A New Approach to Calculate EMEA's Predicted Environmental Concentration for Human Pharmaceuticals in Groundwater at Bank Filtration Sites

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Abstract In recent years, human pharmaceutical substances have been increasingly detected in the aquatic environment. Specific attention has been drawn to the occurrence of pharmaceutical substances at bank filtration sites which are used for drinking water production. In the course of the authorisation application for new pharmaceutical compounds, an environmental risk assessment is required. Currently, the expected concentration of the human pharmaceutical compound in groundwater at bank filtration sites is calculated following the guideline *Pre-Authorisation Evaluation of Medicines for Human Use* issued by the European Medicines Agency (EMEA 2006). A simple estimation is applied: The predicted environmental concentration (PEC_{GW}) is the predicted environmental concentration in surface water (PEC_{SW}) multiplied with 0.25. A new approach considering the hydraulic and hydrogeological characteristics of bank filtration sites as well as transport processes is presented in this study. First, a numerical groundwater flow model was developed to simulate the groundwater flow processes at bank filtration sites in general. Flow times were calculated as a function of the hydraulic and hydrogeological parameters: hydraulic conductivity, shore-well distance, screen depth and extraction rate. In a second step, the PEC_{GW} was calculated based on the compound concentration in surface water and the modelled groundwater flow times considering linear sorption and first-order decay. Sorption and degradation can only be calculated based on the data provided by the pharmaceutical company in the course of the authorisation application. The current approach following the EMEA guideline invariably connects the PEC_{GW} with the PEC_{SW} without considering sorption and/or degradation processes. We introduce an approach that incorporates the hydraulic process bank filtration and the main transport processes sorption and degradation. The new approach is compound specific as well as aquifer, flow and transport specific resulting in a more realistic PEC_{GW} value compared to the old approach.

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1 Introduction

Since the early 1990s, human pharmaceutical substances have been detected in the aquatic environment in surface, ground and drinking water as well as in sewage effluent (Engelmann and Rohde 2009; Halling-Sorensen et al. 1998; Heberer 2002a). Pharmaceutical compounds reach the groundwater via different paths (Fig. 1). A significant amount of pharmaceuticals is excreted as parent products or their metabolites; another part is directly disposed into the toilet. In both cases, pharmaceuticals end up in the sewage system. Leakages may lead to a direct infiltration of sewage into the groundwater (Fenz et al. 2005).

In many cases, pharmaceutical compounds are not completely eliminated in sewage treatment plants (STPs), and the substances are discharged after treatment into the surface water (Halling-Sorensen et al. 1998; Heberer 2002b). During influent aquifer conditions and at bank filtration sites, pharmaceutical substances can reach the groundwater. If this groundwater is used for drinking water purposes, pharmaceuticals may be detected in drinking water. Heberer (2002a) reported pharmaceutically active compounds in groundwater and drinking water samples from water works using bank filtration or artificial groundwater recharge downstream from municipal STPs. The application of sewage sludge in agriculture, the irrigation of sewage and the disposal of pharmaceutical substances at landfills are further sources for (human) pharmaceuticals in groundwater.

During the process of bank filtration, surface water infiltrates the aquifer and the filtrate is extracted at groundwater extraction wells for drinking water production. In Germany, approximately 16% of the drinking water is produced from bank filtration (Schmidt et al. 2004). Research studies at bank filtration sites in the Berlin area show that some pharmaceutical substances such as carbamazepine or primidone are not removed during the subsurface passage (Massmann et al. 2007).

The European Commission has stated in the Council Directive 2001/83/EC (EC 2001) that an environmental impact assessment has to be performed in the course of the marketing authorisation application for new medicinal products for human use. This finally led to the *Guideline on the environmental risk assessment of medicinal products for human use* published by the European Medicines Agency (EMEA 2006). However, the studies during the marketing authorisation application focus in particular on toxicological issues such as acute, subacute and chronic toxicity of adverse effects for a new pharmaceutical substance on the human body (von Keutz and Jekat 1998). The guideline states that an environmental impact should not constitute a criterion for refusal of a marketing authorisation of medicinal products for human use (EMEA 2006). Furthermore, for the pharmaceutical substances, which already have a marketing authorisation, an environmental risk assessment is not requested by the regulatory agencies.

The EMEA guideline is based on the comparison between the predicted environmental concentration (PEC) and the predicted no-effect concentration (Liebig et al. 2006). The stepwise assessment includes the estimation of exposure, the initial prediction of risk, the substance and compartment-specific refinement and the risk assessment. The first phase (phase I) comprises the estimation of exposure and includes the estimation of the PEC_{SW}. The trigger for the performance of a phase II is 0.01 μg/L for the PEC_{SW}. The second phase (phase II) is the environmental risk assessment which is divided in two parts, so-called tier A and tier B. Tier A is the initial prediction of risk, based on a base set of aquatic toxicology and fate data. Tier B includes a substance and compartment-specific refinement and risk assessment, based on an extended data set on emission, fate and effects.

Within the phase II of the environmental risk assessment following the EMEA guideline, an input into groundwater is assumed via bank filtration (EMEA 2006). Therefore, a predicted environmental concentration in groundwater (PEC_{GW}) has to be calculated. The PEC_{GW} is based on the predicted environmental concentration in surface water (PEC_{SW}) using the simple equation

$$PEC_{GW} = 0.25 \times PEC_{SW} \qquad (1)$$

In this equation, the PEC_{GW} is invariably connected to the PEC_{SW} without considering groundwater flow situation or transport behaviour of the pharmaceutical compound. Thus, the aim of the present study was to
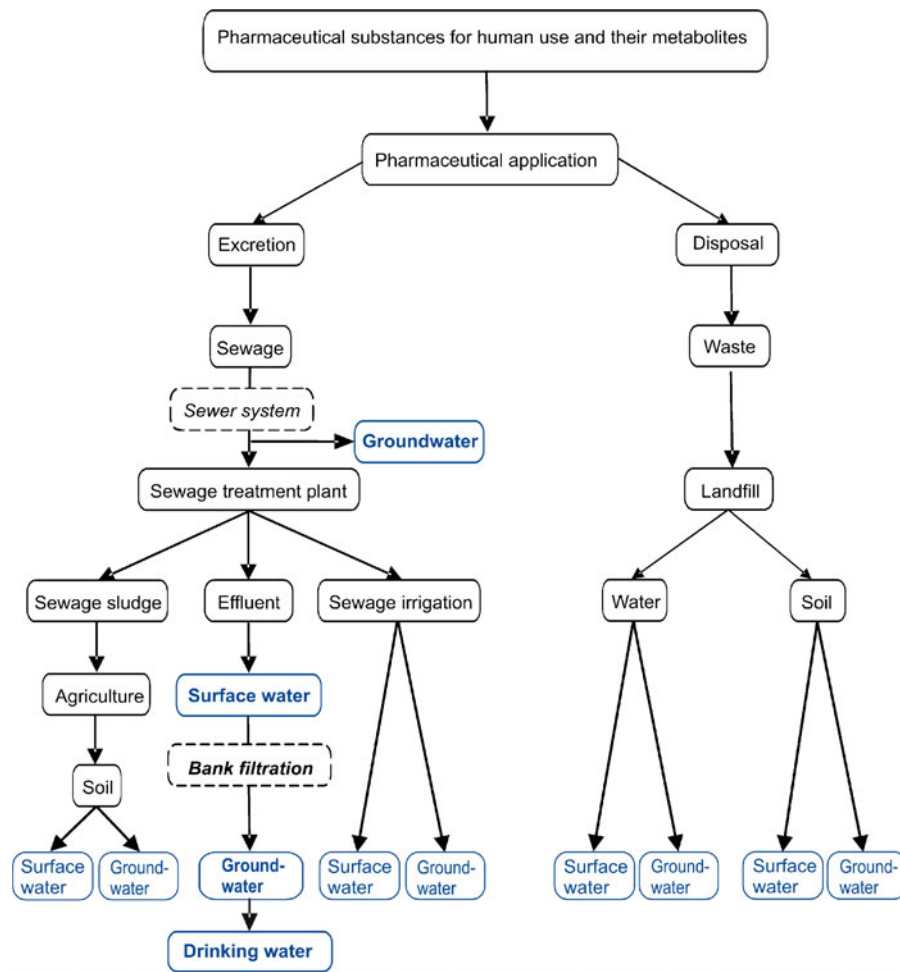
Fig. 1 Input paths into the aquatic environment for human pharmaceuticals

find a compound-specific approach of calculating the PEC_{GW}, based on general hydraulic and hydrogeological conditions at bank filtration sites and the limited sorption and degradation parameters provided by the pharmaceutical companies in the course of an application for marketing authorisation for new pharmaceutical substances (Zippel et al. 2009).

2 Transport Processes During Bank Filtration

Bank filtration is a specifically designed technique to produce drinking water. Groundwater extraction wells are installed on the shore of surface water bodies, and an artificial gradient between surface water and groundwater level induces infiltration of surface water into the aquifer. The physical and chemical transport processes in the aquifer improve the quality of the filtrate (Ray et al. 2002; Hiscock and Grischek 2002).

Due to its nature, the process of bank filtration is limited to the strip between the shore line and the extraction well and to sites comprising a porous aquifer with good hydraulic conductivity. In central Europe, the majority of river bank filtration plants are located along the rivers Danube, Elbe and Rhine (Ray et al. 2002). In Germany, bank filtration is successfully applied for more than 100 years, mostly at the rivers Rhine, Elbe, and in the Berlin area at the rivers Havel and Spree and several lakes (Eckert and Irmscher 2006; Fritz 2003; Lenk et al. 2006).

The occurrence and concentration of pharmaceutical compounds in groundwater wells depend not only on the concentrations in river and its fluctuation but also on the advective transport of the substance and on the reactions along the flow path. The main attenuation processes during bank filtration are diffusion, dilution, dispersion, mixing, biodegradation and sorption occurring within the colmation layer and the aquifer itself (Hiscock and Grischek 2002).

The ratio between the concentration sorbed onto the aquifer sediment and the dissolved solute concentration in water at equilibrium conditions is referred to as a sorption isotherm. The simplest case of an isotherm with a linear correlation between the dissolved and sorbed substance concentration is described by the Henry isotherm.

$$c_{sorb} = K_d \times c_w \qquad (2)$$

c_{sorb} concentration of the substance sorbed onto solid (milligrams per kilogram)
c_w substance concentration in groundwater (milligrams per litre)
K_d Henry sorption coefficient (litres per kilogram)

Sorption depends on the organic carbon content of the aquifer material. By normalizing the sorption coefficient with the organic carbon fraction, a significant reduction of variability is achieved applying the equation

$$K_{OC} = \frac{K_d}{f_{OC}} \qquad (3)$$

K_{OC} partition coefficient with respect to the organic carbon fraction (–)
f_{OC} organic carbon fraction (weight percent)

Scheytt et al. (2006) have shown that even at low organic carbon contents in the aquifer sediment, sorption processes are relevant for the transport of pharmaceutical substances. Beside the organic carbon content of the aquifer material, other parameters such as the mineral content of the sediment or the physicochemical properties of the groundwater (pH, ionic strength) are important for sorption processes.

Retardation is the reduced mobility of a solute in the aquifer at a velocity less than that of the flowing groundwater due to sorption processes. The retardation factor is described by the equation

$$R_f = 1 + \frac{(1-n)}{n} \times \rho_S \times K_d \qquad (4)$$

R_f retardation factor (–)
n porosity (–)
ρ_S solid density (grams per cubic centimetre)

Since only few data on the fate of human pharmaceuticals in the aquifer are available, a focus of the investigations during the past years was the degradation behaviour of pharmaceutical substances. Several laboratory and field studies on the degradation behaviour of pharmaceutical substances for human use in the saturated and unsaturated aquifer zone applying first-order kinetics were performed (Andreozzi et al. 2004; Kunkel and Radke 2008; Loeffler et al. 2005; Scheytt et al. 2006). Loeffler et al. (2005) investigated the environmental fate of ten selected pharmaceuticals in water/sediment systems including both the analysis of water and sediment.

Due to the lack of sufficient data, degradation of pharmaceutical substances in groundwater is often described using a first-order kinetic equation.

$$c = c_0 \times e^{-\lambda \times t_{compound}} \qquad (5)$$

$$\lambda = \frac{\ln 2}{DT_{50}} \qquad (6)$$

c concentration at production well (nanograms per litre)
c_0 surface water concentration (nanograms per litre)
λ decay constant (1 per day)
$t_{compound}$ residence time for the compound (days)
DT_{50} disappearance time of 50% of the compound; here used as half-life time of the compound (days)

3 Method

The general approach for the development of a calculation tool for PEC_{GW} was a stepwise process.

Starting point is the PEC_{SW}, the initial pharmaceutical concentration in surface water. PEC_{SW} is calculated by applying a formula provided in the EMEA guideline, which incorporates the maximum daily dose consumed per inhabitant, the percentage of market penetration, the amount of wastewater per inhabitant per day and a dilution factor.

The aim of the first phase of the study was to construct a groundwater flow model, which does not display one specific site but bank filtration sites in central Europe in general. The groundwater flow model has to consider the geometry of bank filtration sites as well as hydraulic and hydrogeological parameters.

In the second phase, transport processes were considered. The data provided in the application process include values on K_d, K_{OC} and DT_{50}. With these data, sorption and degradation occurring during the transport of the pharmaceutical substance from the shore line to the groundwater extraction well were incorporated in the approach. The available data on the environmental behaviour of new pharmaceutical substances provided in the course of the marketing authorisation define the limits of incorporating transport processes. Finally, it was necessary to combine the results of both phases and to develop a user-friendly computer interface for the estimation of the PEC_{GW} considering the transport time, sorption and degradation (Fig. 2).

3.1 Groundwater Flow Model for Bank Filtration Sites

Based on the evaluation results of available literature (Grischek 2003; Massmann et al. 2008a; HYDOR 2004, 2007; Lenk et al. 2006) and unpublished data of bank filtration sites in central Europe, the variety of hydraulic and hydrogeological parameters typical for bank filtration sites was compiled (Table 1). All bank filtration sites are located in the vicinity of surface water bodies, and the wells are screened in medium to highly permeable unconsolidated sediments. Therefore, geological and hydrogeological properties of the aquifer and the hydraulic settings are quite comparable at all bank filtration sites. The distance between surface water body and the extraction wells varies between 1.5 and 1.00 km, and screen depths reach from 4 to 70 m. Extraction rates are often difficult to acquire, but results from the Berlin area show typical values between 500 and 5,000 m^3/day per extraction well (HYDOR 2004, 2007).

The above-mentioned characteristics that are quite comparable at different bank filtration sites in central Europe do not apply for groundwater flow conditions. Note, data on groundwater flow times are generally rare, although they are essential for describing the solute transport in groundwater. Here, numerical groundwater flow models are capable of calculating these flow times and their variability.

In the present study, a steady-state groundwater flow model was developed using the program code VISUAL MODFLOW (Fig. 3). A horizontal discretization with a 5×5-m grid and a vertical discretization with 20 model aquifer layers with a continuous thickness of 5 m were applied. The river bed has a width of 30 m and was set as a river boundary condition in the groundwater flow model.

The parameters hydraulic conductivity, extraction rate, depth of filter screen and well-shore distance for European bank filtration sites, which characterize the groundwater flow regime, were varied stepwise within defined ranges (Table 2).

The following parameters were set to default values:

- Length of the filter screen—10 m
  This screen length is a mean value for the water works in the Berlin area (HYDOR 2004, 2007). The screen lengths are controlled by the saturated thickness of the aquifer and the desired pump design. Schubert (2002) reports screen lengths for the Lower Rhine Valley of 10 to 15 m.
- Hydraulic conductivity of clogging layer—$1×10^{-5}$ m/s for the river bed area between 0 and 20 m (near to the extraction well) and to $1×10^{-6}$ m/s for the river bed area between 21 and 30 m
  These are again mean values from literature (e.g. Massmann et al. 2008b; Grischek 2003; Doppler et al. 2007).
- Total porosity—0.35, effective porosity—0.2
- The horizontal K_{xx} and vertical K_{zz} hydraulic conductivities are assumed to be constant in each layer. Their ratio $\varepsilon = K_{xx}/K_{zz}$ is the anisotropy coefficient. The anisotropy coefficient was set to a value of 2

In contrast to the diffusive input of pesticides via the land surface, the input of human pharmaceuticals from the surface water can be regarded as a linear source. The effect of dilution is incorporated in the PC-based decision matrix.
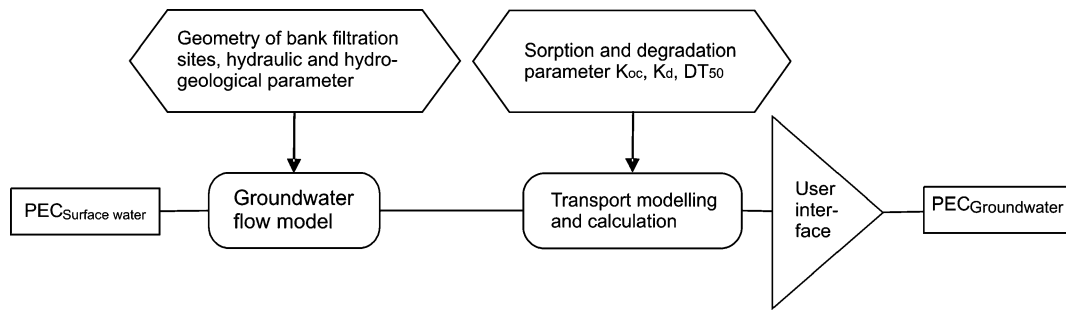
Fig. 2 General approach for development of a calculation tool for PEC$_{GW}$

3.2 Analytical Calculation of PEC$_{GW}$

After the development of the groundwater flow model, it was necessary to incorporate the transport processes sorption and degradation occurring during the transport of the pharmaceutical substance from the shore line to the groundwater extraction well. The environmental assessment according to the EMEA guideline only includes the determination of the distribution coefficients K_d, occasionally the Freundlich sorption isotherm K_F, the partition coefficient normalized by the organic fraction K_{OC} and the disappearance time DT$_{50}$ for the system sediment/water.

Several method descriptions for the determination of the sorption and degradation parameters are provided by various organizations, for example, the Organization for Economic Co-operation and Development (OECD), the European Commission and the International Organization for Standardization.

The determination of the DT$_{50}$ value is described in the OECD guideline 308 *Aerobic and Anaerobic Transformation in Aquatic Sediment Systems* (OECD 2002). The OECD guideline 308 describes degradation tests in artificial water/sediment systems under aerobic and/or anaerobic conditions. DT$_{50}$, DT$_{75}$ and DT$_{90}$ values can be derived from the transformation investigations. The OECD guideline 106 *Adsorption/Desorption using a Batch Equilibrium Method*,

published in 2000, describes adsorption and desorption experiments for the determination of the K_d and K_F describing the mobility of chemical substances in groundwater and soil (OECD 2000). During batch tests as described in the OECD guideline 106, the soil sample is spiked with an aqueous solution of the chemical substance. Afterwards, the soil sample is shook for a defined time. Finally, the distribution of the chemical substance dissolved in water and adsorbed onto soil particles is determined.

In general, the determination of sorption and degradation parameters depends on the laboratory test conditions (e.g. pH, sand, clay and organic carbon fraction). The distribution coefficients are determined at different pH values and in different soil materials as well as DT$_{50}$ values for aerobic and anaerobic conditions. K_d and DT$_{50}$ values derived from laboratory tests following OECD or other guidelines are difficult to apply to real bank filtration sites. However, if the laboratory tests for K_d and DT$_{50}$ are performed under conditions similar to those in the natural aquifer system, these values come quite near to the natural system. Characteristic physicochemical parameters and aquifer material composition at four German bank filtration sites are summarized in Table 3.

In first-order rate laws, the time needed to halve the compound concentration is known as the half-life of the reaction and is independent of the initial

Table 1 Ranges of hydrogeological and hydraulic parameters at bank filtration sites in central Europe (Lenk et al. 2006)

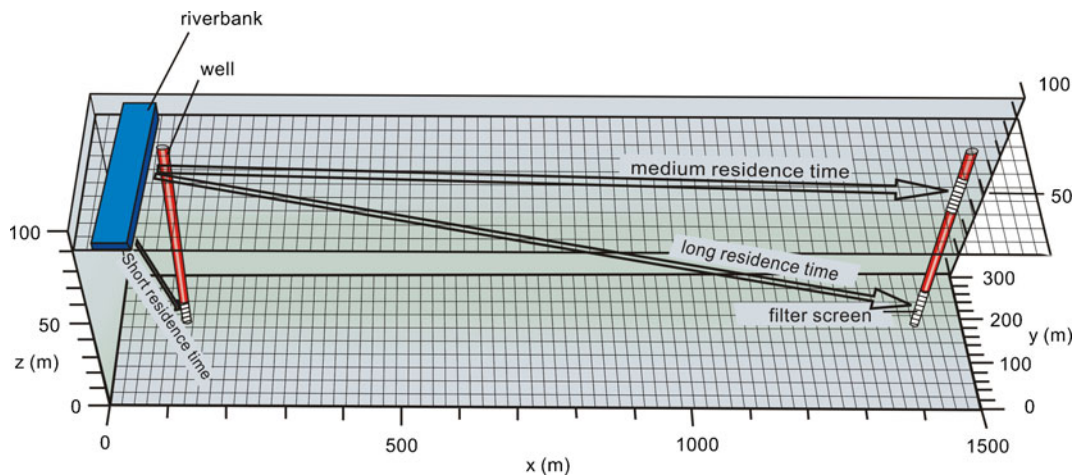| Parameter	Range
Hydraulic conductivity kF (m/s)	1×10^{-2}–1×10^{-4}
Distance between shoreline and extraction well (m)	1.5–1,200
Depth of filter screen (final depth; m)	4–70
Average extraction rates (m^3/day)	500–5,000
Groundwater flow times (days)	<1–>1,100

Fig. 3 Sketch of the groundwater flow model displaying a bank filtration site

concentration. In a more loose sense, the half-life concept is also used for other types of reaction rates, but then the value depends on the initial concentration. According to the OECD guideline, the half-life time ($t_{0.5}$ or $t_{1/2}$) is the time taken for 50% transformation of a test substance when the transformation can be described by first-order kinetics. It is independent of the initial concentration. The disappearance time 50 (DT_{50}) is the time within which the initial concentration of the test substance is reduced by 50%.

Table 4 shows exemplarily a data sheet, which is provided by the pharmaceutical company in the course of the marketing authorisation application. Data are only available on sorption and degradation processes, the K_d and K_{OC} values for the quantification of retardation processes and DT_{50} for quantification of degradation processes occurring during the transport in the aquifer.

Based on the results of the groundwater flow modelling of the first phase, the available sorption and degradation parameters are used for the analytical calculation of the PEC_{GW}. The parameters listed in

Table 4 are the solely available data which are provided in the course of the marketing authorisation for a new pharmaceutical substance for the calculation of PEC_{GW}. The sorption coefficients were used for the calculation of the pharmaceutical compound retardation resulting in a longer residence time of the compound in groundwater compared to the groundwater flow time. Then, the final pharmaceutical compound concentration was calculated analytically applying the first-order decay equation (Eq. 5) and the retarded transport time of the compound. The result is the compound concentration (PEC_{GW}) at the extraction well. Because linear sorption and first-order degradation can be calculated easily, they were not incorporated into a transport model. However, the mathematical calculated results were verified with the transport modelling results (MT3DMS) and the analyzed pharmaceutical compound concentrations for different human pharmaceuticals at two real bank filtration sites: Flehe at the river Rhine and Torgau at the river Elbe.

The EMEA guideline suggests that substances with a high K_{OC} value (>10,000 L/kg) are retained in the STP and will not reach the aquifer during the bank

Table 2 Step sizes for the variables of the groundwater flow modelling

Variables	Step sizes for modelling
Distance between shore line and extraction well (m)	1,000/500/300/100/50/25/5
Hydraulic conductivity (m/s)	$1\times10^{-2}/5\times10^{-3}/3\times10^{-3}/1\times10^{-3}/5\times10^{-4}/1\times10^{-4}$
Depth to filter screen (m b.g.l.)[a]	80–90/50–60/30–40/20–30/10–20/10–15
Extraction rate (m³/day)	5,000/2,000/1,000/750/500/250

[a] Top of ground surface was set to a default value of 100 m, which is the upper model boundary

filtration process. It is therefore assumed that these substances pose no risk for groundwater. The K_{OC} value >10,000 L/kg was integrated as a threshold into the calculation.

4 Results and Discussion

For verification of the groundwater flow model, groundwater flow times were modelled for the bank filtration sites Flehe at the Rhine River and Torgau/Ost at the Elbe River and compared with measured flow times. Furthermore, the quality of the model was tested by calculating a multiple regression to obtain information on the statistical correlation of the hydraulic and hydrogeological parameters and the groundwater flow time. Moreover, the analytical results for human pharmaceuticals analyzed at the two bank filtration sites were compared with the calculation results from the approach discussed in this paper. Finally, the Microsoft Access based application tool for the calculation of PEC$_{GW}$ is introduced.

The results of the groundwater flow model were compiled in a matrix with a total number of 1,290 data pairs displaying shortest flow times and the drawdown at the extraction well depending on the parameter hydraulic conductivity, shore line-well distance, depth of the screened interval, and extraction rate. The main statistical parameters are compiled in Fig. 4.

The median value of the modelled flow times is 110 days, which coincides very well with flow times from real bank filtration sites. A total number of 464 modelled values revealed groundwater flow times <50 days. The minimum and maximum values of the modelled groundwater flow times are 0.07 and 12,791 days. Groundwater flow times at real bank filtration sites range between <1 and 1,100 days (Table 1). It is important to point out that the model displays all groundwater flow times, which are hydraulically possible including extreme high and low values. The mean value of 638 days displays this high range of the modelled values. Therefore, the median value gives a more realistic value.

For the two bank filtration sites Torgau/Elbe and Flehe/Rhine, measured groundwater flow times and pharmaceutical concentrations in surface water and groundwater at the extraction well were taken from Eckert and Irmscher (2004) and Grischek

(2003). The groundwater flow model was adjusted for both sites according to the information from the waterworks operator and literature. For the Flehe site, a groundwater flow time of 30 days was modelled compared with a flow time of 35 days, according to information from the waterworks operator (Eckert and Irmscher 2004). For the Torgau site, a groundwater flow time of 210 days was modelled compared to a medium flow time of >150 days, according to information in Grischek (2003).

The developed groundwater flow model is based on the variation and combination of four different parameters groundwater extraction rate, shore-well distance, depth to filter screen and hydraulic conductivity. A multiple regression allows to assess the relationship between one dependent variable (groundwater flow time) and several independent variables (filter depth, extraction rate, shore-well distance, groundwater drawdown) at the same time. It is suggested that the variation of the groundwater flow time depends on the variation of several different variables. The calculation revealed a squared multiple correlation R^2 of 0.47. The four parameters (see above) thus contribute to 47% of variance of the modelled groundwater flow times. The beta values of 0.63 for the shore-well distance, −0.24 for the extraction rate and 0.22 for the filter depth are in agreement with the correlation factors. From a statistical point of view, a good correlation between the four parameters and the modelled flow time is achieved with the groundwater flow model. Nevertheless, other parameters also influence the groundwater flow time, which were not included in the groundwater flow model, such as river water level, water viscosity (temperature-related) etc.

Another possibility for the illustration of the correlation between the model results and the four parameters is box plots displaying ranges for the groundwater flow times depending on the individual parameter. Figure 5 shows the groundwater flow time as a function of two parameters. At high extraction rates, the filter depth has only a small influence on the groundwater flow time (Fig. 5a). At low extraction rates and increasing depth to filter screen, the groundwater flow times show a higher range (variation). Short flow times result from short shore-well distances and low filter depths (Fig. 5b). In other words, at larger shore-well distances and increasing depth to filter screen, the modelled groundwater flow

Table 3 Groundwater and aquifer sediment characteristics of four German bank filtration sites

	Berlin—Tegeler See	Berlin—Wannsee	Flehe—Rhine	Torgau/Ost—Elbe
Aquifer material/ soil texture (clay content)	Fine- to coarse-grained medium sand	Fine- to coarse-grained medium sand	Sandy gravel (Eckert and Irmscher 2004)	Fine gravel to medium sand (Grischek 2003)
Natural organic matter content aquifer sediment	Total organic carbon content 0.0–2.1 wt. % (Massmann et al. 2007)	Total organic carbon content 0.2–10 wt.% (Massmann et al. 2008a)	Total carbon content ranges between 0.02 and 3.46 wt.% (Eckert 2003, unpublished results)	Total organic carbon content ranges between 0.013 and 0.024 wt.% (Grischek 2003)
Redox condition groundwater	Aerobic (upper aquifer) Anaerobic (lower aquifer; Scheytt et al. 2004)	Aerobic to anaerobic condition (Massmann et al. 2008a)	Aerobic to denitrifying (Schmidt et al. 2004)	Denitrifying conditions (anaerobic conditions) (Grischek 2003)
pH value groundwater	7.4 (mean value; KWB 2007, unpublished results)	7.4 (mean value; KWB 2007, unpublished results)	~7.2–7.8 (Eckert and Irmscher 2004)	6.5–7.4 (Grischek 2003)
Temperature groundwater (°C)	10.7 (mean value; KWB 2007, unpublished results)	11.1 (mean value; KWB 2007, unpublished results)	13.3–14.2 (Eckert 2003, unpublished results)	8.0–12.0 (Grischek 2003)

times show a higher range. Finally, Fig. 5c shows that for the specific boundaries of the model, the extraction rates have a higher influence on the groundwater flow time than short shore-well distances. All three box plots approve the different influence of the parameters on the groundwater flow time. The shore well distance seems to have the highest influence on the flow time followed by the extraction rate and the filter depth.

Following the statistical evaluation of the model results, the mathematical calculation approach was compared with analyzed real-world pharmaceutical concentrations. Table 5 compares the analyzed and calculated concentrations for the pharmaceutical substances carbamazepine (antiepileptic drug) and diclofenac (analgesic, antiarthritic, antirheumatic compound) at the bank filtration sites Flehe and Torgau.

For the transport modelling as well as the analytical calculation, the maximum analyzed concentration of the pharmaceutical substance was chosen as the initial concentration in surface water (PEC_{SW}) in order to represent the worst case. The information on distance between shore line and extraction well and on groundwater flow time were taken from the results of the groundwater flow modelling, from information made available by the waterworks operator or from literature. The DT_{50} and the sorption distribution coefficient were taken from literature.

For this comparison of actually analyzed concentrations and calculated values, diclofenac and carbamazepine were chosen as example compounds because they occur not only in surface water but also in groundwater occasionally. Due to the higher persistency of carbamazepine, documented by the higher half-life time compared to diclofenac, carbamazepine has been detected in groundwater samples from extraction wells. Likewise, the modelled concentrations are also above detection limits for those wells. For diclofenac, modelled values are below the detection limit of 2 ng/L in the groundwater at the extraction wells which coincides very well with analyzed values.

Overall, there are significant differences between the analyzed and modelled concentrations. These differences are mainly due to high variations in concentration in surface water and also due to specific local conditions with respect to the input history, geology and hydrogeology. Albeit these restrictions, the comparison of the analyzed and calculated concentrations shows that the approach for the calculation of PEC_{SW} by combining groundwater flow modelling and analytical calculation of retardation and degradation is a good approximation for the expected concentrations in groundwater. With this tool, it will be possible to identify compounds that have the potential to occur in groundwater even before they are administered.

Table 4 Data sheet with sorption and degradation parameters

| Pharmaceutical substance	Sorption			Characterization test soil			Degradation					Characterization
	K_{OC} (mL/g)	K_d (mL/g)	K_F	pH	% Sand	% O.C.	DT_{50} water aerobic (days)	DT_{50} water anaerobic (days)	DT_{50} sediment aerobic (days)	DT_{50} sediment anaerobic (days)	DT_{50} soil (days)	
Substance A	25	0.568		5.7	77.5	2.29	0.9					Sandy loam pH water 7.98 pH sediment 7.11
	146	1.812		6.8	48.4	1.24	1.1					Silty clay loam pH water 8.17 pH sediment 7.19
	381	7.235		6.7	22.1	1.90		3.06				Silt loam pH water 7.09 pH sediment 7.13
	151	2.202		7.2	14.5	1.46						
	K_{OC} study acc. OECD 106, April 2007						Water/sediment study valid acc. OECD 308, May 2007					
Substance B	55,800			4.3	86	0.5	1		2.8 (whole system)			Sand
	acc. OECD 106, cannot be validated, study report not available, 2007						acc. OECD 308, cannot be validated, study report not available, 2007					
Substance C	2,650	957	1,350 n.s.[a]		Sludge	36.1	11	11				Sand pH 7.6 resp. 6.5
	K_{OC} study valid acc. OECD 302A, July 2003						Water/sediment study valid acc. OECD 308, April 2006					

[a] Not specified
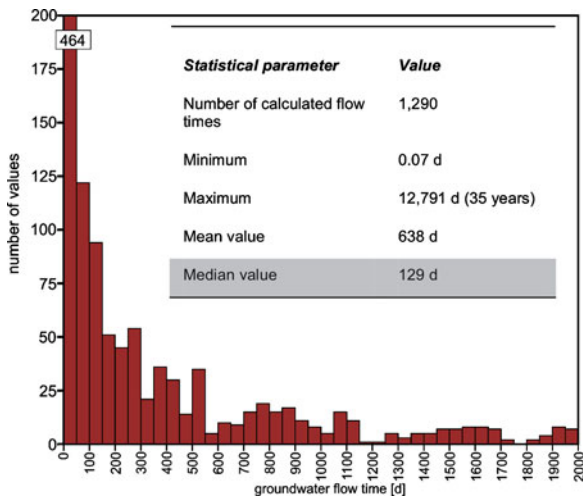
Fig. 4 Descriptive statistics of the modelling results (range of the modelled shortest flow times 0–2,000 days)

Three standard flow times were chosen from the statistical evaluation of the flow model results representing the realistic worst case, the worst case and the median case and correlated with the hydraulic and hydrogeological conditions at real bank filtration sites (Lenk et al. 2006). The shortest flow times result from a combination of small depth to screen, small well-shore-distance and high extraction rate.

The 5/95 percentile was chosen to represent the worst case scenario resulting from short shore-well distance (13 m), high extraction rates of about 3,000 m³/day and high hydraulic conductivity (0.02 m/s). The realistic worst case is represented by the 20/80 percentile with a depth to filter screen of 24 m, shore-well distance of 33 m, extraction rate of 2,500 m³/day and high hydraulic conductivity of 0.0069 m/s. Finally, the median case is characterized by the median values of the modelled flow times. The three scenarios do not represent an individual concrete bank filtration site. Based on these three cases, the groundwater flow time was modelled with the groundwater flow model. Table 6 summarizes the results.

The final step was to develop a PC-based, user-friendly application tool, based on the results of the groundwater flow model and the calculation routines for sorption and degradation. The application applies Microsoft Access and is named "SiMBaFi" (Simulation Model Bank Filtration). The user has two different options for the estimation of PEC_{GW} (Fig. 6).
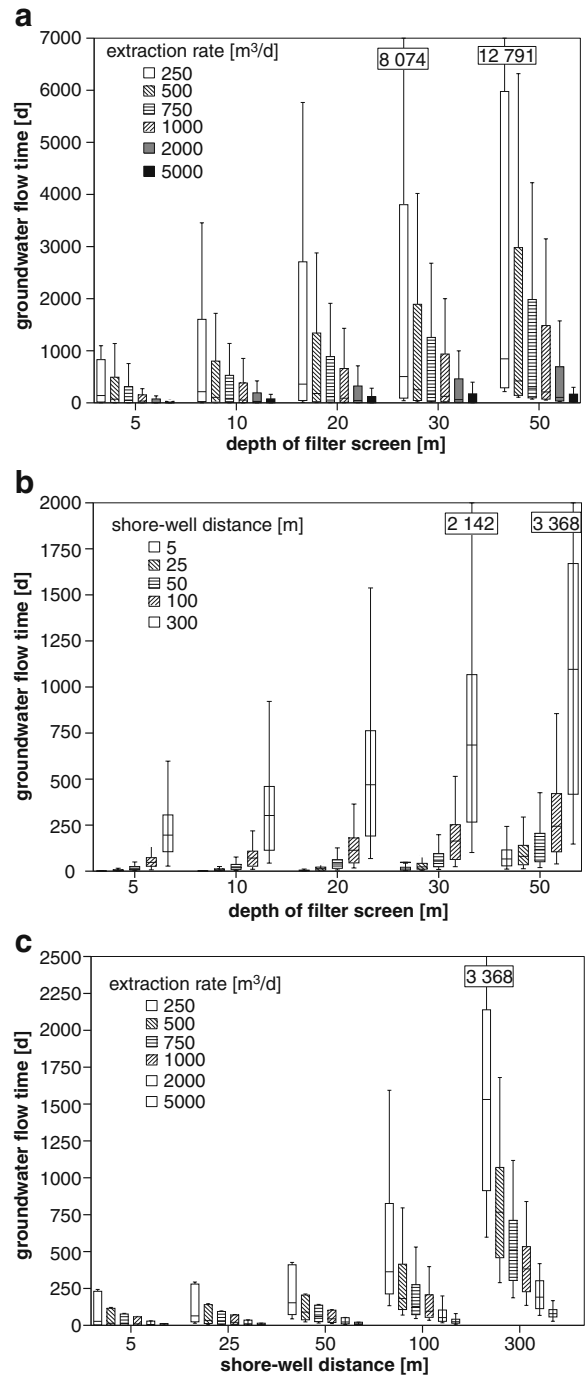

Fig. 5 Box plots showing the relationships between groundwater flow time and hydraulic/hydrogeological parameters. a Influence of different extraction rates and filter depths. b Influence of different shore-well distances and filter depths (maximum flow time 2,000 days). c Influence of different extraction rates and shore-well distances (maximum flow time 2,500 days)

Table 5 Comparison of calculation, flow model and analysis results

Bank filtration site		Flehe/Rhine	Flehe/Rhine	Torgau/Elbe	Torgau/Elbe
Pharmaceutical substance		Carbamazepine	Diclofenac	Diclofenac	Carbamazepine
Substance property					
Sorption distribution coefficient K_d (from literature)	mL/g	0.131[a]	0.572[c]	0.572[c]	0.131[a]
Retardation factor (calculated)		2.30	6.70	6.70	2.30
Half-life time (literature)	days	328[b]	45[a]	45[a]	328[b]
Lambda (calculated)	1/day	0.002113	0.0154	0.0154	0.002113
Initial concentration surface water (maximum concentration)	ng/L	200	110	130	340
Model parameter and boundary conditions					
Shoreline-well distance	m	65	65	300	300
Depth to filter screen	m b.g.l.	10–17	10–17	35–55	35–55
Extraction rate	m³/day	840	840	3,600	3,600
Medium groundwater flow time	days	35	35	>150	>150
Hydraulic conductivity k_F	m/s	0.001	0.001	0.002	0.002
Total porosity		0.35	0.35	0.35	0.35
Effective porosity		0.2	0.2	0.2	0.2
Solid density	g/cm³	2.65	2.65	2.65	2.65
Bulk density	g/cm³	2.0	2.0	2.0	2.0
Results					
Modelled flow time	days	33	33	210	210
Substance concentration at extraction well (analyzed)	ng/L	190	b.d.l.	b.d.l.	86
Substance concentration at extraction well (calculated)	ng/L	177	14	0	164

b.d.l. below detection limit of 2 ng/L

[a] Scheytt et al. 2006

[b] Loeffler et al. 2005

[c] Hanisch et al. 2004

First, PEC_{GW} values can be calculated with three default flow times representing the worst (0.15 days), the realistic worst (5 days) and the median (110 days) case. The calculation routines will only start when a K_{OC} <10,000 L/kg is entered. The K_{OC} serves as a threshold value, and an input is optional. The calculation with a K_{OC} >10,000 L/kg is not feasible following the EMEA guideline, as substances with an average K_{OC} >10,000 L/kg are regarded to be immobile. In the case of an input of a K_{OC} >10,000 L/kg, no further calculation will be performed.

It is furthermore possible to modify the results by choosing the percentage of bank filtrate. The calculated concentration at a flow time of 5 days (realistic

Table 6 Definition of three standard scenarios

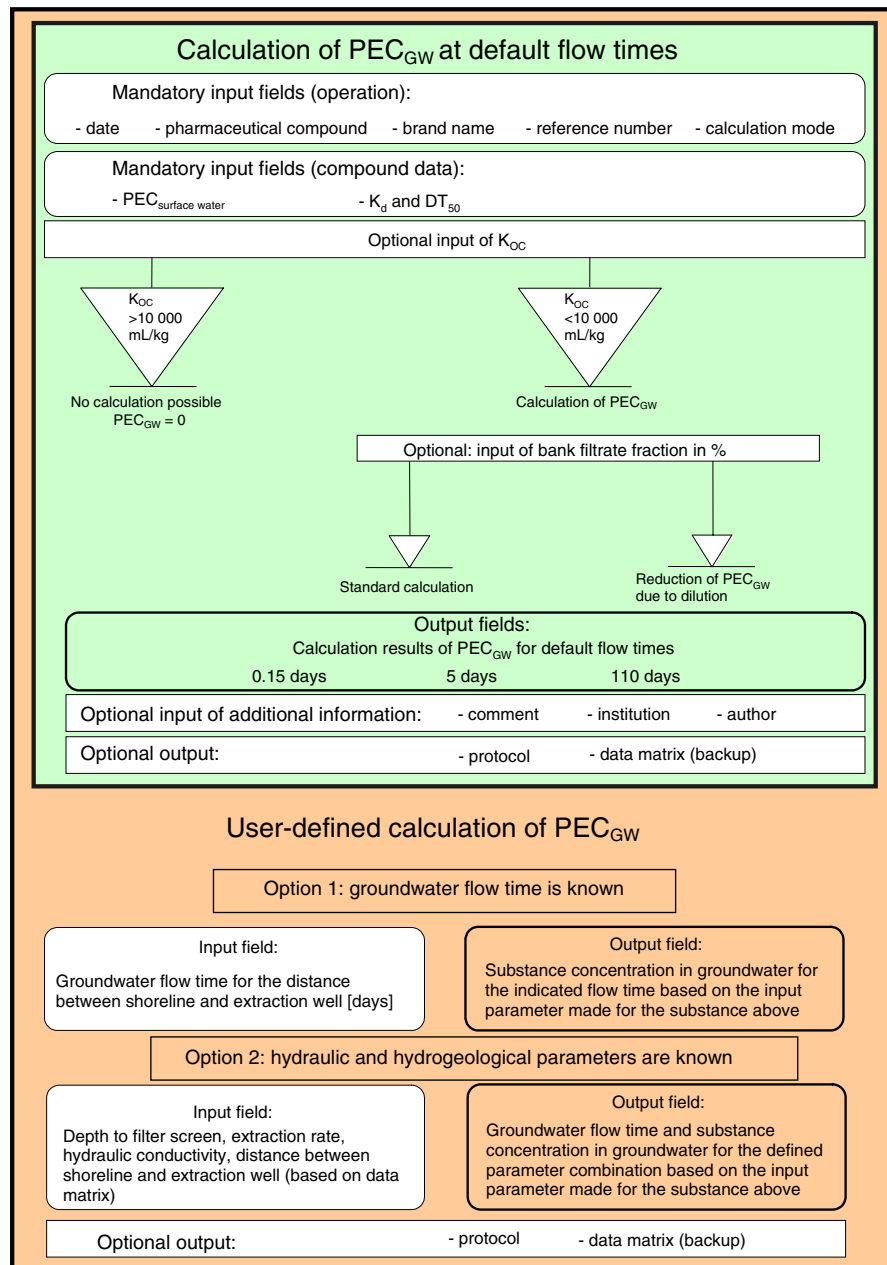| Parameter	Worst case	Realistic worst case	Median case
Hydraulic conductivity (k_F; m/s)	0.02	0.007	0.002
Extraction rate (m³/day)	3,000	2,000	1,000
Well-shore distance (m)	10	30	100
Depth of filter screen (metre below surface water level at 95 m)	5–10	10–20	20–30
Modelled time (days)	0.15	5	110

Fig. 6 Flow chart for application of SiMBaFi

worst case) is referred as the standard case and should be applied in the course of the authorisation process.

Second, PEC_GW values can be calculated with user-defined information on the flow time and/or the hydrogeological and hydraulic parameter. The user can either enter a groundwater flow time manually or can choose values for the hydraulic and hydrogeo-logical properties as screened interval, extraction rate, hydraulic conductivity and surface water to well distance from a dropdown menu. The respective flow time is then recalled from the database, and finally, the PEC_GW values are calculated.

5 Conclusions

A new approach to calculate EMEA's predicted environmental concentration for pharmaceuticals in groundwater has been developed. The current approach of EMEA considers bank filtration and calculates PEC_{GW} merely by multiplying the environmental concentration of surface water (PEC_{SW}) by 0.25. Using this method, PEC_{GW} is invariably connected to PEC_{SW} without considering groundwater travel times or chemical characteristics of the organic compounds. However, in the course of the marketing authorisation for new human pharmaceuticals, some limited data on the characteristics of organic compounds have to be provided by the applying pharmaceutical companies. These data include the sorption coefficient K_d and the value for the disappearance time of the substance. For the new approach, these data are utilized to characterize the basic transport behaviour of the new compounds.

Although bank filtration is applied in Germany for more than 100 years, only very little information on groundwater residence times and the distribution of residence time could be found. As bank filtration sites exhibit quite distinctive patterns for geology, hydrogeology and basic setup at the various sites, a general groundwater flow model revealed that the median value for the residence time is 110 days. This might be a sufficiently long residence time for attenuation processes at bank filtration sites. However, a total number of 464 modelled values revealed groundwater flow times of less than 50 days indicating surprisingly low residence time in groundwater at some locations and along specific flow lines.

The main advantage of the new proposed approach is that the PEC_{GW} is not any longer invariably connected to PEC_{SW} but is calculated using the limited albeit available information on the chemical characteristics of the organic compounds. The two main processes that can be assessed using the available data are sorption, i.e. retardation and degradation/elimination.

Different chemical properties lead to different groundwater transport behaviour. In the case of sorption, this is especially relevant for compounds with very high or very low sorption coefficients. If the sorption coefficient is high, the substance may not be transported far in groundwater due to high retardation.

If the sorption coefficient is very low, sorption can be neglected and the substance is transported by advection with groundwater flow velocity.

In the case of degradation/elimination, again very low or very high degradation exhibits a significant difference compared to the current method. For substances which show low degradation, the calculation following the EMEA approach underestimates the predicted environmental concentration in groundwater.

The introduced calculation tool SiMBaFi is a user-friendly tool for calculation of the predicted environmental concentration for all compounds with available data on sorption and degradation. It can be easily refined to suit more specific demands. Although the calculation is rather rough, it opens the possibility for a fast check on the expected concentration of any organic compound at bank filtration sites.

References

Andreozzi, R., Caprio, V., Ciniglia, C., De Champdore, M., Lo Giudice, R., Marotta, R., et al. (2004). Antibiotics in the environment: Occurrence in Italian STPs, fate, and preliminary assessment on algal toxicity of amoxicillin. *Environmental Science & Technology, 38*(24), 6832–6838.

Doppler, T., Franssen, H. J. H., Kaiser, H. P., Kuhlman, U., & Stauffer, F. (2007). Field evidence of a dynamic leakage coefficient for modelling river–aquifer interactions. *Journal of Hydrology, 347*(1–2), 177–187.

EC. (2001). *Community code relating to medicinal products for human use, Directive 2001/83/EC.* Brussels: European Commission, European Parliament and Council.

Eckert, P., & Irmscher, R. (2004). Modelling of hydrogeochemical processes during bank filtration. In: K. Kovar, Z. Hrkal, & J. Bruthans (Eds.), *Proceedings of the international conference on finite element models* (pp. 193–196). Karlovy Vary, Czech Republic: Fontainebleau, France, International Association of Hydrologic Sciences.

Eckert, P., & Irmscher, R. (2006). Over 130 years of experience with riverbank filtration in Düsseldorf, Germany. *Journal of Water Supply: Research and Technology—AQUA, 55*(4), 283–291.

EMEA. (2006). *Guideline on the environmental risk assessment of medicinal products for human use, Doc. Ref. EMEA/CHMP/SWP/4447/00*. London: European Medicines Agency.

Engelmann, U., & Rohde, S. (2009). Pharmaceutical substances, antibiotics and X-ray contrast media in treated waste water and surface water in the Federal State Saxony (Arzneimittelwirkstoffe, Antibiotika und Röntgenkontrastmittel in Abwassereinleitungen und Oberflächengewässern in Sachsen). *KA Korrespondenz Abwasser, Abfall, 56*(3), 258–268.

Fenz, R., Blaschke, A. P., Clara, M., Kroiss, H., Mascher, D., & Zessner, M. (2005). Monitoring of carbamazepine concentrations in wastewater and groundwater to quantify sewer leakage. *Water Science and Technology, 52*(5), 205–213.

Fritz, B. (2003). Natural processes with a high efficiency: bank filtration and water recharge (Natürliche Prozesse mit hoher Effizienz: Uferfiltration und Wasseranreicherung). *wwt,* 10–11, 10–17.

Grischek, T. (2003). Management of bank filtration sites at the Elbe River (Zur Bewirtschaftung von Uferfiltratfassungen an der Elbe). Habilitation, Technische Universität Dresden Institut für Grundwasserwirtschaft, Dresden.

Halling-Sorensen, B., Nielsen, S. N., Lanzky, P. F., Ingerslev, F., Lutzhoft, H. C. H., & Jorgensen, S. E. (1998). Occurrence, fate and effects of pharmaceutical substances in the environment—a review. *Chemosphere, 36*(2), 357–394.

Hanisch, B., Abbas, B., Kratz, W., & Schüürmann, G. (2004). Human drugs in aquatic ecosystems: approach for the environmental risk assessment of drug residues (Humanarzneimittel im aquatischen Ökosystem: Bewertungsansatz zur Abschätzung des ökotoxikologischen Risikos von Arzneimittelrückständen). *Umweltwissenschaften und Schadstoff-Forschung, 16*(4), 223–238.

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

Hiscock, K. M., & Grischek, T. (2002). Attenuation of groundwater pollution by bank filtration. *Journal of Hydrology, 266*(3–4), 139–144.

HYDOR (2004). Hydrological evaluation of the groundwater resources of the water works Tegel, Spandau, Tiefwerder, Kladow and Beelitzhof in Berlin (Hydrologische Berechnungen zum Nachweis des Grundwasserdargebotes für die Wasserwerke Tegel, Spandau, Tiefwerder, Kladow und Beelitzhof der Berliner Wasserbetriebe). Unpublished report, Berliner Wasserbetriebe, Berlin.

HYDOR (2007). Hydrological evaluation of the groundwater resources of the water works Friedrichshagen, Altglienicke, Johannisthal, Wuhlheide, Kaulsdorf und Buch in Berlin (Hydrologische Berechnungen zum Nachweis des Grundwasserdargebotes für die Wasserwerke Friedrichshagen, Altglienicke, Johannisthal, Wuhlheide, Kaulsdorf und Buch der Berliner Wasserbetriebe). Unpublished report, Berliner Wasserbetriebe, Berlin.

Kunkel, U., & Radke, M. (2008). Biodegradation of acidic pharmaceuticals in bed sediments: Insight from a laboratory experiment. *Environmental Science & Technology, 42*(19), 7273–7279.

Lenk, S., Remmler, F., Skark, C., & Schulte-Ebbert, U. (2006). *Technical concepts and adjusted operational modes for an optimal adaptation of riverbank filtration to local boundary conditions (Technische Konzepte und abgestimmte Betriebsweisen zur optimalen Anpassung der Uferfiltration an lokale Randbedingungen).* Schwerte: Institut für Wasserforschung GmbH Dortmund.

Liebig, M., Moltmann, J. F., & Knacker, T. (2006). Evaluation of measured and predicted environmental concentrations of selected human pharmaceuticals and personal care products. *Environmental Science and Pollution Research, 13*(2), 110–119.

Loeffler, D., Rombke, J., Meller, M., & Ternes, T. A. (2005). Environmental fate of pharmaceuticals in water/sediment systems. *Environmental Science & Technology, 39*(14), 5209–5218.

Massmann, G., Heberer, T., Grützmacher, G., Dünnbier, U., Knappe, A., Meyer, H., et al. (2007). Drinking-water production in urban environments—bank filtration in Berlin (Trinkwassergewinnung in urbanen Räumen—Erkenntnisse zur Uferfiltration in Berlin). *Grundwasser, 12*, 232–245.

Massmann, G., Nogeitzig, A., Taute, T., & Pekdeger, A. (2008a). Seasonal and spatial distribution of redox zones during lake bank filtration in Berlin, Germany. *Environmental Geology, 54*, 53–65.

Massmann, G., Sültenfuß, J., Dünnbier, U., Knappe, A., Taute, T., & Pekdeger, A. (2008b). Investigation of groundwater residence times during bank filtration in Berlin: A multi-tracer approach. *Hydrological Processes, 22*, 788–801.

OECD. (2000). *OECD guidelines for the testing of chemicals/Section 1: Physical–chemical properties test no. 106: Adsorption–desorption using a batch equilibrium method.* Paris: Organisation for Economic Co-operation and Development.

OECD. (2002). *OECD guidelines for the testing of chemicals/Section 3: Degradation and accumulation test no. 308: Aerobic and anaerobic transformation in aquatic sediment systems.* Paris: Organisation for Economic Co-operation and Development.

Ray, C., Melin, G., & Linsky, R. B. (Eds.). (2002). *Riverbank filtration—improving source-water quality.* Dordrecht: Kluwer Academic.

Scheytt, T., Mersmann, P., & Heberer, T. (2006). Mobility of pharmaceuticals carbamazepine, ibuprofen, diclofenac, ibuprofen, and propyphenazone in miscible-displacement experiments. *Journal of Contaminant Hydrology, 83*, 53–69.

Scheytt, T., Mersmann, P., Leidig, M., Pekdeger, A., & Heberer, T. (2004). Transport of pharmaceutically active compounds in saturated laboratory columns. *Ground Water, 42*(5), 767–773.

Schmidt, C. K., Lange, F. T., & Brauch, H.-J. (2004). Assessing the impact of different redox conditions and residence times on the fate of organic micropollutants during riverbank filtration. In R. Gimbel, N. Graham, & M. R. Collins (Eds.), *Recent progress in slow sand and alternative biofiltration processes* (pp. 561–569). London: IWA.

Schubert, J. (2002). Hydraulic aspects of riverbank filtration—field studies. *Journal of Hydrology, 266*, 145–161.

von Keutz, E., & Jekat, F.-W. (1998). Toxicological studies in the course of a marketing authorization application for human pharmaceuticals (Toxikologische Untersuchungen im Rahmen der Zulassung von Humanarzneimitteln). In Hessische Landesanstalt für Umwelt (Ed.), *Arzneimittel in Gewässern* (pp. 65–69). Wiesbaden: Hessische Landesanstalt für Umwelt.

Zippel, M., Scheytt, T., Hannappel, S., & Müller, B. (2009). Mathematical transport simulation of pharmaceutical compounds in groundwater during bank filtration (Mathematische Simulation des Eintrages von Arzneimitteln aus Oberflächengewässern in das Grundwasser durch Uferfiltration). In Umweltbundesamt (Ed.), *Texte 14/2010* (p. 162). Dessau: Umweltbundesamt.