Management of pharmaceutical substances in the environment: Lithuanian case study
Inga Baranauskaitė-Fedorova, Jolanta Dvarioniene and Vladimir A. Nikiforov

ABSTRACT
Investigation on the sources, discharges and related risks for the environment of the pharmaceutical substance (PhS) diclofenac (DCF) was performed in Lithuania, a country of the Baltic Sea region, for the first time. The investigation only refers to DCF as a PhS for human use; emissions from animal husbandry were not considered. In the first stage of the research, the main sources and pathways of DCF via substance flow analysis were identified within the country. During the second stage, DCF flows along the wastewater treatment plants (WWTPs) in two different cities were measured in order to assess the current levels of pharmaceutical residues in the environment. Furthermore, environmental risk assessment was carried out by taking into account the parameters of consumption data and elimination rate in WWTPs. Then, the assessment of different technical and managerial removal approaches was accomplished in an environmental management model of wastewater containing PhS, based on the framework of environmental systems theory.

Key words | diclofenac, pharmaceutical substance management, pharmaceuticals in wastewater, risk assessment, substance flow analysis

ABBREVIATIONS
BOD | biochemical oxygen demand
DCF | diclofenac
DDD | defined daily dose
LSMCA | Lithuanian State Medicines Control Agency
LC/MS | liquid chromatography/mass spectrometry
MEC | measured environmental concentration
NOEC | no-observed-effect concentration
PEC | predicted environmental concentration
PhS | pharmaceutical substances
PNEC | predicted no-effect environmental concentration
SFA | substance flow analysis
WWTP | wastewater treatment plant

INTRODUCTION
Chemical pollution of surface water poses a threat to the aquatic environment. The effect can be acute and enduring: toxicity in aquatic organisms, accumulation of pollutants in ecosystems and decline of biodiversity, as well as risk to human health. In 2013, three pharmaceutical substances (PhSs), diclofenac (DCF), 17-β-estradiol (E2) and 17-α-ethinyl-estradiol (EE2), were included in the watch list in accordance with the directive 2013/39/EC in order to gather monitoring data for facilitating the determination of appropriate measures that address the risk posed by those substances (Directive 2013/39/EU). A holistic approach to current sources of PhS, discharges into the environment, the interaction between substances and the natural environment, their ability to disintegrate and remain in the environment, and most significantly the dangers and risks they pose are especially important for the purpose of being able to predict and manage these substances and their compounds in the environment. In spite of the fact that the presence of PhS in the environment is a sensitive issue for the whole world and has been under discussion for decades, no studies involving these precise compounds have been conducted in Lithuania, a country of the Baltic region.

According to the publicly accessible database of the Lithuanian State Medicines Control Agency (LSMCA)
concerning human drug usage in 2013, with reference to the drug usage in the Baltic States, DCF occupied the twelfth place in Estonia, the third place in Latvia and the fifth place in Lithuania. Since 2010, the demand for DCF and drugs with this active substance has grown by 10.7%. A statistical analysis has revealed growth in DCF consumption. DCF has been used for pain relief more frequently than other medical products; the analgesic consumption may have increased due to its effectiveness, low price, usage in the market for many years, and a variety of manufacturers and pharmaceutical forms (Lasinskas & Kaduševičius 2008). It is likely that in the future the increase in the consumption of this substance will also be observed; due to this fact, the occurrence of this PhS in the environment should become a global concern.

Therefore, this research is important for both the actual substance measurements in the aquatic environment and the current potential toxicological risk posed to the environment and human health. As the literature review has revealed, the substance flow analysis (SFA) approach provides an explicit basis for sustainable management of the environment, allowing the quantification of material flows over social and economic systems (e.g., at business, industrial, city or state level). Therefore, the issue of the consumption of resources as well as the reduction of the environmental pollution could be discussed at the substance management level (Montangero et al. 2006; Huang et al. 2012). Due to these reasons, SFA was chosen as the most appropriate management tool for discovering the main sources and pathways of DCF at the country level. Investigations only refer to DCF as a PhS for human use. The main purpose of this research is to determine the quantity of DCF entering the environment at the country level, to assess the environmental risk and to provide an environmental PhS management model for improving the environmental protection efficiency.

**MATERIAL AND METHODS**

**Scientific literature analysis**

The research consists of five phases. A literature survey (Baranauskaite & Dvarioniene 2014a) was carried out where the data on the DCF analgesic’s consumption were estimated using the international anatomic therapeutic chemical classification system and the defined daily dose (DDD) methodology (WHO 2005). DCF consumption (kg/y) was recalculated from the drug’s DDD value in units of 1,000 inhabitants per day by the period of 2013, publicly available on the LSMCA drugs consumption database.

**Diclofenac substance flow analysis**

SFA was based on the idea proposed by the researcher Chèvre (Chèvre et al. 2015). The substance flow balance was analytically formed on the basis of statistical data, practices in other countries and scientific research, when estimating potential substance flows into the environment by anthropogenic activities. SFA is presented by a Sankey diagram with loads of DCF given in kg/y. The input in the system for DCF is the human consumption at the country level.

**Case studies of Kaunas and Marijampole wastewater treatment plants**

Twenty-four-hour composite samples from the influent and effluent of wastewater treatment plants (WWTPs) were collected during one sampling from each WWTP (March 2014). Wastewater samples were analysed by using a liquid chromatography/mass spectrometry (LC/MS) method for the DCF determination (Nikiforov et al. 2014; Zeng et al. 2014). DCF was extracted separately by using two methods: liquid–liquid extraction and solid phase extraction (Nikiforov et al. 2014). The chemical substance analysis included the following phases: the collection of samples; the sample storage; taking a representative aliquot; using the recovery standard for determining the degree of extraction; the extraction from matrix; a multi-step sequence of operations to remove interferences; an instrumental analysis; a calculation and a report. LC/MS analysis was based on DCF quantity in a sample. In order to detect the target substance, the liquid chromatography/mass spectrometers LCMS-IT-TOF (Shimadzu) and LTQ Orbitrap (Thermo Finnigan) were employed (Nikiforov et al. 2014). Tests were performed in an electro-spray ionisation mode with the detection of negative ions. Quantitative calculations were performed by using an internal standard method (according to the isotope-labelled internal standard).

The efficiency of the treatment of wastewater containing PhS is calculated according to the formula:

\[ \eta = \frac{C_{int} - C_{eff}}{C_{int}} \times 100 \]
where:

\[ C_{\text{inf}} \] is the average PhS concentration measured in the raw influent, ng/L;

\[ C_{\text{eff}} \] is the average PhS concentration measured in the effluent, ng/L.

**Environmental risk assessment**

To assess the risk, a methodology published by European Medicines Agency was employed, *Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use*, EMEA/CHMP/SWP/4447/00 (EMA 2006; Mustafa 2011).

**Predicted environmental concentration, adapted to local conditions of DCF in WWTP influent and effluent wastewater**

The quantitative evaluation of PhS was carried out by taking into account a 1 year period (2013). In Kaunas and Marijampole city municipalities \((A_{\text{area},j} (j = 1, 2))\), the quantity of consumed substances was evaluated according to Formula (2). The \(A_{\text{area},j}\) value is in direct proportion to the drug consumption at the national level \((A_{\text{Lithuania},j})\) and depends on the population size \((P_{\text{Lithuania}})\) (Mustafa 2011). According to the Statistical Department data, the population in Lithuania in 2013 was 2,958,182, in Kaunas – 305,493, and in Marijampole city municipality – 59,099.

\[
A_{\text{area},j} = \frac{A_{\text{Lithuania},j} \times P_{\text{area}}}{P_{\text{Lithuania}}} \quad (2)
\]

The predicted environmental concentration \((\text{PEC}_{j,k})\) for substance \((j)\) for both influent \((k = \text{inf})\) and effluent \((k = \text{eff})\) from WWTPs was calculated in accordance with the following formula (Mustafa 2011):

\[
\text{PEC}_{j,k} = \frac{A_{\text{area},j} \times 10^9 \times E_j \times (1 - R_j)}{Q_{\text{inh}} \times P_{\text{area}} \times 365 \times D} \quad (3)
\]

where:

\(E_j\) is excretion coefficient;

\(R_j\) is wastewater treatment coefficient;

\(Q_{\text{inh}}\) is water quantity consumed by one person (L/day) in the study area. According to EMA (2006), \(Q_{\text{inh}}\) is L/(inh·day).

During the calculations of \(\text{PEC}_{j,\text{inf}}\), the wastewater treatment coefficient was taken to be \(R_j = 0\), due to the fact that the treatment had not been performed yet.

**PEC in surface waters**

The PEC for DCF in surface waters was calculated by taking into account the wastewater dilution in the river water.

\[
\text{PEC}_{\text{SW}} = \frac{A_{\text{area},j} \times 10^9 \times E_j \times (1 - R_j)}{Q_{\text{inh}} \times P_{\text{area}} \times 365 \times D} \quad (4)
\]

where:

\(D\) is the factor for dilution of wastewater by surface water flow rate, \(D = 10\) (EMA 2006).

**Environmental management model**

An environmental management model was based on environmental systems theory according to Staniškis (2001).

**RESULTS AND DISCUSSION**

**DCF flow analysis in Lithuania**

**System definition**

Flows of the DCF for human use in Lithuania are evaluated with reference to the LSMCA database of consumed drugs in 2013. Several generally accepted assumptions have been made (Bound & Voulvoulis 2005; Zhang et al. 2008; Längin et al. 2009; Corrigan 2011; Martín et al. 2012; Plant et al. 2012; Li 2014). For analytical calculations, an assumption was made that all the purchased drugs had been consumed orally. Topical applications (ointments) are not considered. The main processes evaluated in the system were substance consumption and disposal, metabolism and the prevalence in the environment. *Functional unit* is a quantity of the target substance consumed in a year (kg/y). The purpose of SFA analysis is to determine potential emerging pollutant sources and the migration pathways in the environment, as well as to identify the most suitable facility or point where the amount of DCF pollution in the environment can be determined.

**Data analysis**

The considered SFA system was divided into three interrelated elements: the phases of consumption, disposal and distribution in the environment.
In the consumption phase, the following aspects were evaluated:

- **Private and public consumption.** This is the consumption of PhS in households, recreation and retreat centres and other public (non-health care) institutions where the waste and discharges of the target substances may form. Based on the conducted literature analysis, 17.7% of all sold drugs are not consumed; they are disposed of with waste or flushed into the sewage networks (Längin et al. 2009). Up to 89% of the population of Lithuania dispose of expired drugs with domestic waste; the rest return them to pharmacies (Kruopienė & Dvarionienė 2007). Upon the basis of previous studies, it was determined in the balance that 17% of all unconsumed drugs with DCF are flushed directly into the sewage (non-compliant disposal), 72% are disposed of with domestic waste, and 11% are returned to pharmacies. It was assumed that 65% of orally consumed DCF is excreted through urine (Zhang et al. 2008; Plant et al. 2012).

- **Hospitals and health care facilities.** This special source includes hospitals, sanatoria, rest homes, nursing homes and other public and private health care facilities. According to the Lithuanian Statistical Department data, in 2012 there were 27,079 beds in Lithuanian hospitals including tilting beds; according to the water allowance (RSN 26-90 1991), the water usage per bed in such facilities is 0.24 m³/day. It was estimated that hospital wastewater constituted 2.6% of the annually consumed water for agriculture and household needs in 2012. The research of Chèvre et al. (2013) of DCF flows in a Swiss city revealed that the portion of DCF from hospitals constituted 9.1% of the whole flow of PhS into the wastewater collection system. For our research, an assumption was made that water consumed for agriculture and household needs in Lithuania is considered as a deviation when evaluating only household wastewater; also larger quantities of the drug, when comparing daily private and public consumption, are consumed at health care facilities. Therefore, it was assumed that hospital wastewater constitutes approximately 8% of the consumed DCF, and all the wastewater from the hospitals and health care facilities is transported directly into WWTPs.

- **PhS production plants.** After the analysis of the literature and the interview with LSMCA specialists, it was concluded that DCF is not manufactured in Lithuania, although the substance may be used in laboratory research. An assumption is made that the quantity used in laboratories constitutes approximately 0.1% of all the annually consumed drugs, and 10% of these substances will be disposed of as hazardous waste, while the rest goes into wastewater collection systems.

In the disposal phase, the following was evaluated:

- **Wastewater collection systems.** As the analysis of the literature revealed (RL ME 2012), only 79% of residents have declared measures of wastewater management. In 2010, wastewater management services were available to 65.05% of the population. The wastewater disposed of via sewage systems amounted to 62% in that year. An assumption was made that the leakage from wastewater collection systems to surface waters due to damaged or poor quality wastewater collection systems constitutes 1%, and leakage into the soil is also 1%.

- **Untreated wastewater.** According to the conducted analysis, it was determined that approximately 35% of household wastewater is released directly to surface waters or is collected from wastewater pits. A careful estimation was made that the flow would be divided into two parts: leaking effluent to the soil and to the surface waters, 40% and 60%, respectively.

- **WWTPs.** The main flow consists of wastewater from wastewater collection systems (62%). Due to the fact that most WWTPs in Lithuania employ the traditional activated sludge technology, the WWTP DCF removal efficiency value of 26.4% was used in further calculations (Martín et al. 2012).

- **Wastewater pits, septic tanks and private WWTPs.** 1.78% of Lithuanian residents employ wastewater pits. With reference to the report submitted to the Ministry of the Environment of the Republic of Lithuania, wastewater collected from wastewater pits is pumped out by specialists providing decontamination services and transported to WWTPs specified in the contracts (RL ME 2012). An assumption is made that 70% of DCF will leak into the soil, and 30% will be transported to WWTPs.

- **Combustion.** All unconsumed drugs accumulated in pharmacies are collected by hazardous waste managers and dispatched for combustion. Flows of this waste from households (55.7%), hospitals (44.0%) and laboratories (0.3%) will be reflected in the substance flow scheme. It is assumed there is no active DCF remaining in solid incineration residues (Corrigan 2011).

- **Landfilling.** According to the literature analysis, as well as the report by the National Audit Office of the Republic of Lithuania into medical waste management, 72% of unused pharmaceutical waste is disposed of with household waste, and thus it later enters landfills (Bound & Voulvoulis 2005; NAOL 2010). Due to the improved landfill...
In the distribution phase, the following was evaluated:

- **Air.** DCF is non-volatile and combustible; therefore, its release into air is considered to be negligible.
- **Sludge.** For the SFA research, according to the previously conducted studies in Lithuania (EPA 2012), it was accepted that 57.4% of sludge is stored in sludge collection sites, 0.9% of sludge is disposed of in landfills, and 20.1% is used in agriculture for fertilisation. The rest (21.6%) is managed by other treatments. In the SFA, an assumption is made that all the DCF remaining in sludge will enter the soil.
- **Surface waters.** As has been analysed previously, PhS will enter surface waters with untreated wastewater due to the leakage from wastewater collection systems and by landfilling.
- **Soil.** The PhS will enter the soil from untreated wastewater (39%); by leaking from wastewater collection systems (1%), septic tanks (100%), and wastewater pits (70%); and by disposing of PhS in landfills (15%).
- **Groundwater.** In this study, all the PhS that enter surface waters are assumed to migrate, and, after being affected and absorbed by aquacultures and precipitate, will enter the groundwater. Substances that enter the soil by means of filtration will enter the aeration zone and later the groundwater.

**Results of SFA**

Approximately 92% of DCF (for oral human uses) is consumed in households, where the main environmental contamination by PhS originates. Distribution of DCF in Lithuania in 2013, determined by SFA analysis, is presented in Figure 1. A summarised SFA scheme in the Appendix (available with the online version of this paper) shows the detailed DCF flow (in kg/year) through the currently ordinary ways of DCF penetration to the environment.

Of all the sold DCF, 56.3% enters wastewater. As much as 28% of DCF currently remains in untreated wastewater: it happens due to the fact that households are not connected to common wastewater collection and disposal systems. Nevertheless, the biggest part (49.2%) of DCF from households enters the environment, i.e., surface waters, through WWTPs, the rest is distributed among landfilling, combustion, untreated wastewater, and private wastewater treatment systems (see Figure 1).

The DCF flow analysis shows that private and public consumption is the main pollution source, and WWTPs are the main facilities through which the biggest part of pharmaceutical pollutants are released into the environment.

**Levels of DCF in Kaunas and Marijampole wastewater**

**Study area**

Kaunas is in the geographical centre of Lithuania, with its WWTP located on the left bank of the river Nemunas, whereas Marijampole is in the south-western part of Lithuania, with its WWTP located near the river Sesupe, also belonging to the Nemunas river basin. Both wastewater treatment technologies consist of mechanical–biological treatment plants, thus applying activated sludge technology. The domestic wastewater is predominant (approximately 55%) in Kaunas WWTP with some industrial wastewater (30%, the rest generated by the other types of consumers), while industrial wastewater constitutes more than 60% in Marijampole WWTP. Other characteristics of the study area are shown in Table 1.

<table>
<thead>
<tr>
<th>Size of population in 2013, Inhab.</th>
<th>Volume treated (m³/day)</th>
<th>Percentage of inhabitants using wastewater treatment services in the study area, %</th>
<th>Average river debit near sampling point, m³/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Municipal WWTP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kaunas*</td>
<td>306,888</td>
<td>66,400</td>
<td>95*</td>
</tr>
<tr>
<td>Marijampole**</td>
<td>59,483</td>
<td>22,000</td>
<td>76.7b</td>
</tr>
</tbody>
</table>

*River Nemunas.
**River Sesupe.
Strategic plan update of Kaunas, No. T-332 (Kauno miesto 2005).
Strategic action plan of Marijampole municipality, No. 1–1 (Marijampolės savivaldybės 2014).
Both WWTPs meet the set of legal requirements (Lietuvos Respublikos Aplinkos Ministro 2006). The treatment efficiency of the studied WWTPs in the first quarter of 2014 was similar, and was higher than 95% for biochemical oxygen demand (BOD), total phosphorus and suspended solids; total nitrogen was 43.2% for Kaunas WWTP and 78.6% for Marijampole WWTP.

The results of DCF analysis in wastewater

Twenty-four hour samples were taken for both WWTPs on 4 March (2014). The experimentally determined concentrations of DCF in wastewater were 1,590 ng/L at Kaunas WWTP and 1,520 ng/L at Marijampole WWTP. In the effluent, the concentrations were 1,420–1,470 and 1,060 ng/L, respectively. The average treatment efficiency for DCF in Kaunas WWTP was 12.25%. The treatment efficiency in Marijampole was 30.3% (see Table 2).

Determined DCF concentrations are also similar to the ones measured in such countries as Austria and Spain (Clara et al. 2005; Jelic et al. 2011).

In order to evaluate the surface water contamination, the DCF concentration was recalculated, taking into account the pollutant dilution in a receiver (see Formula (5), applied according to Bolster et al. (2005) and Keller et al. (2006)).

\[
C_T = \frac{Q_1 \cdot C_1}{Q_1 + Q_2}
\]

where:

- \(C_T\) is PhS concentration in a river, ng/L;
- \(Q_1\) is average effluent wastewater flow rate, m³/day;
- \(C_1\) is PhS concentration in wastewater, ng/L;
- \(Q_2\) is average multiannual river flow rate, m³/day.

The DCF concentrations in water, compared to annual average environmental quality standards (100 ng/L according to Loos (2012)), reveal no risk for aquatic organisms and are lower by 17.8 times in Nemunas and 5.6 times in Sesupe. This kind of pollution estimate does not include the pollution of the river stream before discharge of the WWTP effluents. It is believed that additional effluents of wastewater may cause higher pollution concentrations of surface water flow.

Comparison with Saint Petersburg. Saint Petersburg is the second biggest city in Russia and the biggest one in the whole Baltic Sea region. The population of Saint Petersburg is over 5 million, which is 16.5 higher than in Kaunas and 85.1 higher than in Marijampole. Estimated consumption of DCF is 700 kg/year (Nikiforov et al. 2014), which is only three times higher than estimated consumption in Kaunas (see Table 3).

Considering which part of the consumed DCF reaches the WWTP for the two Lithuanian cities, almost identical values (16%) were obtained. This is an experimental confirmation of the model validity. The estimated value for St Petersburg (37%) is 2.3 times higher. Possible cause for this difference can be underestimation of consumption in St Petersburg (it can be higher than country-wide average) or overestimation of consumption in Kaunas and Marijampole (not every household connected to the city sewers).

### Table 2 | DCF concentration in wastewater

<table>
<thead>
<tr>
<th>PhS</th>
<th>WWTP in Kaunas</th>
<th>WWTP in Marijampole</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCF</td>
<td>Influent, ng/L</td>
<td>Effluent, ng/L</td>
</tr>
<tr>
<td></td>
<td>1,590</td>
<td>1,420–1,370</td>
</tr>
</tbody>
</table>

### Table 3 | Comparison of DCF consumption and release in Russia (Nikiforov et al. 2014) and Lithuania

<table>
<thead>
<tr>
<th>City</th>
<th>Population in 2013</th>
<th>Wastewater volume, 1,000 m³/day</th>
<th>DCF estimated consumption*, kg/y</th>
<th>Release into wastewater, g/day</th>
<th>Release into wastewater, kg/y</th>
<th>Release/consumption ratio</th>
<th>DCF in wastewater, ng/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPb</td>
<td>5,028,000</td>
<td>2,180*</td>
<td>700</td>
<td>890</td>
<td>325</td>
<td>0.37</td>
<td>408</td>
</tr>
<tr>
<td>K</td>
<td>305,493</td>
<td>66.4*</td>
<td>268</td>
<td>106</td>
<td>39</td>
<td>0.16</td>
<td>1,590</td>
</tr>
<tr>
<td>M</td>
<td>59,099</td>
<td>13.3*</td>
<td>37</td>
<td>20</td>
<td>7.4</td>
<td>0.16</td>
<td>1,520</td>
</tr>
</tbody>
</table>

SPb – St Petersburg, Russia; K – Kaunas, Lithuania; M – Marijampole, Lithuania.

*Estimated only consumers of DCF who are connected to centralised wastewater collection systems.


http://www.suduvosvandenys.lt/.

A different structure of consumption or different practice of administration in the two countries can also contribute to the observed difference.

Environmental risk assessment

Estimated concentrations of DCF in wastewater

It was assumed that approximately 65% of DCF oral dosage is excreted through urine and enters the environment with wastewater (Zhang et al. 2008; Martín et al. 2012; Plant et al. 2012). It is a theoretical value, hereinafter Ej. The PhS treatment efficiency (Rj, %) from wastewater was evaluated, taking into account the wastewater management technology (Strenn et al. 2004; Zhang et al. 2008; Martín et al. 2012; Zhou et al. 2013). This value refers to the percentage of the substance removed from wastewater by the means of sludge adsorption, hydrolysis and biodegradation together. The wastewater treatment technology of both Kaunas and Marijampole is comparable; therefore, the same Rj is applied. In 2013, 10% of all the products containing DCF in the Lithuanian market were sold in Kaunas, while the share of Marijampole was only about 2% (see Table 4).

Predicted DCF concentrations in surface waters

After the evaluation of the treated wastewater distribution in a receiver, an unacceptable theoretical environmental effect of DCF concentrations (PEC/PNEC > 1) was determined (see Table 5).

A predicted no-effect concentration (PNEC) was chosen after the assessment of the worst scenario; however, a series of conducted studies reveals that the no-observed-effect concentration (NOEC) may be much lower. According to the overview of the literature, the most sensitive test is an early life stage toxicity test (fish) (see Table 6).

For DCF concentration at locations where treated wastewater is released, the quotient MEC/PNEC is > 9 (MEC: measured environmental concentration). Due to this fact, a risk arises for the biota located near the WWTP (see Table 7). However, after the evaluation of the wastewater dilution, DCF concentration was reconsidered as acceptable.

The PEC/MEC value indicates whether the method application is suitable (Mustafa 2012). PEC/MEC < 4 shows that the assessment methodology is acceptable for Marijampole city with a slight possible variance. PEC/MEC > 4 indicates significant variations.

It is important that only treated wastewater diluted in river water was evaluated for the PEC, but not the emissions from influent river waters. The conducted risk assessment analysis revealed that the predicted concentrations calculated by this methodology of risk analysis may be significantly higher in the areas where the population size is higher, and in contrast, it may be suitable for the areas where the population size and density are smaller. It may depend on a variety of social indicators determining the drug use in a given area, for example, the standard of living and the residents’ age.

### Table 4

<table>
<thead>
<tr>
<th>Target area</th>
<th>DCF consumption, kg/year</th>
<th>PECinf, ng/L</th>
<th>PECj,inf, ng/L</th>
<th>Ej, %</th>
<th>Rj, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaunas</td>
<td>268.00</td>
<td>8185.0</td>
<td>6024.2</td>
<td>65</td>
<td>26.4</td>
</tr>
<tr>
<td>Marijampole</td>
<td>36.63</td>
<td>5483.2</td>
<td>4035.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Plant et al. (2012).

*Plant et al. (2012).

### Table 5

<table>
<thead>
<tr>
<th>Location</th>
<th>PECinf, ng/L</th>
<th>PNEC, ng/L</th>
<th>PEC/PNEC, ng/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>River Nemunas, near Kaunas</td>
<td>602.4</td>
<td>100*</td>
<td>6.02</td>
</tr>
<tr>
<td>River Sesupe, near</td>
<td>403.6</td>
<td>4.04</td>
<td></td>
</tr>
</tbody>
</table>

*Ort et al. (2009).

### Table 6

<table>
<thead>
<tr>
<th>Maximum daily dose, mg</th>
<th>PNEC</th>
<th>Algal growth inhibition test</th>
<th>Daphnia sp. reproduction test</th>
<th>Early-life stage toxicity test (fish)</th>
</tr>
</thead>
<tbody>
<tr>
<td>450**</td>
<td>0.1 μg/L*</td>
<td>NOEC</td>
<td>NOEC</td>
<td>0.5 μg/L*</td>
</tr>
</tbody>
</table>

*Ort et al. (2009).

**Hamre (2006).

### Table 7

<table>
<thead>
<tr>
<th>Location</th>
<th>MEC</th>
<th>MEC/PNEC</th>
<th>PEC/MEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influent wastewaters, μg/L</td>
<td>1.59</td>
<td>1.52</td>
<td>5.1</td>
</tr>
<tr>
<td>Effluent wastewaters, μg/L</td>
<td>1.40</td>
<td>1.06</td>
<td>4.2</td>
</tr>
</tbody>
</table>

K – Kaunas, M – Marijampole.
Application of the environmental management system theory to manage the concentrations of PhS in wastewater

An efficient management system must exhibit three main properties:

- It must be broad-based and include all the activities of a considered facility.
- The system and its procedures must be understandable for the participants of the whole system.
- The system should allow for a constant improvement of the environmental protection effectiveness and it should be open for analysis (Staniškis et al. 2010).

One of the actual examples of the environmental management system usage is a decision support system proposed and adapted for Kaunas wastewater treatment facility in order to manage one of the most important aspects, as is the input required by the system. The system allowed us to identify the river water quality, to predict the system behaviour and to evaluate different management scenarios. Thereby, it was determined that Kaunas WWTP BOD could be reduced by 8–10% in the mechanical treatment stage, and by 8–15% in the biological treatment stage (Vaitiekūnienė & Vincevičienė 2001).

In theory, the main task of the management system is to find such a management effect $U(t)$ and appropriate strategic factors that would allow the set objectives of the management system ($X_{in}(t)$) to be achieved (Staniškis 2003). The main task of the management system is to reduce the negative environmental impact of installing the tools for pollution prevention by the most cost-effective means.

**Management system.** Selection of the management system type for a specific environment depends not only on available management tools, but also on deviations that enter the system. The proposed environmental management system is a structure of a closed-loop feedback–feedforward control. Theoretically, an interference compensation device measures the interference $D(t)$ influencing the facility and forms a signal to the regulation device, a controller, that eliminates the influence of an interference to a regulating parameter $X_{out}(t)$. A forming management impact $U(t)$ compensates the process output variable deviation from the set value, and determines the DCF concentration change in wastewater in order to improve environmental protection efficiency. For the system to work effectively, and the conditions not to change, the deviation should be equal to 0 ($\Delta = 0$). The management system is presented in Figure 2.

The main object of this study, for which the management system was developed, is household wastewater that contains DCF. Significant object parameters and system state variables are the consumption quantity per year, at the average country level (kg/year) and DCF concentration in wastewater (ng/L). The object control parameter is DCF concentration in wastewater (ng/L). The goal of the system is $X_{in}(t) = 0$. The main strategic decision in the area of water policy is a gradual

![Figure 2](https://iwaponline.com/wst/article-pdf/74/6/1255/458336/wst074061255.pdf)

**Figure 2** Environment management scheme of wastewater containing PhS (Baranauskaitė & Dvarioniene 2014b).
reduction of the contamination with PhS and the leakage termination. In order to achieve the goal of the management system \( X_{\text{out}}(t) \), it is suggested to gradually reduce it; i.e., until 2020: \( X_{\text{in}} \rightarrow \frac{1}{4} X_{\text{out}}; \) from 2020 to 2025: \( X_{\text{in}} \rightarrow \frac{1}{2} X_{\text{out}}; \) from 2025 to 2030: \( X_{\text{in}} \rightarrow 0 X_{\text{out}}. \)

To achieve the management goal of the object chosen for the study in the area of wastewater management and water policy, the following is suggested:

1. Integration of economical and efficient (from the point of view of the environmental protection) treatment processes into city WWTP.
2. Separation of wastewater flows from health care facilities.

SFA allowed us to determine the consumption location where the bulk of waste with DCF residue is generated in households. During SFA, it was determined that the biggest part of DCF from households (49.2%) enters the environment with wastewater after flowing through the WWTP (see Figure 1). Therefore, the main purpose of this management system is to reduce the DCF leakage from households to surface waters to a minimum, i.e., 0. The system output parameters can be checked by direct and indirect measurements. In order to check the parameters, the same tests conducted in this study should be employed, i.e., pharmaceutical substance flow analysis at the country level (kg/year) and qualitative analysis of PhS in wastewater (ng/L) (see Figure 2). If the management tools suggested for the management model are effective, the DCF leakage from households into WWTP will be reduced by a quarter until 2020, i.e., to the value 571.9 kg/y in wastewater according to SFA; also, after the measurements are performed, the PhS quantity in wastewater (ng/L) should also be reduced accordingly at the same ratio. The PhS risk assessment should indicate the declining values of substances of concern in the aquatic environment. The resulting interferences, such as lack of research, lack of legal regulations, or additional costs, should be compensated for by interference compensators: studies and research, materials modification and limitation of consumption, etc. (see Figure 2). Thus, with the operating management system, one-half of the DCF primary pollution should be detected in wastewater by 2025, and by 2030 the leakage should have disappeared.

The system was analysed only regarding the DCF, but due to its properties, it may also be adapted for a wider spectrum of micropolllutants. The proposed model could help to reduce the PhS discharges into the environment. It is a system that privileges the end-of-pipe technology, but together with integrated preventive measures, the discharge into the environment may be stopped. It is known that as long as PhS compounds are used in human activities and there are no substitutes without negative impacts, the PhS residues will enter the environment following excretion. These residues will need to be managed in order to avoid negative impacts. In any case, as the SFA study revealed and as the six system compensators have demonstrated (see Figure 2), the solution of the PhS waste generation problem has to start with raising the consumer's environmental awareness. Waste management is the second stage.

**CONCLUSIONS**

The SFA results revealed that 56.3% of DCF that was commercially available in Lithuania was discharged into wastewater through different pathways. Households were the main source of PhS pollution. The biggest part of household DCF, 49.2%, was released to the environment through WWTPs, 27.7% entered wastewater and reached biota without appropriate treatment, 17.9% was disposed of in a landfill, 2.7% was treated by combustion, and 2.4% was managed in private wastewater treatment systems.

A qualitative DCF analysis of Kaunas inlet wastewaters revealed that DCF concentration is 1,590 ng/L, while in Marijampole it is 1,520 ng/L. Twenty-four-hour composite samples from the influent and effluent of WWTPs were collected during one sampling in March (2014). They might have contributed to the obtained average wastewater treatment efficiency (determined as 12% for Kaunas WWTP and 30% for Marijampole WWTP). This study also revealed that conventional wastewater treatment with activated sludge technology used in Kaunas and Marijampole is not efficient for the prevention of pharmaceutical waste discharging into the natural environment.

DCF was found to be a compound of potential concern in the aquatic environment, which requires additional management. It was determined that the PEC is not acceptable (PEC/PEC > 1) for surface waters near Kaunas and Marijampole, 6.02 and 4.04, respectively (treated wastewater dilution was included). The application of the risk assessment model revealed that PEC calculated by this methodology may be significantly higher in the areas where the number of residents is higher, and on the contrary, it is suitable in the areas where the number of residents and the density are smaller.

The prepared environmental model gives a possibility to demonstrate the optimal management of PhS in the environment, to enable resource efficiency and waste prevention as
well as striving to meet legislative demands. The recommendations integrated into the suggested environment management system of PhS included: substance substitution and consumerism restriction, education of consumers and interested parties, exchange of information between target groups, development of new drugs, legislative amendments, as well as studies and research on the current situation. With the application of the main system controllers (technological solutions) and compensators (prevention tools), the expected efficiency of the environmental protection is the reduction of up to 49.2% of the PhS leakage from households by the year 2030.

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