C1.4 - Environmental risk

TIERED APPROACH FOR ENVIRONMENTAL RISK ASSESSMENT OF EMERGING POLLUTANTS IN AQUATIC SYSTEMS

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ABSTRACT

During the last three decades the presence of emerging pollutants such as pharmaceuticals, personal care products, disinfection by-products and industrial additives in aquatic systems has been the focus of much public concern and also scientific consideration. The continuously increasing contamination of surface and ground-waters with these pollutants is one of the key environmental problems. To solve the water quality problems caused by these hazardous micropollutants a complex and efficient risk management strategy is required.

Hungarian CDFILTER project aimed to develop new cyclodextrin-based sorbents suitable for monitoring bioactive micropollutants and for removal of these pollutants from drinking water and treated wastewater. The most important decision support tool of the CDFILTER research was the risk-based evaluation and management where the river Danube used both as a source of drinking water resource and as a wastewater receiver has been played central role.

As part of the risk management a tiered strategy for environmental risk characterization of micropollutants in aquatic ecosystems has been developed.

Hereby this paper presents the main results of first tier of the tiered strategy, the prioritization approach with the scoring (ranking) system and the CDFILTER Priority List.

Keywords*: cyclodextrin-based sorbent, emerging pollutant, micropollutant, prioritization, priority list, risk management*

INTRODUCTION

The occurrence of organic micropollutants in ground- and surface waters has become an important concern, mainly because of possible related environmental and health effects (Khetan and Collins 2007, Kümmerer 2009, NTP 2008, Pal *et al* 2010, Yoon et al 2010).

Numerous studies have been published on the occurrence, fate and effects of emerging pollutants in different parts of the world, including a wide range of sources and aquatic systems (Bendz *et al* 2005, Khan *et al* 2004, Schäfer et al 2002, Sedlak *et al* 2005, Smital *et al* 2004). Although most of these chemicals are present at trace concentrations, there has been emerging concern about many micropollutants because of their biological activities adversely impacting aquatic life and human health (Fent *et al* 2006, Ferrari *et al* 2006). Primary effects of these substances are well known, but their long-term effect on the ecosystem and their secondary effects are largely unknown (Crane *et al* 2006, Ferrari *et al* 2006).

So this worldwide growing pollution of surface and ground-waters with a vast number of synthetic or natural organic compounds has been one of the key environmental problems facing civilization recently (Angelakis and Durham 2008, Boyd *et al* 2003, Daughton 2004). The number and frequency of detections of emerging pollutants are increasing and the detectable levels are reducing due to the improving analytical techniques (Daughton 2004).

Water policy has listed some of these emerging compounds as priority hazardous pollutants, but many of them are not listed in official registries (Directive 2011/0429/EC, ICPDR 2003).

The literature shows, that many of these micropollutants survive biodegradation, and finally being discharged into receiving waters, e.g. surface waters (Carballa *et al* 2004, Dlugolecka *et al* 2006, Gomes *et al* 2003, Kahn *et al* 2004, Miege *et al* 2009, Oulton *et al* 2010, Yu-Chen *et al* 2010).

Therefore the environmental and health risk associated with these previously unknown or unrecognized chemicals in the aquatic systems has been a very important concern recently (Carlsson *et al* 2006, Enick and Moore 2007, Webb 2001).

Prioritization models and schemes for emerging contaminants have been developed in order to support decisions in connection with monitoring and risk reduction (Guillén *et al* 2012, Murray *et al* 2010, Sanderson and Thomsen 2009, Stuart *et al* 2012).

Regarding the water quality problem caused by these hazardous micropollutants a complex and efficient risk management system involving risk assessment and risk reduction is necessary. First of all, tools to assess the long-term impact and risk of these pollutants on aquatic ecosystems and human health must be developed or refined and implemented (Koschorrek *et al* 2002, Schwarzenbach *et al* 2006). Secondly, effective waste water treatment technologies are necessary, because conventional techniques do not provide effective elimination of these organic contaminants (Castigloni *et al* 2006, Oulton *et al* 2010, Schaar *et al* 2010, Schwarzenbach *et al* 2006, Verlicchi 2010).

Addressing these issues the Hungarian CDFILTER project aimed to develop new cyclodextrin-containing sorbents suitable for monitoring bioactive micropollutants and for removal of these pollutants from drinking water and treated wastewater (Gruiz *et al* 2011). The most important decision support tool of the CDFILTER research was the risk-based evaluation and management (Figure 1).

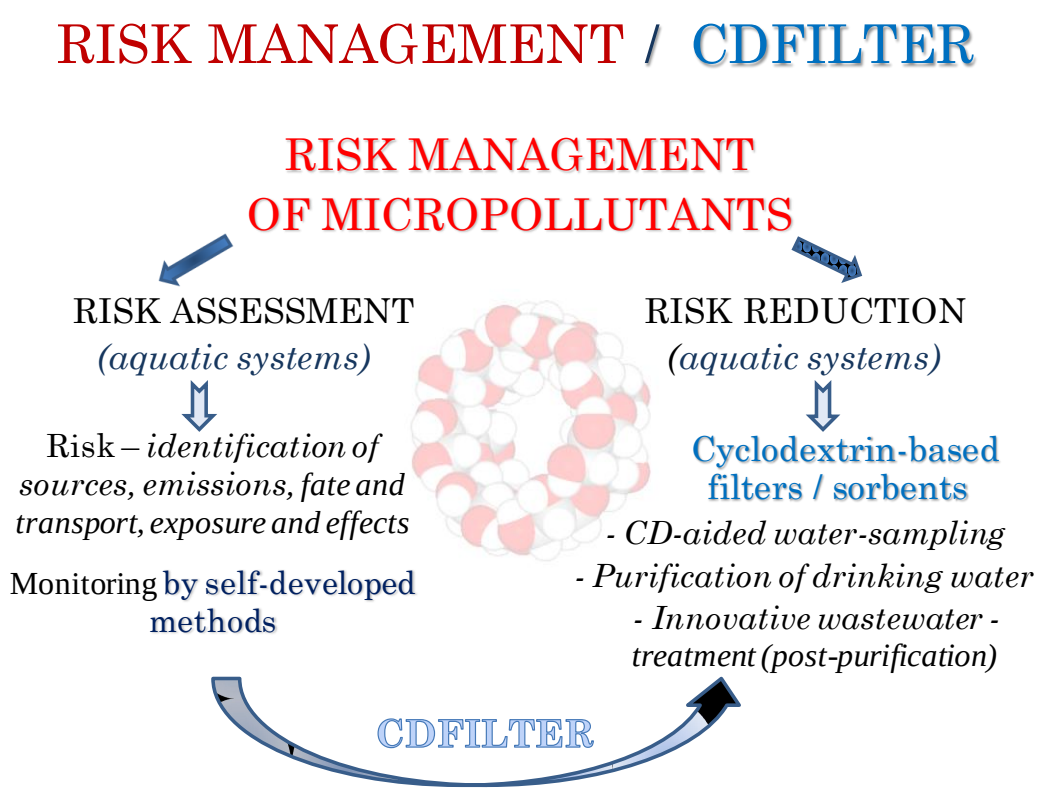

Figure 1. Risk management concept of CDFILTER project for micropollutants in water systems

To focus our research on the large and complex topic as risk assessment and risk reduction of organic micropollutants inventory of chemicals had to be drawn up.
To cope with the vast amount of organic micropollutants occurring in the environment, a priority list of organic micropollutants was worked out and the assessment of removal possibilities with cyclodextrin-based filters have been focused on the high priority chemicals of the list.
The river Danube used both as a source of drinking water resource and as a wastewater receiver has been played central role in the project.

TIERED STRATEGY FOR ENVIRONMENTAL RISK ASSESSMENT OF EMERGING POLLUTANTS

As part of the CDFILTER risk management a three-step tiered strategy for environmental risk characterization of micropollutants in aquatic systems has been developed. This tiered approach provided a systematic way of determining what level of investigation is appropriate for the site of concern, minimising unnecessary investigations, and allowing more efficient risk management tasks.

As the first tier of the tiered strategy, a qualitative risk assessment system was developed and applied. Hereby we present the main results of first tier: the prioritization approach with the scoring (ranking) system and the CDFILTER Priority List.

Emerging pollutants in aquatic systems

The Danube River is one of the most important natural axes in South-East-Europe. From source to mouth, the Danube passes 10 countries, 4 capitals and draws water from 19 nation states. This makes the Danube River Basin the most international one in the World (ICPDR).

The river absorbs raw sewage from cities, pesticides from agriculture as well as chemicals and waste from factories and oil from transport by ships. Numerous industrial factories and plants in oil refining, chemicals, pulp, metallurgy and refining often release pollutants into the many small rivers and tributaries that feed into the Danube River. Inadequately treated waste water often still ends up in the Danube so hazardous and toxic compounds are also a major hazard. Therefore anthropogenic activity has severely affected the Danube ecosystems leading to serious problems with water quality and quantity, and significant reductions in biodiversity (ICPDR).

The river Danube has been played central role in CDFILTER risk management tasks where the river used both as a source of drinking water resource and as a wastewater receiver.

CDFILTER Inventory of micropollutants

Prioritizing of micropollutants in aquatic systems can be carried out in different ways, depending on the selection criteria used. The selection method proposed in our research was developed from the perspective of the surface waters and drinking water quality, related to environmental and human health. Potentially hazardous, risky micropollutants were selected for screening exercise taking into account their occurrence in surface waters, in the river Danube and treated waste waters in Hungary, moreover their production / use volumes. Low removal efficiency in the wastewater treatment was also taken into considerations in set up of micropollutants inventory.
This preliminary list is comprised of about 58 emerging contaminants including pharmaceuticals, industrial compounds, pesticides, nanomaterials, flame retardants and surfactants, personal care products, as well as caffeine and nicotine.

Substance data sheet of emerging pollutants

Detailed substance data sheets were worked out for each chemical, including information about the volume of production, its use, and the physical, chemical, biological properties of the substance. Details of their occurrence and fate in the aquatic ecosystems moreover environmental and human toxicity data were also provided. Data and characteristics of the substances were collected from data bases with environmental aspects and from own measurements. Data sheets of chemicals have been prepared by scientific experts and peer reviewed.

Prioritization approach

The *Tier 1* was intended to be a qualitative screening process.
A comprehensive protocol was developed and set up to determine the rank of substances in the Priority List. Amount of production and consumption, physicochemical data, biodegradability as well as environmental and human health effects were taken into account aiming prioritization.
Prioritization system (Table 1) was developed to serve as a risk management tool in scoring and ranking of chemicals of CDFILTER inventory.

Table 1. Scoring and ranking system for micropollutants in surface waters

PARAMETERS	**Ranking classification**	***SCORE***
Production (use)	< 1 kg/year 1–100 kg/year 100–1 000 kg/year 1 t–10 t/year more than 10 t	***0*** ***1*** ***3*** ***5*** ***10***
K_{ow} - *Octanol-water partition coefficient*	100 000–1 000 000 10 000–100 000 1 000–10 000 100–1 000 10–100 <10	***0*** ***1*** ***2*** ***3*** ***5*** ***10***
Abiotic degradability	readily: $t_{1/2}$= 0–2 days moderately: $t_{1/2}$= 2 days–1 week $t_{1/2}$= 1 week–1 month $t_{1/2}$= 1 month–1 year persistent: $t_{1/2}$= more than 1 year	***0*** ***1*** ***2*** ***3*** ***5***
Biodegradability	readily: $t_{1/2}$= 0–2 days moderately: $t_{1/2}$= 2 days–1 week $t_{1/2}$= 1 week–1 month $t_{1/2}$= 1 month–1 year persistent: $t_{1/2}$= more than 1 year	***0*** ***1*** ***2*** ***3*** ***5***
Endocrine disrupting effects	no possibly yes	***0*** ***3*** ***5***
Immune system disrupting effects	no possibly yes	***0*** ***3*** ***5***
Tissue (dermal) lesion	no possibly yes	***0*** ***3*** ***5***
Mutagen	no possibly yes	***0*** ***3*** ***5***
Carcinogen	no possibly yes	***0*** ***3*** ***5***
Reproduction / development effects	no possibly yes	***0*** ***3*** ***5***
Lowest acute toxicity data (LC_{50}, EC_{50})	>100 mg/L 100–10 mg/L 1–10 mg/L >1 mg/L	***0*** ***2*** ***3*** ***5***
Lowest chronic toxicity data (ecotoxicological) NOEC/LOEC	>100 mg/L 100–10 mg/L 1–10 mg/L <1 mg/L	***0*** ***2*** ***3*** ***5***

Key to the table above:

$t_{1/2}$ *Half-life : the time taken for the concentration of the compound in a defined compartment (e.g. soil, water) to decline by 50%*

LC_{50} *the concentration of the compound that is lethal to 50% of the test organisms*

EC_{50} *the effective concentration of the compound that produces a specific measurable effect in 50% of the test organism*

NOEC the no observed effect concentration

LOEC the lowest observed effect concentration

Priority List

Following the first scoring step chemicals were ranked on the base of the calculated risk scores (*Ranking 1).* In the next step the interaction between the selected chemicals and cyclodextrins was also considered in order to obtain efficient risk reduction (*Ranking 2*).

In the *Ranking 2* phase following criteria (CDFILTER score) were taken into account to determine the final composite score of micropollutants in the list:

- complexation with cyclodextrin - the interaction between the selected chemicals and cyclodextrins
- availability of analytical methods for measuring trace concentration of micropollutants in aquatic systems,
- availability of ecotoxicity methods to determine the long term effect of micropollutants for aquatic systems and
- availability of own measured values.

The CDFILTER Priority List with risk score and composite score of chemicals is shown in *Table 2*.

Table 2. CDFILTER Priority List

Ranking 1.	***Chemicals***	***CAS number***	***Risk score***	***Composite score****	***Ranking 2.***
1	**nicotine**	54-11-5	57	*87*	***1***
2	**bisphenol A**	80-05-7	57	*86*	***2***
25	**oestradiol**	50-28-2	44	*75*	***3***
8	**carbamazepine**	298-46-4	51	*73.5*	***4***
30	**di(2-ethylhexyl)-phthalate (DEHP)**	117-81-7	42	*73*	***5***
31	**dibutyl-phthalate (DBP)**	84-74-2	42	*73*	***6***
18	**gemfibrozil**	25812-30-0	46	*71*	***7***
21	**cotinine**	486-56-6	45	*70*	***8***
33	**2,6-Di-tert-butylphenol**	128-39-2	41	*70*	***9***
28	**diclofenac**	15307-86-5	43	*69*	***10***
38	**progesterone**	57-83-0	40	*68*	***11***
43	**naproxen**	22204-53-1	38	*68*	***12***
40	**ketoprofen**	22071-15-4	39	*67*	***13***
53	**ibuprofen**	15687-27-1	35	*67*	***14***
9	**doxorubicin**	23214-92-8	50	*66.5*	***15***
3	**sulfamethoxazole**	723-46-6	55	*66*	***16***
20	**simazine**	122-34-9	45	*65.5*	***17***
5	**diuron**	330-54-1	52	*65*	***18***
11	**paracetamol**	103-90-2	50	*65*	***19***
26	**atrazine**	1912-24-9	43	*65*	***20***
39	**fenofibrate**	49562-28-9	40	*65*	***21***
37	**norethisterone/ norethindrone**	68-22-4	40	*64*	***22***
44	**metoprolol**	37350-58-6	38	*64*	***23***
14	**carboplatin**	41575-94-4	46	*62.5*	***24***
16	**pentachlorophenol (PCP)**	87-86-5	46	*62*	***25***
46	**triclosan**	3380-34-5	37	*62*	***26***
47	**2,4-dichlorobenzoic acid**	50-84-0	37	*62*	***27***
24	**ethinyloestradiol**	57-63-6	44	*61*	***28***
34	**trifluralin**	1582-09-8	41	*61*	***29***
45	**caffeine**	58-08-2	38	*60*	***30***

Ranking 1.	*Chemicals*	*CAS number*	*Risk score*	*Composite score**	*Ranking 2.*
13	**verapamil**	52-53-9, hydrochloride: 152-11-4	46	*59*	***31***
6	**nonylphenol**	25154-52-3	51	*58*	***32***
17	**benzothiazole**	95-16-9	46	*58*	***33***
19	**epoxiconazole**	135319-73-2	45	*58*	***34***
23	**bezafibrate**	41859-67-0	44	*58*	***35***
4	**metamizole (sodium salt)**	68-89-3	52.5	*57.5*	***36***
10	**bis(tributyltin) oxide**	56-35-9	50	*57*	***37***
15	**cyproterone**	2098-66-0, acetate: 427-51-0	46	*57*	***38***
36	**daunorubicin**	20830-81-3, hydrochloride: 023541-50-6	40	*56.5*	***39***
7	**urethane/ethyl carbamate**	51-79-6	51	*56*	***40***
27	**isoproturon**	34123-59-6	43	*56*	***41***
29	**simvastatin**	79902-63-9	43	*56*	***42***
32	**chlorpyrifos**	2921-88-2	41	*56*	***43***
48	**medroxyprogesteron**	520-85-4, acetate: 71-58-9	37	*55*	***44***
12	**aminophenazone**	58-15-1	48.5	*53.5*	***45***
22	**2,4-dichlorophenoxyacetic acid (2,4-D)**	94-75-7	44	*53*	***46***
42	**benzotriazole**	95-14-7	38	*49*	***47***
49	**metolachlor**	51218-45-2	36	*49*	***48***
50	**S-metolachlor**	87392-12-9	36	*49*	***49***
35	**phenylbutazone**	50-33-9	41	*47*	***50***
55	**penicillins**	penicillin G: 61-33-6, penicillin: 1406-05-9	34	*47*	***51***
41	**sodium glutamate, glutamic acid**	sodium glutamate: 142-47-2, glutamic acid: 56-86-0	39	*46*	***52***
54	**benfluralin**	1861-40-1	34	*46*	***53***
56	**diflubenzuron**	35367-38-5	33	*45*	***54***
51	**nanoTiO_2**	13463-67-7	36	*44*	***55***
57	**tris(nonylphenyl) phosphite (TNPP)**	26523-78-4	31	*43*	***56***
52	**taurine**	107-35-7	35	*40*	***57***
58	**propofol**	2078-54-8	27.5	*32.5*	***58***

**Composite score* – The composite score is the sum of the risk score completed with the CDFILTER score

The highest priority pollutants for further risk management task included industrials (BPA, DEHP, DPA), pesticides (diuron) and PPCPs (carbamazepine) because they occur frequently in the freshwater environment and pose environmental and human health risk. Overall, the qualitative predictions are roughly in agreement with literature values.

Further risk management task and results

The prioritized chemicals were assessed in the second tier by a generic quantitative risk assessment methodology. The generic risk quotient ($RQ_{generic}$) was calculated for selected micropollutants based on generic exposure assessment and effect assessment. The *Predicted Environmental Concentration* (PEC) was determined using European default parameters where the produced/used volume of chemicals was taken into account. The *Predicted No Effect Concentration* (PNEC) was also calculated, that is the concentration of chemicals that causes no adverse effect to the environment.
The PEC/PNEC ratio was calculated used as an indicator of risk (RQ= PEC/PNEC).

The last tier was the site specific risk assessment which gave a more detailed picture on the local risks. In the case of *Site specific Risk Assessmen*t the PEC/PNEC approach was also applied too, but instead of default values the site specific measured concentrations and site specific environmental parameters were used. Local risk quotient was calculated for the river Danube and treated wastewater discharging surface water bodies in the case of selected micropollutants (Figure 2).

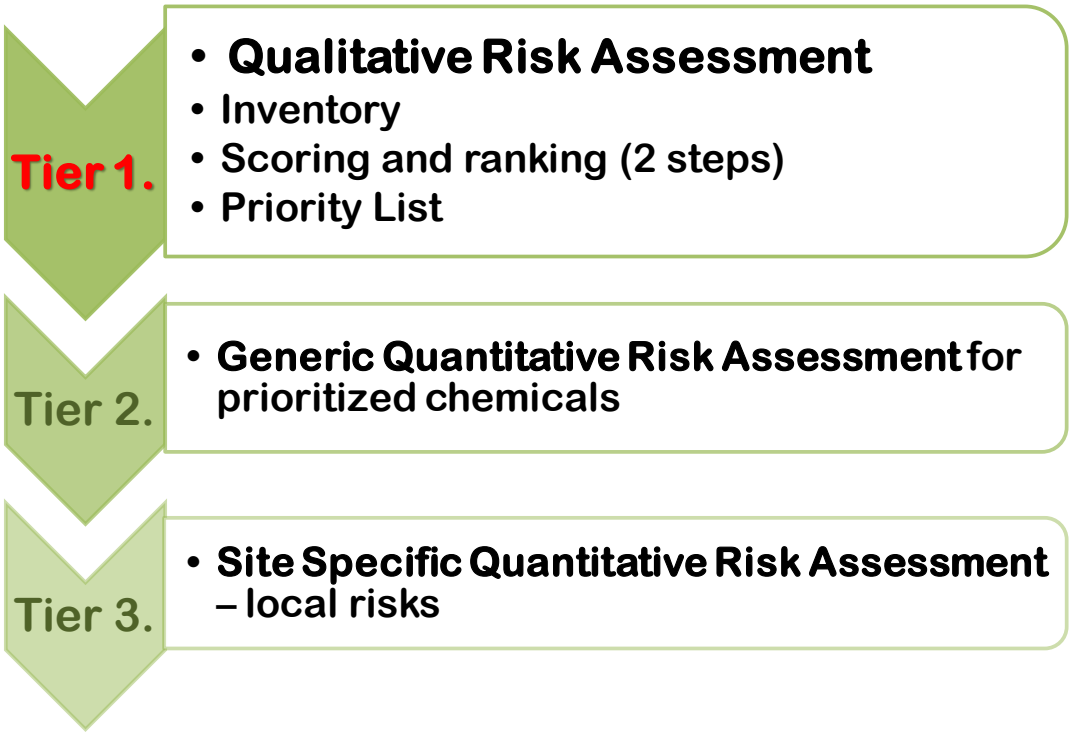

Figure 2. CDFILTER - tiered risk assessment methodology for micropollutants in water

The application of the developed risk assessment methodology during the research resulted in more accurate risk characterisation of the selected micropollutants both in qualitative and quantitative terms. On the basis of the comprehensive risk assessment results and the performed establishing experiments the technology for risk reduction using cyclodextrin sorbents was developed.

In the case of higher priority pollutants such as bisphenol-A and β-estradiol the outstanding risk reduction capability of cyclodextrin filters has been demonstrated.

ACKNOWLEDGEMENT
The financial support of National Innovation Office (TECH_08-A4/2-2008-0161, CDFILTER and TECH_09-A4-2009-0129, SOILUTIL project) is greatly acknowledged.

REFERENCES

Angelakis, A.N. and Durham, B. (2009) Water recycling and reuse in EUREAU countries: Trends and challenges. *Desalination*, 218, 3–12

Bendz, D., Paxéus, N.A., Ginn, T.R. and Loge, F.J. (2005). Occurrence and fate of pharmaceutically active compounds in the environment, a case study: Höje River in Sweden. *Journal of Hazardous Material*, 122, 195–204

Boyd, G.R., Reemtsma, H., Grimm, D.A. and Mitra, S. (2003) Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario, Canada. *Science of the Total Environment* 311, 135–149

Carballa, M., Omil, F., Lema, J.M., Llompart, M., García-Jares, C., Rodríguez, I., Gómez, M. and Ternes, T. (2004) Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant. *Water Research*, 38, 2918–2926

Carlsson, C., Johansson, A-K., Alvan, G., Bergman, K. and Kühler, T. (2006) Are pharmaceuticals potent environmental pollutants? Part I: Environmental risk assessments of selected active pharmaceutical ingredients. *Science of the Total Environment* 364, 67–87

Castiglioni, S., Bagnati, R., Fanelli, R., Pomati, F., Calamari, d. and Zucccato, E. (2006) Removal of pharmaceuticals in sewage treatment plants in Italy. *Environmental Science and Technology*, 40, 357–363

Crane, M., Watts, C. és Boucard, T. (2006) Review, Chronic aquatic environmental risks from exposure to human pharmaceuticals. *Science of the Total Environment*, 367, 23–41

Daughton, C. G. (2004) Non-regulated water contaminants: emerging research. *Environmental Impact Assessment Review*, 24(7–8), 711–732

Directive 2011/0429/EC Brussels, 31.1.2012, COM(2011) 876. DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. http://ec.europa.eu/environment/water/water-dangersub/pdf/com_2011_876.pdf

Dlugolecka, M., Dahlberg, A.G. and Plaza, E. (2006) Low concentrations of high priority – pharmaceutical and personal care products (PPCPs); occurence and removal at wastewater treatment plants. *Vatten*, 62, 139–148

Enick, O.V. and Moore, M.M. (2007) Assessing the assessments: Pharmaceuticals in the environment. *Environmental Impact Assessment Review*, 27, 707–729

Fent, K., Weston, A. A. and Caminada, D. (2006) Review, Ecotoxicology of human pharmaceuticals. *Aquatic Toxicology,* 76, 122–159

Ferrari, B., Paxeus, N., Giudice, R. L., Pollio, A., Garric J. (2003) Ecotoxicological impact of pharmaceuticals found in treated wastewaters: study of carbamazepine, clofibric acid, and diclofenac, *Ecotoxicology and Environmental Safety,* 55, 359–370

Gomes, R.L., Scrimshaw, M.D. and Lester, J.N. (2003) Determination of endocrine disrupters in sewage treatment and receiving waters. *Trends in Analytical Chemistry*, 22(10), 697–707

Gruiz, K., Molnár, M., Fenyvesi, É., Hajdú, Cs., Atkari, Á. and Barkács, K. (2011) Cyclodextrins in Innovative Engineering Tools for Risk-based Environmental Management. *Journal of Inclusion Phenomena and Macrocyclic Chemistry*, 70:(3-4) 299–306

Guillén, D., Ginebreda, A., Farré, M., Darbra, R.M., Petrovic, M., Gros, M. and Barceló D. (2012) Prioritization of chemicals in the aquatic environment based on risk assessment: Analytical, modeling and regulatory perspective. *Science of the Total Environment,* 440, 236–252

ICPDR - International Commission for the Protection of the Danube River (2003) List of Priority Substances for the Danube River Basin. – http://www.icpdr.org

ICPDR JDS2 - International Commission for the Protection of the Danube River, Joint Danube Survey 2. (2007) – http://www.icpdr.org/main/activities-projects/joint-danube-survey

Khan, S.J., Wintgens, T., Sherman, P., Zaricky, J. and Schäfer, A. I. (2004). Removal of hormones and pharmaceuticals in the Advanced Water Recycling Demonstration Plant in Queensland, Australia. *Water Science and Technology*, 50 (5), 15–22

Khetan, S.K. and Collins, T.J. (2007) Human Pharmaceuticals in the Aquatic Environment: A Challenge to Green Chemistry. *Chemical Reviews*, 107 (6), 2319–2364

Koschorreck, J., Koch, C. and Rönnefahrt, I. (2002) Environmental risk assessment of veterinary medicinal products in the EU—a regulatory perspective. *Toxicology Letters, 131*, 117–124

Kümmerer, K. (2009) Review, The presence of pharmaceuticals in the environment due to human use – present knowledge and future challenges. *Journal of Environmental Management*, 1, 1–13

Miege, C., Choubert, J.M., Ribeiro, L. Eusebe, M. és Coquery, M. (2009) Fate of pharmaceuticals and personal care products in wastewater treatment plants – Conception of a database and first results. *Environmental Pollution*, 157(5) 1721–1726

Murray, K.E,, Thomas, S.M. and Bodour, A,A. (2010) Prioritizing research for trace pollutants and emerging contaminants in the freshwater environment. *Environmental Pollution*, 158, 3462–3471

NTP National Toxicology Program U.S. Department of Health and Human Services NTP-CERHR (2008) Monograph on the Potential Human Reproductive and Development al Effects of Bisphenol A. NIH Publication No. 08-5994

Oulton, R.L., Kohn, T. and Cwiertny, D.M. (2010) Pharmaceuticals and personal care products in effluent matrices: A survey of transformation and removal during wastewater treatment and implications for wastewater management. Critical Review. *Journal of Environmental Monitoring*, 12, 1956–1978

Pal, A., Gin. K.Y., Lin, A.Y. and Reinhard M. (2010) Impacts of emerging organic contaminants on freshwater resources: review of recent occurrences, sources, fate and effects. *Science of the Total Environment,* 408(24), 6062–6069

Sanderson, H. and Thomsen, M. (2009) Comparative analysis of pharmaceuticals versus industrial chemicals acute aquatic toxicity classification according to the United Nations classification system for chemicals. Assessment of the (QSAR) predictability of pharmaceuticals acute aquatic toxicity and their predominant acute toxic mode-of-action, *Toxicology Letters,* 187, 84–93

Schaar, H., Clara, M., Gans, O. and Kreuzinger, N. (2010) Micropollutant removal during biological wastewater treatment and subsequent ozonization step. *Environmental Pollution*, 158, 1399–1404

Schäfer, A.I., Mastrup, M. and Lund Jensen, R. (2002). Particle interactions and removal of trace contaminants from water and wastewater. *Desalination,* 147, 243–250

Schwarzenbach, R.P., Escher, B.I., Fenner, K., Hofstetter, T.B., Johnson, C.A., von Gunten, U. and Wehrli, B. (2006) The challenge of micropollutants in aquatic systems. Review. *Science*, 313, 1072–1077

Sedlak, D. L., Pinkston, K. and Huang, Ch.-H. (2005). Occurrence survey of pharmaceutically active compounds. AWWA Research Foundation and American Water Works Association, U.S.A.

Smital, T., Luckenbachb, T., Sauerborna, R., Hamdounb, A.M., Rebecca L. Vegab, R.L. and Epelb, D. (2004) Emerging contaminants—pesticides, PPCPs, microbial degradation products and natural substances as inhibitors of multixenobiotic defense in aquatic organisms. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis,* 552 (1–2), 101–117

Stuart, M., Lapworth, D., Crane, E. and Hart, A. (2012) Review of risk from potential emerging contaminants in UK groundwater. *Science of the Total Environment,* 416, 1–21

Verlicchi, P., Galletti, A., Petrovic, M. and Barcelo, D. (2010) Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options. *Journal of Hydrology*, 389, 416–428

Webb, S.F. (2001) A data-based perspective on the environmental risk assessment of human pharmaceuticals I - collation of available ecotoxicity data. In: Kümmerer, K. (Ed.), Pharmaceuticals in the Environment – Sources, Fate, Effects and Risks. Springer, Berlin, pp. 175–201

Yoon, Y., Ryu, J., Oh, J., Choi, B-G. és Snyder, S. A. (2010) Occurrence of endocrine disrupting compounds, pharmaceuticals, and personal care products in the Han River (Seoul, South Korea). *Science of the Total Environment*, 408(3), 636–643

Yu-Chen Lin, A., Wang, X-H. and Lin, C-F. (2010) Impact of wastewaters and hospital effluents on the occurrence of controlled substances in surface waters. *Chemosphere*, 81, 562–570