log K_{ow}$	4.51[1,8]
Henry's constant K_H (atm*m^3/mol)	4.73E-12 at 25 °C[1,3]
$\log K_{oc}$	0.78 (Diclofenac-Na)[5]
Dissociation constant K_a [pK_a]	4.15[1,3]
Degradation	
Excretion as parent compound (%)	15.5 ± 0.7
Excretion as metabolite (%)	55 ± 50.7
Elimination Rate in conventional STPs (%)	35.6 ± 29.4
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	0.1
NOEC fish (µg·L^{-1})	1
Sales/ Production volumes	
Consumption (t/a)	14.9 (France, 1998)[4] 85.8 (Germany)[2] 3.8 (Switzerland, 2000)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

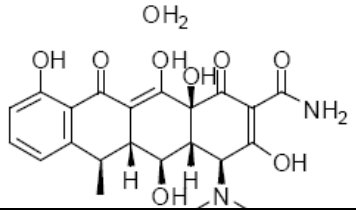
2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Ternes & Joss 2006

5 (Hanisch, Abbas et al. 2002)

A.14 Doxycycline

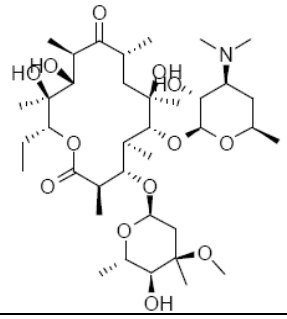
Data on priority PhAC	
Class of PhAC	Antibiotic
CAS-no.	564-25-0
Molecular formula	C22-H24-N2-O8
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	462.46
Water solubility (mg/l)	630 at 25°C[1]
Vapour pressure (mm Hg)	1.42E-23 at 25°C[1]
$\log K_{ow}$	-0.02[1]
Henry's constant K_H (atm*m^3/mol)	4.66E-24 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	>70[3]
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	n.a.
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	12.34 (Germany,2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 Hirsch et al. 1999

A.15 Erythromycin

Data on priority PhAC	
Class of PhAC	(Macrolide) antibiotic
CAS-no.	114-07-8
Molecular formula	C37-H67-N-O13
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	733.9
Water solubility (mg/l)	1.440 at 25°C[1]
Vapour pressure (mm Hg)	2.28E-27 at 25°C[1]
$\log K_{ow}$	3.06[1]
Henry's constant K_H (atm*m^3/mol)	5.42E-29 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	8.88 at 25°C[1,3]
Degradation	
Excretion as parent compound (%)	61.3 ± 51.9 >60[4]
Excretion as metabolite (%)	4[4]
Elimination Rate in conventional STPs (%)	23.2 ± 32.9
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	0.02
EC_{50} algae (µg·L^{-1})	20
Sales/ Production volumes	
Consumption (t/a)	19 (Germany, 2001)[2] 0.17 (Switzerland 1999)[5]

1 http://chem.sis.nlm.nih.gov/chemidplus/

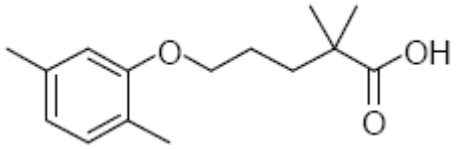
2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Lienert et al. 2007

5 Giger 2005

A.16 Gemfibrozil

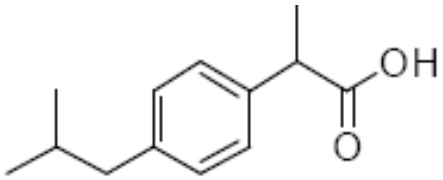
Data on priority PhAC	
Class of PhAC	Lipid Regulator
CAS-no.	25812-30-0
Molecular formula	C15-H22-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	250.3
Water solubility (mg/l)	n.a.
Vapour pressure (mm Hg)	n.a.
$\log K_{ow}$	4.770[1]
Henry's constant K_H (atm*m^3/mol)	n.a.
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	6[3]
Excretion as metabolite (%)	40 ± 14.1
Elimination Rate in conventional STPs (%)	50 ± 26.9
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	5.2 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 Lienert et al. 2007

A.17 Ibuprofen

Data on priority PhAC	
Class of PhAC	Antirheumatic agent, Analgesic
CAS-no.	15687-27-1
Molecular formula	C13-H18-O2
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	206.3
Water solubility (mg/l)	21 at 25 °C[1,3]
Vapour pressure (mm Hg)	1.35E-03[5] 1.86E-04 at 25°C[1]
$\log K_{ow}$	3.97[1,3]
Henry's constant K_H (atm*m^3/mol)	1.50E-07 at 25°C[1]
$\log K_{oc}$	4.06[5]
Dissociation constant Ka [pKa]	4.91[1,3] 5.2[3]
Degradation	
Excretion as parent compound (%)	11.8 ± 15.8
Excretion as metabolite (%)	62 ± 43
Elimination Rate in conventional STPs (%)	81.5 ± 18.6
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	60
NOEC daphnia (µg·L^{-1})	3000
Sales/ Production volumes	
Consumption (t/a)	166.2 (France, 1998)[4] 344.9 (Germany, 2001)[2] 15.7 (Switzerland, 2000)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

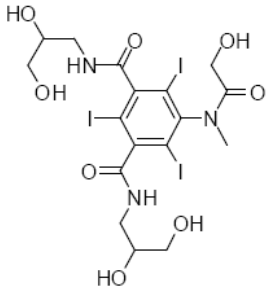
2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Ternes & Joss 2006

5 (Hanisch, Abbas et al. 2002)

A.18 Iomeprol

Data on priority PhAC	
Class of PhAC	Contrast media
CAS-no.	78649-41-9
Molecular formula	C17-H22-I3-N3-O8
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	777.1
Water solubility (mg/l)	n.a.
Vapour pressure (mm Hg)	n.a.
$\log K_{ow}$	n.a.
Henry's constant K_H (atm*m^3/mol)	n.a.
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	100[3]
Excretion as metabolite (%)	-
Elimination Rate in conventional STPs (%)	0[4]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	83.4 (Germany, 2001)[1] 1.7 (Switzerland 2004)[2]

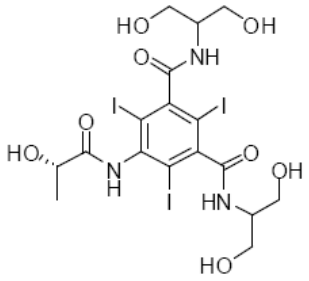
1 BLAC 2003

2 Lienert et al. 2007

3 LANUV 2007

4 Ternes & Hirsch 2000

A.19 Iopamidol

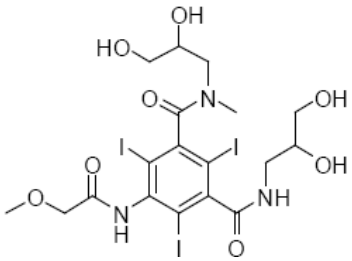
Data on priority PhAC	
Class of PhAC	Contrast media
CAS-no.	62883-00-5
Molecular formula	$C_{17}H_{22}I_3N_3O_8$
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	777.08
Water solubility (mg/l)	n.a.
Vapour pressure (mm Hg)	n.a.
$\log K_{ow}$	n.a.
Henry's constant K_H (atm*m^3/mol)	n.a.
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	100[2]
Excretion as metabolite (%)	-
Elimination Rate in conventional STPs (%)	0[3]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	42.9 (Germany, 2001)[1]

1 BLAC 2003

2 LANUV 2007

3 Ternes & Hirsch 2000

A.20 Iopromide

Data on priority PhAC	
Class of PhAC	X-ray contrast media
CAS-no.	73334-07-3
Molecular formula	C18-H24-I3-N3-O8
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	791.1
Water solubility (mg/l)	23.8 at 25°C[1]
Vapour pressure (mm Hg)	1.59E-28 at 25°C[1]
$\log K_{ow}$	-2.05E+00[1]
Henry's constant K_H (atm*m^3/mol)	1.00E-28 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	100[3]
Excretion as metabolite (%)	-
Elimination Rate in conventional STPs (%)	0[6]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	100000
NOEC daphnia (µg·L^{-1})	1000000
Sales/ Production volumes	
Consumption (t/a)	73.4 (France, 1998)[4] 64.1 (Germany, 2001)[2] 5.3 (Switzerland 2003)[5]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

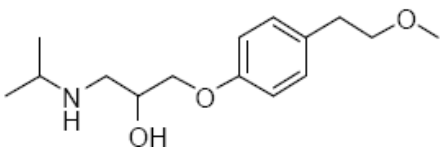
3 LANUV 2007

4 Ternes & Joss 2006

5 Blüm at al. 2005

6 Ternes & Hirsch 2000

A.21 Metoprolol

Data on priority PhAC	
Class of PhAC	Beta blocker
CAS-no.	37350-58-6
Molecular formula	C15-H25-N-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	267.4
Water solubility (mg/l)	1.69E+04 at 25°C[1]
Vapour pressure (mm Hg)	2.88E-07 at 25°C[1]
$\log K_{ow}$	1.88[1,3]
Henry's constant K_H (atm*m^3/mol)	1.40E-13 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	9.7[4]
Degradation	
Excretion as parent compound (%)	8 ± 2.6
Excretion as metabolite (%)	85.5 ± 0.7
Elimination Rate in conventional STPs (%)	68.5 ± 2.1
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	7.3
EC_{50} algae (µg·L^{-1})	7300
Sales/ Production volumes	
Consumption (t/a)	93 (Germany, 2001)[2]

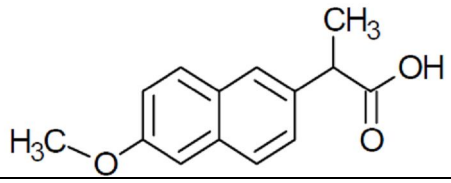
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 (Hanisch, Abbas et al. 2002)

A.22 Naproxen

Data on priority PhAC	
Class of PhAC	Analgesic, Antiphlogistic
CAS-no.	22204-53-1
Molecular formula	C14-H14-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	230.3
Water solubility (mg/l)	15.9 at 25°C[2]
Vapour pressure (mm Hg)	1.89E-06 at 25°C[2]
$\log K_{ow}$	3.0[1] 3.18[2]
Henry's constant K_H (atm*m^3/mol)	3.39E-10 at 25°C[2]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	4.15[2,4]
Degradation	
Excretion as parent compound (%)	10[1]
Excretion as metabolite (%)	88[1]
Elimination Rate in conventional STPs (%)	69 ± 20.8
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	28
EC_{50} daphnia (µg·L^{-1})	140000
Sales/ Production volumes	
Consumption (t/a)	37.3 (France)[10] 5 (Germany)[3]

1 Hanisch et al. 2002

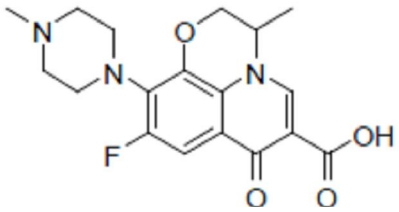
2 http://chem.sis.nlm.nih.gov/chemidplus/

3 BLAC 2003

4 http://toxnet.nlm.nih.gov

5 Webb 2001

A.23 Ofloxacin

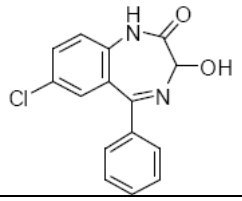
Data on priority PhAC	
Class of PhAC	Antibiotic
CAS-no.	82419-36-1
Molecular formula	C18-H20-F-N3-O4
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	361.4
Water solubility (mg/l)	2.83E+04 at 25°C[1]
Vapour pressure (mm Hg)	1.55E-13 at 25 °C[1]
$\log K_{ow}$	-0.39[1]
Henry's constant K_H (atm*m^3/mol)	4.98E-20 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	n.a.
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	57[3]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	2.3 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 Castiglioni et al. 2006

A.24 Oxazepam

Data on priority PhAC	
Class of PhAC	Anticonvulsant, Sedative
CAS-no.	604-75-1
Molecular formula	C15-H11-Cl-N2-O2
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	286.7
Water solubility (mg/l)	179 at 25°C[1] 200 at 22 °C[3]
Vapour pressure (mm Hg)	3.76E-12 at 25 °C[1] 4.2E-12 at 25 °C[3]
$\log K_{ow}$	2.24[1,8]
Henry's constant K_H (atm*m^3/mol)	5.53E-10 at 25 °C[1,3]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	1.55 (-C=N-)[3]
Degradation	
Excretion as parent compound (%)	n.a.
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	n.a.
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	6.2 (France)[4] 1.1 (Germany, 2001)[2]

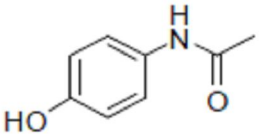
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Webb 2001

A.25 Paracetamol

Data on priority PhAC	
Class of PhAC	Analgesic
CAS-no.	103-90-2
Molecular formula	C8-H9-N-O2
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	151.2
Water solubility (mg/l)	1.40E+04 at 25°C[1,3]
Vapour pressure (mm Hg)	7.00E-06 at 25°C[1] 6.29E-5 at 25 °C[3]
$\log K_{ow}$	0.46[1] 0.27[6]
Henry's constant K_H (atm*m^3/mol)	6.42E-13 at 25°C[1,3]
$\log K_{oc}$	0.14[7]
Dissociation constant Ka [pKa]	9.38[1,3]
Degradation	
Excretion as parent compound (%)	5.25 ± 1.8
Excretion as metabolite (%)	84.5 ± 7.8
Elimination Rate in conventional STPs (%)	96.7 ± 4.9
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	46
EC_{50} daphnia (µg·L^{-1})	9200
Sales/ Production volumes	
Consumption (t/a)	3303 (France)[4] 654 (Germany, 2001)[2] 128 (Switzerland, 2004)[5]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

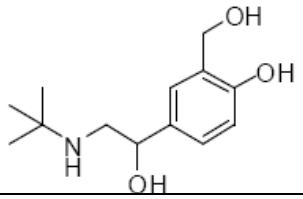
4 Webb 2001

5 Lienert et al. 2007

6 (Yamamoto, Hayashi et al. 2005)

7 (Hanisch, Abbas et al. 2002)

A.26 Salbutamol (Albuterol)

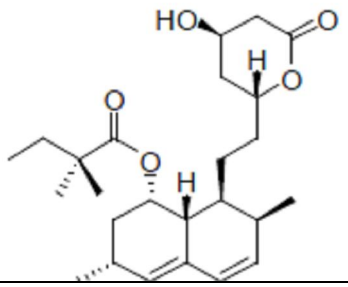
Data on priority PhAC	
Class of PhAC	Bronchodilator
CAS-no.	18559-94-9
Molecular formula	C13-H21-NO3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	239.3
Water solubility (mg/l)	1.43E+4[1,3]
Vapour pressure (mm Hg)	8.9E-9 at 25 °C[3]
$\log K_{ow}$	0.640[1,3]
Henry's constant K_H (atm*m^3/mol)	6.4E-16at 25 °C[3]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	9.2 (amine nitrogen)[3]; 10.7 (phenolic -OH)[3]
Degradation	
Excretion as parent compound (%)	n.a.
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	59.5 ± 51.8
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	0.46 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

A.27 Simvastatin

Data on priority PhAC	
Class of PhAC	Antihyperlipidemic
CAS-no.	79902-63-9
Molecular formula	C25-H38-O5
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	418.56
Water solubility (mg/l)	0.765 at 25°C[1,3]
Vapour pressure (mm Hg)	6.41E-13 at 25°C[1,3]
$\log K_{ow}$	4.68[1,3]
Henry's constant K_H (atm*m^3/mol)	2.81E-10 at 25°C[1,3]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	n.a.
Excretion as metabolite (%)	n.a.
Elimination Rate in conventional STPs (%)	n.a.
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test (µg·L^{-1})	n.a.
Sales/ Production volumes	
Consumption (t/a)	6.9 (France)[4] 0.34 (Germany, 2001)[2]

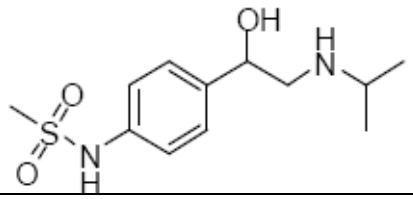
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Webb 2001

A.28 Sotalol

Data on priority PhAC	
Class of PhAC	Beta-Blocker
CAS-no.	3930-20-9
Molecular formula	C12-H20-N2-O3-S
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	272.4
Water solubility (mg/l)	5510 at 25°C[1]
Vapour pressure (mm Hg)	5.30E-09 at 25°C[1]
$\log K_{ow}$	0.24[1]
Henry's constant K_H (atm*m^3/mol)	2.49E-14 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	n.a.
Degradation	
Excretion as parent compound (%)	91.25 ± 11.8
Excretion as metabolite (%)	0[4,5]
Elimination Rate in conventional STPs (%)	40-50[3]
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	n.a.
test	n.a.
Sales/ Production volumes	
Consumption (t/a)	26.7 (Germany, 2001)[2]

1 http://chem.sis.nlm.nih.gov/chemidplus/

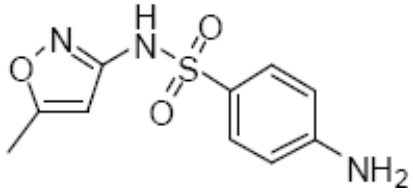
2 BLAC 2003

3 MUNLV 2006

4 Lienert et al. 2007

5 LANUV 2007

A.29 Sulfamethoxazole

Data on priority PhAC	
Class of PhAC	Antibiotic (Sulfonamide)
CAS-no.	723-46-6
Molecular formula	C10-H11-N3-O3-S
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	253.3
Water solubility (mg/l)	610 at 37 °C[1,3]
Vapour pressure (mm Hg)	6.93E-8 at 25 °C[1,3]
$\log K_{ow}$	0.89[1,8]
Henry's constant K_H (atm*m^3/mol)	6.42E-13 at 25 °C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	pKa1 = 1.6[8]; pKa2 = 5.7[3]
Degradation	
Excretion as parent compound (%)	19.2 ± 3.8
Excretion as metabolite (%)	76.5 ± 2.1
Elimination Rate in conventional STPs (%)	37 ± 18.4
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	0.1
NOEC duckweed (µg·L^{-1})	10
Sales/ Production volumes	
Consumption (t/a)	22.4 (France, 1998)[4] 53.6 (Germany, 2001)[2] 2.5 (Switzerland, 2000)[4]

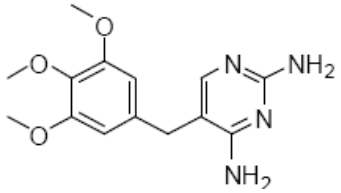
1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Ternes & Joss 2006

A.30 Trimethoprim

Data on priority PhAC	
Class of PhAC	Antibiotic
CAS-no.	738-70-5
Molecular formula	C14-H18-N4-O3
Physical-chemical parameters	
Structural formula	
Molecular weight (g/mol)	290.3
Water solubility (mg/l)	400 at 25 °C[1,3]
Vapour pressure (mm Hg)	9.88E-09 at 25°C[1]
$\log K_{ow}$	0.91[1,3]
Henry's constant K_H (atm*m^3/mol)	2.39E-14 at 25°C[1]
$\log K_{oc}$	n.a.
Dissociation constant Ka [pKa]	7.12[1,3]
Degradation	
Excretion as parent compound (%)	58.3 ± 7.6
Excretion as metabolite (%)	10-20[5]
Elimination Rate in conventional STPs (%)	n.a.
Ecotoxicity **(PNEC and toxicological test which leads to PNEC value in (µg·L^{-1})**	
PNEC (µg·L^{-1})	3
LC_{50} fish (µg·L^{-1})	3000
Sales/ Production volumes	
Consumption (t/a)	11.4 (Germany, 2001)[2] 0.7 (Switzerland, 2003)[4]

1 http://chem.sis.nlm.nih.gov/chemidplus/

2 BLAC 2003

3 http://toxnet.nlm.nih.gov

4 Blüm at al. 2005

5 Adam 2005

Appendix B

Analytical Methods of the Monitoring Campaigns

B.1 Berlin

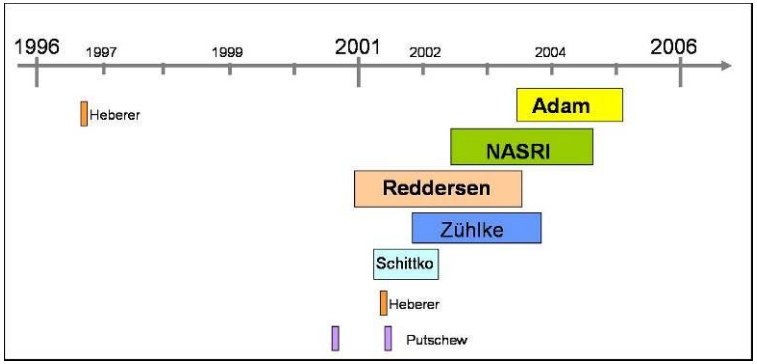


Table 19 Information about analytical methods, limit of detection (LOD), and limit of quantification (LOQ) used in the different monitoring campaigns in Berlin.

Campaign	Analytical Method	Analysed Compound	LOD (ng/L)	LOQ (ng/L)	Reference
Marc Adam	for methods see Reddersen, K.	Acetyl-salicylic-acid, atenolol, bezafibrate, carbamazepine, ciprofloxacin, clarithromycin, clofibric acid, codeine, cyclophosphamide, diazepam, diclofenac, erythromycin-H2O, gemfibrozil, ibuprofen, naproxen, ofloxacin, oxazepam, paracetamol, salbutamol, acetyl-sulfamethoxazole, sulfamethoxazole, trimethoprim	see Reddersen	see Reddersen	(Reddersen and Heberer 2003)

Campaign	Analytical Method	Analysed Compound	LOD (ng/L)	LOQ (ng/L)	Reference
NASRI	1. SPE, derivatisation (PfBBr/MTBSTFA), detection by GC-MS with SIM 2. for antibiotics: SPE, two step elution (1. acetonitrile 2. acetonitrile/water/triethylamine) , high performance liquid chromatography with positive electrospray ionization and tandem mass spectrometic detection (LC/ESI-MS/MS)	bezafibrate carbamazepine clofibric acid diclofenac gemfibrozil ibuprofen naproxen oxazepam all antibiotics	n.a. n.a. n.a. n.a. n.a. n.a. n.a. n.a. n.a.	50 5 10 5 5 5 5 20 n.a.	Non antibiotics: (Reddersen and Heberer 2003) Antibiotics: (Jekel and Heberer 2005)
Reddersen, K.	1. Method Solid phase extraction (SPE), chem. derivation with pentafluorobenzyl bromide (PFBBr), detection by GC-MS with selected ion monitoring (SIM) 2. Method: SPE, chem. derivatisation with N-(t-butyldimethylsilyl)-N-methyltrifluoro-acetamide (MTBSTFA), detection by GC-MS with SIM	bezafibrate clofibric acid (1.Method) (2.Method) diclofenac (1.Method) (2.Method) gemfibrozil (1.Method) (2.Method) ibuprofen (1.Method) (2.Method) naproxen (1.& 2. Method) carbamazepine (2.Method) oxazepam (2.Method)	n.a. <1 5 <1 1 <1 1 1 <1 <1 <1 5	n.a. 2 20 1 4 2 4 4 1 1 2 20	(Reddersen and Heberer 2003; Reddersen 2004)
Zühlke, S.	SPE, LC/MSMS	carbamazepine	3	50	(Zühlke 2004)
Schittko, S.	SPE, LC/MSMS	iopromide amidotrizoic acid iopamidol	n.a. n.a. n.a.	20 50 20	(Schittko, Putschew et al. 2004)

Campaign	Analytical Method	Analysed Compound	LOD (ng/L)	LOQ (ng/L)	Reference
Heberer, Th. (2001)	n.a.	clofibric acid diclofenac bezafibrate carbamazepine	1 to 10		(Heberer, Verstraeten et al. 2001)
Heberer, Th. (1998)	see Reddersen	clofibric acid diclofenac ibuprofen	see Reddersen	see Reddersen	(Heberer, Schmidt-Bäumler et al. 1998)
Putschew, Jekel	SPE, HPLC-MS-MS with SIM	Iopromide Amidotrizoic acid	4 4	n.a. n.a.	(Putschew and Jekel 2001)

B.2 Canton Zurich

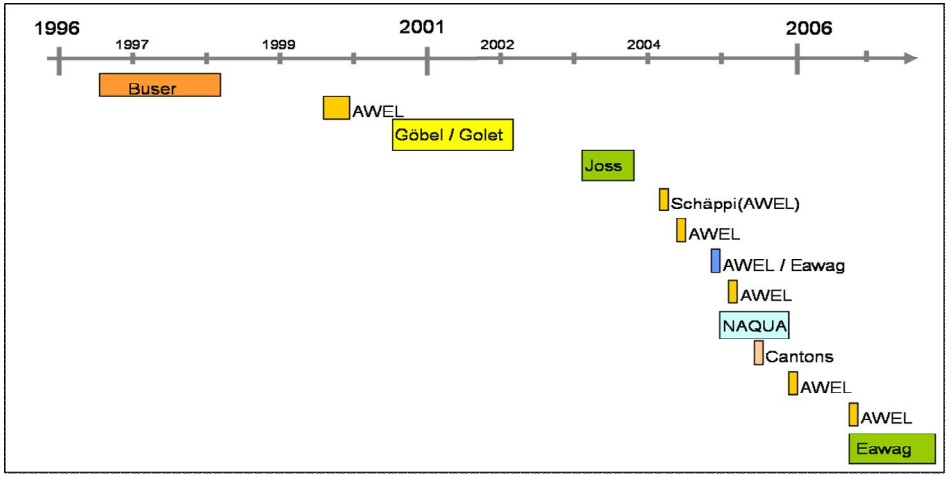


Table 20 Information about analytical methods, limit of detection (LOD), and limit of quantification (LOQ) used in the different monitoring campaigns in the Canton (not for all campaigns information were available).

Campaign	Analytical Method	Analysed Compound	LOD (ng/L)	LOQ (ng/L)	Reference (Method)
Buser	1. SPE, HRGC-MS with SIM 2. SPE, GC-MS with SIM 3. SPE, GC-MS with SIM	clofibric acid (1) diclofenac (2) ibuprofen (3)	n.a. <10 <1	n.a.	(Buser, MÃ¼ller et al. 1998b) (Buser, Poiger et al. 1998a) (Buser, Poiger et al. 1999)
Golet		ofloxacin ciprofloxacin	5 2.5	17 9	(Golet 2002a)
Göbel	HPLC-MS	clarithromycin erythromycin-H2O sulfamethoxazole n4-acetyl-sulfamethoxazole trimethoprim		2 6 11 22 4	(Göbel 2004a)
Joss	1. SPE, LC-MS 2.SPE, GC/MC with SIM 3.SPE GC/MS	1.Iopromide 2.diclofenac, ibuprofen, naproxen 3.carbamazepine	n.a. n.a. n.a.	n.a. n.a. n.a	1.(Hirsch et al. 2000; Ternes et al. 2005) 2.(Ternes et al. 1998; Ternes, Bonerz et al. 2005)
Schäppi	1. GC-MS 2.HPLC-ESI-MS-MS 3.HPLC-ESI-MS-MS 4&5.HPLC-ESI-MS-MS	1analgesics, antipyretics, antiphlogistics, lipid lowering drug antiepileptic 2.analgesics, beta blocker, bronchodilator, cytostatics, lipid lowering drug 3.radio contrast agents 4/5. antibiotics	n.a. n.a. n.a. n.a.	n.a. n.a. n.a. n.a.	(Sacher, Lange et al. 2001)

Campaign	Analytical Method	Analysed Compound	LOD (ng/L)	LOQ (ng/L)	Reference (Method)
Awel/Eawag Oct 2004	1&2.. LC-MS-MS 3. TZW Karlsruhe	1.macrolides 2.sulfonamide antibiotic 3.radio contrast agents		STP eff 10/ SW 2 STP eff5/ SW2 STP eff 50/ SW10	1&2. (Göbel et al. 2004b) 3. (Sacher, Lange et al. 2001) (Blüm, McArdell et al. 2005)
Awel Nov 2004	LC-MS/MS (TZW Karlsruhe)	78 compounds	n.a.	n.a.	(AWEL 2005)
NAQUA	analysed at TZW Karlsruhe	1.diclofenac, ibuprofen, naproxen, bezafibrate, clofibric acid, gemfibrozil, symvastatin, carbamazepine, diazepam, atenolol, metoprolol, sotalol, salbutacyclophosphamide, amidotrizoic acid, iomeprol, iopamidol, iopromide, sulfamethoxazole, clarithromycin, erythromycin 2. ciprofloxacin, ofloxacin, amoxicillin, trimethoprim		10 20	(Sacher, Lange et al. 2001; Hanke, Singer et al. 2007)