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Emerging contaminants in surface waters and their relevance for the production of drinking water in Europe

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An increasing part of drinking water in Europe is prepared from surface water. At the same time, a growing number of emerging contaminants is being discovered in surface water. This review provides an overview of classes of emerging contaminants nowadays detected in the aquatic environment that are of relevance for drinking water production. These comprise e.g. endocrine disrupting compounds, such as hormones and compounds with hormone-like properties, pharmaceuticals, illicit and non-controlled drugs, sweeteners, personal care products, complexing agents, nanoparticles, perfluorinated compounds, flame retardants, pesticides, and fuel additives. The individual compounds are observed in concentrations that are generally considered too low to cause acute effects. Nevertheless, health effects due to long-term exposure to a mixture of low concentrations of all kinds of emerging contaminants cannot be excluded with current knowledge. Moreover, contamination of drinking water with man-made substances is considered unwanted in principle. The precautionary principle is used to motivate that prevention of emission of emerging contaminants into the environment is the preferred approach to safeguard sustainable drinking water production. In the mean time, extensive monitoring of the sources and development and application of advanced treatment techniques are used to prepare safe drinking water.

Keywords: emerging substances; endocrine disruption; pharmaceuticals; aquatic environment; drinking water; risk assessment

1. Introduction

The availability of safe drinking water is essential for health and well-being of humans all over the world. Traditionally, microbiological quality of drinking water attracted most attention and this still is the most important issue in a large part of the world. The provision of safe drinking water with respect to pathogens since the second half of the nineteenth century virtually eliminated the spread of infectious waterborne diseases, such as typhoid fever and cholera in developed countries. During the last decades, the attention for chemical quality of drinking water has grown because the knowledge on chemical compounds and their possible toxic effects has increased.

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In Europe, millions of people depend for their need of drinking water on surface waters, such as the Rivers Danube, Meuse, Rhine, and Tagus (Figure 1). These surface waters are contaminated with thousands of chemical compounds originating from industry, agriculture, and household uses and their number is still increasing. This confronts drinking water companies with the challenge and responsibility to deal with contaminants in their sources and still prepare safe drinking water.

This article gives an overview of classes of chemical pollutants that have been recently detected in surface waters, so called “emerging contaminants”, that are of concern for the production of drinking water. The article does not include inorganic compounds as nutrients and metals, but is confined to organic chemicals, i.e. compounds predominantly composed of the chemical elements carbon, hydrogen, and oxygen. To keep focus, the review only considers compounds that are detected in surface waters, and does not pay attention to compounds mainly detected in ground waters or compounds formed during treatment processes. In addition to the overview of compounds (section 3), the article discusses the possibility of health risks (section 4), current legislation, and the position of drinking water companies with respect to the protection of surface waters, such as drinking water sources (section 5) and gives an outlook on future possibilities to assess emerging contaminants (section 6). This article describes the drinking water production often with the situation in the Netherlands as an example. The same applies however for other European countries. If not, the differences are described.



Figure 1. Map showing examples of European rivers from where water is abstracted for the preparation of drinking water.

2. Safe drinking water in a contaminated environment

2.1. Drinking water production in Europe: historical perspective

Surface water from rivers, creeks, and canals long served as source for drinking water without any prior treatment. Thanks to the self-purifying capacity of natural waters, people could sustainably use surface water streams both as source for drinking water and as means to dispose their waste water. Industrialization, concomitant expansion of the population living in cities, and increasing population density in the nineteenth century changed this situation in large parts of Europe. Human impact on surface water quality often surpassed this self-purifying capacity. A famous and disastrous example of the consequences of contamination of drinking water with human waste is the 1854 cholera epidemic in London. London, at that time the largest city in the world, suffered from poor sanitary circumstances. The cause of this epidemic was mixing of drinking water with waste water in a pumping well that was used by inhabitants of Broad Street, Golden Square, and adjoining streets in London (Colwell 1996). From the nineteenth century onwards, growing knowledge on civil engineering opened the door for wastewater treatment and drinking water treatment and supply.

In the Netherlands, the first drinking water supply was introduced in 1853 with the installation of a pipeline transporting freshwater filtered by the dunes near Haarlem to the city of Amsterdam. There, the freshwater was distributed at the price of “one cent a bucket” (De Moel et al. 2004). Since then, numerous private companies were founded. Afterwards, drinking water supply became a responsibility of the government leading to a limited number of supplies covering the whole country. Similar developments have taken place in surrounding European countries. In the nineteenth century, drinking water in Europe was almost completely made from ground water. Nowadays, surface water is increasingly used because of ground water shortage. Two main systems for the production of drinking water from surface water currently used are storage in basins followed by extensive treatment and pre-treatment, infiltration in ground, river banks or dunes, abstraction and limited purification afterwards (De Moel et al. 2004). The production of drinking water by desalination of brackish (ground) water is expensive and thus applied only in countries where freshwater is scarce, such as Malta. In contrast to most other European countries, in the Netherlands, and parts of Germany drinking water is distributed without prior post-disinfection with chlorine. Currently, 99.8% of the Dutch households are connected to a drinking water distribution network and 98% to sewage treatment. At the same time, due to easy availability and use for other purposes besides drinking, average water consumption per person per day increased from about 10 l per person per day in 1850 to 120–160 l nowadays throughout Europe.

2.2. Sources of contaminating compounds in surface water

Surface water is available in large quantities from rivers, canals, and lakes. Whereas ground water generally is of high bacteriological and constant chemical quality, surface water quality varies considerably due to upstream activities, and varying discharge volumes and flow properties. As rivers often pass several countries, upstream activities might influence water quality in other countries downstream, making surface water quality a transboundary issue.

Contaminants are introduced by all kinds of human activities, such as agriculture, shipping, industry, and use of chemicals in households. We can distinguish incidental spills, structural spills, and diffuse emissions (Wuijts and Van Rijswijk 2008). *Incidental spills* are unexpected, and may influence water quality considerably, albeit usually only temporarily. Examples are shipping accidents, industrial accidents, and sewage overflows. *Structural spills*, such as the discharge of effluents of industrial and municipal waste water treatment plants, are often of better known composition and have a continuous influence on water quality. *Diffuse emissions*, such as agricultural and road run off, are characterized by a strong seasonal variation and poorly traceable origins (Wuijts and Van Rijswijk 2008), because of the many possible sources.

At first hand, one might think that large incidental spills from point sources such as a chemical industry plant are most important. And indeed, incidents from the past have shown disastrous consequences for the aquatic environment. One example is a fire at the chemical plant Sandoz near Basel in 1986 that led to the poisoning of the river Rhine between Basel and Koblenz with 20 tons of pesticides and consequently to an interruption of water intake for drinking water production in the Netherlands for 9 days (RIWA Vereniging van Rivierwaterbedrijven 2003). Nevertheless, continuous contamination by structural spills or diffuse sources might have an at least as substantial impact on drinking water production. In contrast to incidental spills, drinking water companies cannot deal with them by just temporarily interrupting the intake. Figure 2 shows the most relevant pathways by which emerging contaminants are introduced in the aquatic environment and might end up in waters used as source for drinking water production.

Organic compounds such as polyaromatic hydrocarbons, polychlorinated biphenyls, and organochlorine pesticides were a focus of interest last decades

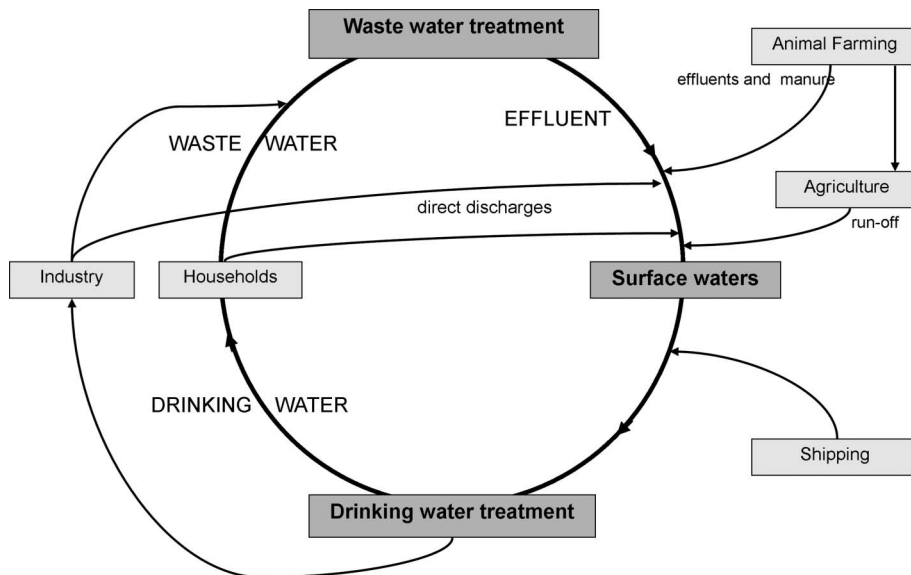


Figure 2. Schematic representation of a water cycle, showing pathways by which emerging contaminants are introduced in the surface waters and thus end up in waters used as source for drinking water preparation.

and were monitored intensively. Because of their persistent and often lipophilic nature, they could be present in the environment for a very long time before being degraded and could accumulate in sediment and in living organisms. They originated predominantly from diffuse sources such as agriculture and from industries. Maximum allowed concentrations in water distracted for the production of drinking water and in drinking water itself for these compounds are laid down in legislation. Nowadays, regulatory measures against application of various persistent compounds have come into force and have aided to reduce emissions and environmental concentrations of these compounds. For these reasons, these compounds gradually have become less relevant for drinking water preparation (Jones et al. 2005).

2.3. Emerging contaminants

At the same time, large new groups of as yet unregulated contaminants have attracted attention. These groups of so-called “emerging contaminants (substances)” comprise various compounds used in everyday life, such as human and veterinary pharmaceuticals, plasticizers, and various industrial additives. Although often less persistent in the environment than conventional contaminants, their continuous introduction might lead to negative effects. Therefore, emerging contaminants belong to the most important chemical contaminants currently found in the environment (Field et al. 2006).

The term “emerging contaminants” does not necessarily solely cover newly developed compounds. In fact, the term is used for at least three categories of compounds attracting the concern of current environmental toxicologists and chemists. The first consists of compounds that are newly introduced into the environment, e.g. industrial compounds that have only recently been developed.

The second category comprises compounds that, although possibly around for longer times, have only recently been detected in the environment. The analysis of emerging contaminants is really challenging for analytical chemists, because of the diversity in chemical properties, the complexity of matrices, and generally very low concentrations at which they are found – usually to even low nanogram or picogram per liter levels. However, major advances in chemical analytical technologies achieved last decades have widened the scope of compounds that can be detected and identified enormously. Current techniques, such as liquid chromatography coupled with tandem mass spectrometry, hyphenated chemical screening techniques (Ferrer and Thurman 2003; Houtman et al. 2006a), and biological analysis methods (bioassays) (Houtman et al. 2004a, 2007) now permit the routine analysis of all kinds of polar organic chemicals, which could not be observed before with the gas chromatographic approaches, that led to the early discovery of many persistent and non-polar organic pollutants. Furthermore, instrumental sensitivity has improved enormously (Giger 2009; Richardson 2009). Over the last 40 years, a sensitivity gain of a factor 1000 to even 100,000 has been achieved (de Boer 2010), thus enabling the detection of most compounds at the concentrations in which they are indeed present in the environment.

The third category emerging contaminants consist of compounds that, although possibly known for a longer time, are only recently recognized as potentially causing adverse effects on ecosystems or humans (Petrovic and Barcelo 2006). This is, for example, the case with hormones (see section 3).

How long the contaminants keep their “emerging” status depends largely on the time needed to assess their persistency and toxicity for humans and wildlife. This requires time and resource-intensive studies on environmental fate and toxicological properties. As a result, contaminants may keep their emerging status for several years (Field et al. 2006).

3. Classes of emerging contaminants

3.1. Endocrine disrupting compounds

Since the 1990s, evidence has accumulated that certain synthetic and natural chemicals in the environment can disturb the hormonal (endocrine) system of exposed organisms by mimicking or blocking the action of hormones (Colborn et al. 1993; Fairley et al. 1996). Exposure might lead to adverse health effects – collectively referred to as “endocrine disruption” – concerning all kinds of processes in the body that are controlled by hormones, such as growth, development, fertility, and reproduction (Colborn et al. 1993; Fairley et al. 1996). Most attention has been given to estrogenic compounds, i.e. compounds that act as the female sex hormone 17β -estradiol. The most notable effect in this respect is the intersexuality of male fish that is observed at large scale in the UK (Jobling et al. 1998; Allen et al. 1999a,b; Kirby et al. 2004) and other countries (Sole et al. 2003; Barnhoorn et al. 2004; Vethaak et al. 2005; Bjerregaard et al. 2006; Houtman et al. 2007). Intersex male fish developed female characteristics, i.e. produced egg yolk sac protein and developed egg cells in their testes (Jobling et al. 1998).

The human endocrine system is comparable to that of animal vertebrates like fish. Therefore, exposure to endocrine disrupting compounds might imply a certain health risk for humans also. A link between environmental contaminants and reproductive health of humans has been suggested in terms of declining sperm counts, increased incidences of other reproductive disorders related with male infertility, testicular cancer, and breast cancer (Sharpe and Skakkebaek 1993; Wolff et al. 1993; European Environment Agency 1997), however, a causal relationship has not been established (Safe 1995, 2000; Daston et al. 2003).

Laboratory research has shown that a large number of different chemicals can exert estrogenic effects (Blair et al. 2000; Legler et al. 2000; Nishihara et al. 2000; Houtman et al. 2004b), including the natural estrogenic hormones 17β -estradiol, estriol and estrone, the synthetic estrogenic hormone and contraceptive pill ingredient 17α -ethynylestradiol, and phytoestrogens like isoflavonoides and coumestrol. Furthermore, various pesticides and industrial compounds, such as alkylphenols, alkylphenoethoxylates, and bisphenol A, which are applied as surfactants, plasticizers, and raw materials for the production of polycarbonate plastic, are estrogenic. The latter groups were never intended to act like hormones, but similarities in their chemical structure with hormones enable them to act similarly in the body, although generally much higher concentrations are needed to cause an effect. Picogram to nanogram per liter concentrations of estrogenic activity have been found throughout the aquatic environment, e.g. in wastewater, surface water, and sediment (Jobling et al. 1998; Belfroid et al. 1999; Bolz et al. 2001; de Alda and Barcelo 2001; Petrovic et al. 2002; Houtman et al. 2004b; Peck et al. 2004; Cespedes et al. 2005; Houtman et al. 2006a; Morteani et al. 2006).

Field investigations have identified very low concentrations of natural and synthetic estrogenic hormones as main causes of estrogenic effects in the aquatic

environment (Desbrow et al. 1998; Houtman et al. 2004b; Gibson et al. 2005; Sumpter 2005; Houtman et al. 2006a; Houtman et al. 2007; Sumpter and Johnson 2008). They are excreted by humans and livestock and discharged in the environment with effluents of sewage treatment plants (Kolpin et al. 2002; Legler et al. 2002; Snyder et al. 2003) or with agricultural run off (Lange et al. 2002; Johnson et al. 2006; Matthiessen et al. 2006). Only at certain specific locations, estrogenic activities were partly or fully caused by high concentrations of alkylphenols (Sheahan et al. 2002; Fenet et al. 2003; Cespedes et al. 2004; Quiros et al. 2005).

Several studies have investigated the presence of estrogens in drinking water. Fawell et al. (2001) did not detect estrogenic compounds in drinking water prepared from UK river water. On the other hand, two studies in Southern Germany reported estrogenic steroid hormones in some drinking water samples at levels to 1.4 ng/l for ethynylestradiol and 2 ng/l for estradiol, suggesting that estrogenic hormones are not in all cases completely removed during sewage treatment and water treatment (Adler et al. 2001; Kuch and Ballschmiter 2001).

In addition to estrogens, research focuses nowadays also on other classes of hormones and compounds with comparable or opposite activities such as anti-estrogens, androgens (male sex hormones), anti-androgens, progestagens (female pregnancy hormones), glucocorticoids (hormones controlling energy balance and inflammation), and compounds showing thyroid hormone-like activities. Many hormone-like compounds are used as pharmaceuticals and might enter the environment via similar routes as estrogens. The amount of, e.g. androgens and progestagens that is excreted by humans via urine is estimated to be several orders of magnitude higher than that of estrogens (Shore and Shemesh 2003). The exposure to androgens has been linked with masculinization of fish. The exposure to glucocorticoids is associated with impairment of the immune system, reproduction, and development. Various hormones are known to be used by fish as chemical compounds excreted to communicate with other fish (reproductive pheromones) (Chang et al. 2009). The issue of endocrine disruption is even more complex as mixtures of compounds with different endocrine effects might enhance or counteract each other or act independent of each other (Brian et al. 2005; Houtman et al. 2006b; Weiss et al. 2009). Several surveys have demonstrated the presence of (anti-) androgens, glucocorticoids, and thyroid hormone activities in the environment (Houtman et al. 2004a; Van der Linden et al. 2008; Chang et al. 2009; Weiss et al. 2009). However, thyroid hormone activity was not detected in a survey investigating drinking water prepared from the French river Seine (Jugan et al. 2009).

3.2. *Pharmaceuticals*

Pharmaceuticals are chemical compounds used for the diagnosis, treatment, or prevention of diseases in humans and animals. It is impossible to imagine our modern Western society without them; hundreds or thousands of different pharmaceuticals are currently used and distributed including pain killers, antibiotics, anti-diabetics, β -blockers, lipid regulators (anti-lipemics), anti-depressants, anti-epileptics, and X-ray contrast media (Richardson 2008). The use of pharmaceuticals still rises due to increasing use to prevent instead of to cure diseases, due to applying them as additives in food products and due to aging of population in Western-European countries (RIWA Vereniging van Rivierwaterbedrijven 2008; Van der Aa et al. 2009).

The possibility of emission of pharmaceuticals in the environment has been recognized in environmental science since several decades. However, its significance remained unnoticed for long, perhaps partly because regulation of pharmaceuticals is often in the hands of health agencies with limited expertise in environmental issues (Daughton and Ternes 1999). Since 1990s, implementation of increasingly sensitive analysis techniques opened the door for multiple investigations that demonstrated the presence of traces of various classes of pharmaceuticals in surface waters at nanogram to microgram per liter level (Hilton and Thomas 2003; Hilton et al. 2003; Stolker et al. 2004; Ellis 2006; Hernando et al. 2006a; Jjemba 2006; Gibson et al. 2007; Kasprzyk-Hordern et al. 2007; Batt et al. 2008; Kasprzyk-Hordern et al. 2008; Sacher et al. 2008; Gros et al. 2009; Meng 2009; Matamoros et al. 2010; Ter Laak et al. 2010). Figure 3 shows pharmaceuticals, including X-ray contrast media, detected in surface water at an intake site of a drinking water treatment plant along the River Meuse. In the figure, each bar represents the sum of concentrations of individual compounds. Up to 10 different pharmaceuticals were observed in varying concentrations over time.

As observed for endocrine disruptors, municipal sewage treatment plants appeared to play an important role in the introduction of pharmaceuticals in the environment. Conventional sewage treatment plants purify household waste water mainly by subsequent application of bacterial degradation of organic matter, and coagulation/flocculation for the removal of suspended solids and phosphates. In these processes, which are predominantly optimized for the degradation of waste of natural origin, organic contaminants are primarily removed by bacterial degradation and sorption to solids. The past decades have shown that this treatment is rather inadequate in removing (synthetic) organic contaminants, such as pharmaceuticals. This results in the detection of pharmaceuticals in effluents and receiving waters in their original form, or as degradation products

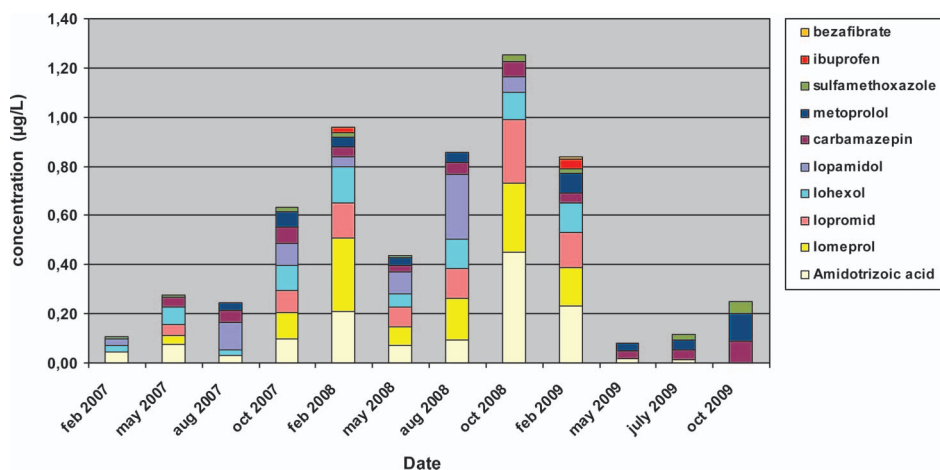


Figure 3. Pharmaceuticals detected in surface water at an intake site of a drinking water treatment plant along the River Meuse. Bezafibrate is used to treat elevated blood concentrations of cholesterol (lipid regulator), ibuprofen is used as pain killer, sulfamethoxazole as antibiotic, metoprolol as β -blocker (treatment of hypertension), carbamazepin as anti-epileptic, other shown compounds are used as X-ray contrast media.

(Hilton and Thomas 2003; Gagne et al. 2006; Gomez et al. 2006; Hernando et al. 2006b; Kuster et al. 2008). Besides household sewage, other emission sources of human pharmaceuticals are waste waters from manufacturers, hospitals, and disposal of unconsumed drugs via solid waste. It is estimated that up to 65% of sold pharmaceuticals are never consumed (Ruhoy and Daughton 2008). Furthermore, large quantities of pharmaceuticals, e.g. antibiotics and inflammatory drugs do not pass sewage treatment. They are used in veterinary practice to treat cattle feedlot and directly contaminate surface water by means of run off during rainfall (Daughton and Ternes 1999; Brooks et al. 2009). Several studies have reported that some pharmaceuticals are not completely removed by drinking water treatment and are found at trace levels in drinking water (Versteegh et al. 2007; Kuster et al. 2008; Benotti et al. 2009; Cooney 2009).

3.3. *Illicit drugs, non-controlled drugs, and sweeteners*

Using similar methodologies as for pharmaceuticals, it was demonstrated that our environment is also contaminated with drugs with predominantly non-medical applications. It is estimated that up to 5% of the world population uses illicit drugs, like cocaine, heroin, cannabinoids (hashish, marijuana), and amphetamine-like stimulants (such as ecstasy) (Castiglioni et al. 2008). In 2005, Zuccato et al. published a first systematic study on the presence of cocaine and its degradation product benzoylecgonine in surface and waste water samples from the Italian river Po. The results were interesting not only from an environmental but also from a societal-forensic point of view; based on the measured concentrations, the authors calculated that cocaine consumption in the area was considerably higher than estimated at that time (Zuccato et al. 2005). Since then, several studies have investigated the presence of cocaine and other illicit drugs as cannabinoids, amphetamins in surface and waste waters throughout Europe. In addition, also non-controlled stimulatory compounds, such as caffeine from coffee, tea, and soft drinks and nicotine from tobacco were often included in these investigations. Illicit and non-controlled drugs were structurally found at nanogram per liter concentrations to low microgram per liter concentrations in waste and surface waters. Degradation in sewage treatment plants varied considerably between different drugs. The most frequently found compound was benzoylecgonine, pointing to the use of cocaine (Kasprzyk-Hordern et al. 2008, 2009; Zuccato et al. 2008). A Spanish study concluded that during the production of drinking water from the Llobregat River illicit drugs were eliminated to undetectable levels, whereas only traces of caffeine and degradation products of nicotine and cocaine survived treatment (Huerta-Fontela et al. 2008).

One of the newest groups of emerging contaminants are artificial sweeteners. These compounds are consumed in large volumes as low-calorie sugar alternatives in food and drinks. Examples are acesulfame, saccharin, cyclamate, and sucralose (Richardson 2009). Some of them, such as acesulfame, are heat-stable – and therefore used for baking purposes – and are very persistent in liquids – and as such applied in soft drinks with long expiry dates. These properties, combined with the fact that certain sweeteners are not degraded by the human body but excreted unchanged, makes sweeteners the next class of compounds that proved to end up widespread in surface waters after use, as was demonstrated by Scheurer et al. (2009) in German waste and surface waters.

3.4. *Personal care products*

Personal care products comprise active ingredients of cosmetics, toiletries, and fragrances. They are applied as preservative or to alter odor, appearance, touch, or taste. In most cases, personal care products are not meant for ingestion, but are applied directly on the human body (Daughton and Ternes 1999).

One group of personal care products consists of compounds used as fragrance, such as polycyclic musks. A second group comprises preservatives like parabens applied in shampoos, creams, and toiletries to prevent bacterial decay. Furthermore, disinfectants like triclosan and chlorophene are used on a large scale. Triclosan for example has been used for decades in a wide variety of consumer products, ranging from toothpaste and hand soap to toys and socks (Petrovic et al. 2003). In addition, compounds such as benzophenone in sun screen lotions that block UV light have gained interest of environmental chemists and biologists. The last examples mentioned here are alkylated siloxanes, compounds used in soaps, hair-care products, etc. Personal care products enter the environment via sewage treatment effluent as a result of showering, washing off, washing clothes, etc., but are also directly released in surface waters by recreational activities as swimming and sunbathing. Personal care products are observed regularly in effluents and surface waters worldwide (Daughton and Ternes 1999; Kasprzyk-Hordern et al. 2008; Kuster et al. 2008; Rahman et al. 2009). Some of them can accumulate in exposed organisms. This was illustrated by our observation of triclosan and chlorophene in bile from bream in the Dutch River Dommel (Houtman et al. 2004b). Some personal care products are suspected to have potentially adverse potencies, such as estrogenic hormone-like activity (UV blockers, parabens), developmental toxicity (UV blockers), and extreme bioaccumulation (musks) (Daughton and Ternes 1999; Richardson 2009).

3.5. *Nanoparticles*

Nanoparticles constitute a rapidly growing research area. They are extremely small in size with diameters between 1 and 100 nm and have properties that differ from smaller (molecules) or larger (bulk materials) particles of the same composition (Wiesner et al. 2009). Besides inorganic compounds, such as titanium dioxide and nanosilver, and also organic compounds, such as carbon nanotubes and “nano-C₆₀” are examples of nanoparticles. They can be of natural origin as well as manufactured and a wide variety of applications is foreseen or already implemented, for example, in medicine and in food industries. Meanwhile, questions about their environmental fate and possible human-health risks arise. Due to their small size, their surface is relatively large and their chemical reactivity and biological activity remain relatively high. Nanoparticles can enter the body and cells more easily than larger particles. It is suggested that they might evoke inflammatory responses and DNA damage. However, very little is as yet known about possible toxic properties of nanoparticles (Wiesner et al. 2009). Although currently environmental data are scarce, techniques for the analysis of nanoparticles in environmental samples are developing fast, and it is expected that monitoring data will become available soon (Isaacson et al. 2009).

3.6. Flame retardants

Flame retardants are a class of chemicals that are widely used in plastics, textiles, and furnishing foams, such as computers, televisions, clothes, and sofas to slow down inflammation in the event of a fire. As such, they are supposed to have contributed considerably to the reduction of fire risks (Rahman et al. 2001). In the past, mainly polybrominated biphenyl and polybrominated diphenyl ethers were used for this purpose. These compounds are structurally similar to “conventional” contaminants as polychlorinated biphenyls, and likewise is their behavior in the environment. Brominated flame retardants are structurally detected in tissues, blood and breast milk of wildlife and humans (Rahman et al. 2001). This is worrying, as convincing evidence has been obtained last years that these compounds and their degradation products have several potentially toxic properties, such as the ability to disrupt the thyroid, androgenic and estrogenic hormone systems (Legler 2008); toxicity for the nervous system and they might also be carcinogenic (Richardson 2009). Because of their low solubility in water, they tend to sorb to sediments in rivers (Rahman et al. 2001) instead of reaching high concentrations in water.

Another class are organophosphate flame retardants, with tributylphosphate and tris(2-chloroethyl)phosphate as important representatives. Their widespread use may even increase since many brominated flame retardants have been banned (Reemtsma et al. 2008). Organophosphate flame retardants, for which toxicity data still are scarce, are persistent, although better soluble in water than brominated ones, and several studies have reported their presence in surface and waste waters (Andresen et al. 2007; Stackelberg et al. 2007; Focazio et al. 2008; Reemtsma et al. 2008; Terzic et al. 2008).

3.7. Perfluorinated compounds

Perfluorinated compounds such as perfluorooctanoic acid and perfluorooctane sulphonic acid are compounds with extraordinary chemical properties; they repel water as well as lipids and oil. They are used as water, dirt, or grease repellent coatings and sprays for leather, textile, and in PTFE (Teflon) non-stick cookware. Concern about perfluorinated compounds is growing as they appear to be persistent; accumulate in organisms and have a wide range of toxic properties, including developmental interference and carcinogenicity (Skutlarek et al. 2006; McLachlan et al. 2007). In addition, perfluorinated compounds are found in a wide variety of wildlife species worldwide and in investigated human serum and tissues (Farre et al. 2008; Richardson 2009; Kwadijk et al. 2010). Water appears to be the major reservoir in the environment and an important medium for their transport (Prevedouros et al. 2006).

Various studies report the detection of perfluorinated compounds in surface waters throughout Europe (Ahrens et al. 2009; Loos et al. 2009; Kwadijk et al. 2010). Reported levels at diffusely contaminated locations vary between 1 and 50 ng/l. However, incidentally higher concentrations (to over 1 µg/l) have been found, suggesting that concerned sites were influenced by specific (industrial) sources (Skutlarek et al. 2006; McLachlan et al. 2007; Kwadijk et al. 2010). Skutlarek et al. reported the presence of perfluorinated compounds in surface water and in drinking water samples (between lesser than detection limit and 519 ng/l) from the

Ruhr–Rhine area, concluding that they were not successfully removed during water treatment (Skutlarek et al. 2006).

3.8. Organic solvents MTBE and ETBE

Several industrially used organic solvents, such as diglyme, triglyme, and diisopropylether are regularly detected in surface waters (RIWA Vereniging van Rivierwaterbedrijven 2008) (Figure 4). The organic solvents methyl tertiary butylether (MTBE) and ethyl tertiary butylether (ETBE) are used as fuel additives to optimize combustion, reduce emissions, and to help prevent engine knocking. As such, they replaced tetra-ethyl lead, which was in use for this purpose in Europe till 1988. However, MTBE and ETBE have some adverse properties: they disperse rapidly in the environment due to high volatility and solubility and show poor biodegradability and are therefore frequently detected in surface waters at the low $\mu\text{g/l}$ concentrations. Most literature data for MTBE and ETBE are available for the Rhine catchment area (e.g. refer Van Wezel et al. 2009). Unfortunately, MTBE and ETBE are not easily removed during drinking water production. MTBE concentrations in drinking water samples supplied by works along the Rhine and the Main are reported between <10 and 100 ng/l (Kolb and Puttmann 2006). A study in the Dutch part of the Rhine found low levels (10 – 28 ng/l) in drinking water (Morgenstern et al. 2003). Although toxicity is probably low (Swartjes et al. 2004),

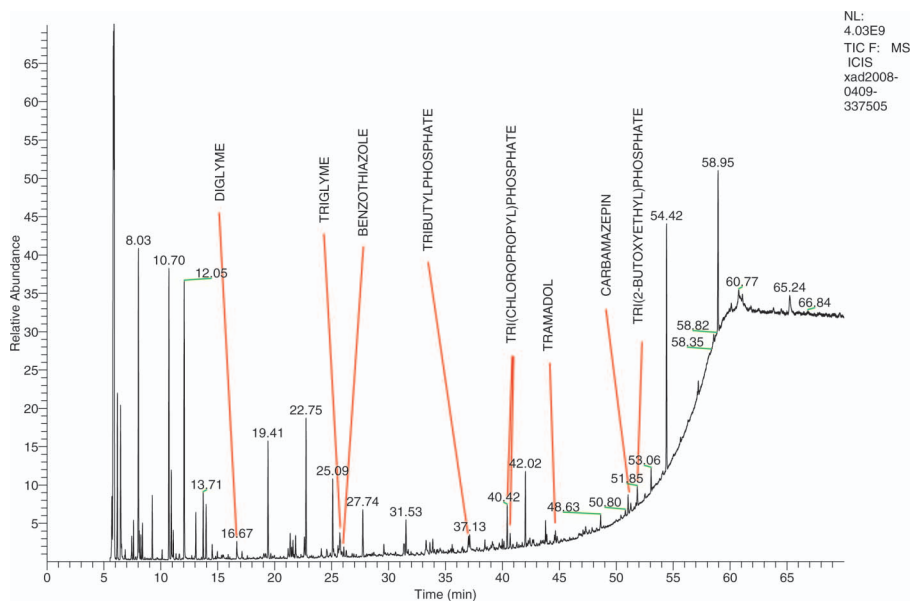


Figure 4. Chromatogram showing the results of a screening analysis of surface water from the Amsterdam Rhine Channel. Each peak denotes a different compound present in the sample. This sample simultaneously contained diglyme and triglyme (organic solvents), tributylphosphate, tri(chloropropyl)phosphate and tri(2-butoxyethyl)phosphate (flame retardants), tramadol and carbamazepin (pharmaceuticals), and benzothiazole (industrial compound). The figure shows that surface water is contaminated with a mixture of multiple emerging contaminants at low concentrations.

they are of concern as low $\mu\text{g/l}$ concentrations can already negatively affect water taste and odor (Fischer et al. 2005; RIWA Vereniging van Rivierwaterbedrijven 2008; Van Wezel et al. 2009).

3.9. Complexing agents

Complexing agents are organic compounds that can bind metals. An example used in common products as soap and toothpaste is EDTA. Other examples are 1H-benzotriazoles, used as coating to protect metals in contact with fluids against corrosion, e.g. in engine coolants, aircraft de-icers, or anti-freezing liquids, and for silver protection in dish washing liquids. They are soluble in water, resistant to biodegradation and poorly removed in waste water treatment (Weiss et al. 2006). As a consequence, they have been found in surface and drinking water (Hogenboom et al. 2009). One complication of complexing agents is that, once emitted in the environment, they have the ability to detach heavy metals from sediments and keep them dissolved in the aqueous phase. This hampers the efficient removal of metals during drinking water production and, moreover, enhances their bioavailability for aquatic organisms.

3.10. Pesticides

Pesticides, such as herbicides, fungicides, insecticides, plant growth regulators, bactericides, and defoliants have been a topic of concern for surface water quality for decades. Extensive use in agricultural practice and industrial emission during their production are important sources of pesticides and their residues in the aquatic environment.

After the Second World War, introduction of relatively non-polar and very persistent pesticides, such as chlordane, aldrin, and DDT, enabled impressive increases in food production and crop security. However, their bioaccumulation potential led to detrimental effects on the environment, particularly on birds, as was demonstrated in 1962 by Rachel Carson. Her bestseller “Silent Spring” (Carson 1962) has been of tremendous help to launch the environmental movement.

Pesticides registered nowadays are more polar and less persistent (Kuster et al. 2009). After application on the field, they contaminate surface waters by drift, run off, drainage, and leaching. Meanwhile, they undergo degradation by hydrolysis, oxidation, biodegradation, or photolysis. For some compounds, degradation products can be present at greater levels in the environment than the parent pesticide. Currently registered pesticides include hundreds of different compounds, such as glyphosate, triazines, organophosphorus herbicides, thiocarbamates, and chlorophenoxy acetic acids, of which the latter are used in highest volume worldwide (Petrovic et al. 2003).

Because pesticides have been in use for a long time, the European Union sets limits for pesticides in drinking water: 100 ng/l for individual compounds and 500 ng/l for the sum of pesticides (Council of the European Communities 1998). A maximum concentration for total pesticides in surface water intended for abstraction of drinking water is set that varies between 1 and 5 $\mu\text{g/l}$ depending on the method of water treatment (Directive 75/440/EEC).

The presence of pesticides in European surface waters is intensively investigated and monitored (e.g. Petrovic et al. 2003; Rodrigues et al. 2007; Kuster et al. 2009;

Loos et al. 2009; Palma et al. 2009; Vryzas et al. 2009). The occurrence of pesticides in drinking water was investigated for water prepared from the Llobregat River and reported to be undetectable (Lopez-Roldan et al. 2004) or below 100 ng/l (Kuster et al. 2008).

4. Is there a health risk related to emerging contaminants?

The above listing of emerging contaminants shows that numerous compounds used in everyday life in Europe are released into the aquatic environment. Therefore, depending on their fate in the environment and during drinking water preparation, there might be a possibility that humans are exposed to emerging contaminants through drinking water abstracted from contaminated surface waters. As a matter of definition, information about related health risks is not yet sufficiently available for contaminants still in their “emerging” stage and further research is warranted.

Risk assessment of emerging contaminants for humans includes assessment of the exposure dose and assessment of the dose at which possible adverse health effects can occur. From the latter, benchmarks representing safe doses that are assumed to be safe are derived. Subsequently, the ratio between exposure dose and benchmark determines if there is a risk related to the exposure.

4.1. Exposure assessment

The first step in risk assessment is to investigate the extent to which exposure takes place. Typical for emerging contaminants are the low concentrations (nanograms to micrograms per liter) in which they are detected in the environment. Acute toxicity for most of these compounds is tested and observed only at relatively high doses, and not expected at low environmental concentrations (Schriks et al. 2009). However, the case of estrogenic hormones in the environment disrupting the endocrine systems of fish has shown that exposure to low concentrations can lead to subtle but severe adverse effects.

In contrast to fish and other aquatic organisms, exposure to emerging contaminants by direct exposure to surface waters is only of minor importance for humans. More common exposure routes for humans include oral administration (hormones, pharmaceuticals, illicit drugs), food consumption (additives, non-controlled drugs, sweeteners, traces of contaminants in vegetables and meat), direct application on the body (personal care products), exposure via inhaled air and exposure to drinking water. Given the multiple routes, the relevance of drinking water as exposure route depends on fraction drinking water contributes to the total dose. The contribution of drinking water can differ between compounds and depends, for example, on the concentrations in drinking water relative to those in other matrices, exposure volumes, on efficiency of uptake after exposure.

For many contaminants, exposure via drinking water is estimated to be low compared to that by other routes. For example, exposure assessments published for PFOA and PFOS in Germany and for estrogenic hormones in the USA concluded that the contribution of drinking water for the general population was only in the order of 0.7–2% of the total daily intake of the general population (Fromme et al. 2009; Caldwell et al. 2010). Another example is pharmaceuticals. In contrast to many known polluting compounds, they are intentionally designed to exert at low concentrations a specific biological effect in the body. Especially for this class of

contaminants, effects might thus be expected at low concentrations. Exposure to drinking water is likely life-long and may extend to over 80 years. Using current environmental concentrations, the “worst case” assumption of no removal at all during drinking water production, and an estimated consumption of 2 l of water per day, it can be calculated that for most pharmaceuticals the dose that might be obtained by life-long consumption of drinking water is lower than the dose obtained from a single medical treatment with the same pharmaceutical (Webb et al. 2003). It is therefore often concluded that traces of pharmaceuticals in drinking water likely do not represent an acute health risk problem (Daughton and Ternes 1999; Webb et al. 2003; Versteegh et al. 2007; Johnson et al. 2008). However, although exposure assessment calculations do indicate the relative significance of drinking water as exposure route, one should be aware that as such they do not give an indication of the likeliness of adverse health effects other than the therapeutic one.

4.2. Risk assessment

To assess the health risks of exposure to emerging contaminants via drinking water, doses (or concentrations) determined in the exposure assessment step are compared with toxicity-based benchmarks that represent estimates of exposure that are assumed to be safe. These benchmarks are derived from toxicity data. Examples of such benchmarks are the acceptable daily intake (ADI), provided by the World Health Organisation (World Health Organisation 2006), and the Threshold of Toxicological Concern (TTC) as proposed by an International Life Sciences Institute expert group (Kroes et al. 2000, 2004). Whether or not drinking water exposure exceeds these benchmarks indicates whether the exposure may be associated with adverse health risks.

In applying such benchmarks for emerging contaminants in drinking water, several aspects have to be taken into account. Vulnerability for certain effects might differ between gender, and also during life stages, such as growth, pregnancy, or older age. As emerging contaminants are not incidentally released in drinking water sources, but are continuously present, exposure might continue life-long. Long-term effects might follow different biological mechanisms and occur at much lower concentrations than acute effects. Therefore, also possible other effects than the acute (therapeutic) one have to be investigated, as well as the possible consequences of exposure to mixtures. Another important aspect is namely the fact that in the environment more than one contaminant is present at the same time and location. Real-life exposure seldom is to a single compound, but in general to a mixture. Compounds in a mixture might act independently or might enhance or inhibit each other's effects. Such combined behavior makes predictions of health risks of exposure even more complex. Figure 3 exemplified the presence of more pharmaceuticals at the same time. In reality, the composition of surface water is even more complex, as contaminants other than pharmaceuticals – flame retardants, solvents, etc – can be detected in the same sample, as is shown in the chromatogram showing the results of a screening analysis of a water sample from the River Rhine in Figure 4.

Generally, toxicity benchmarks deal with mentioned aspects by applying safety factors to estimated safety values, e.g. a factor 10 for sensitive populations as applied in the ADI.

Caldwell et al. (2010) performed a risk assessment using ADI and TTC values for estrogenic hormones potentially present in drinking water in the USA and concluded

that they do not cause adverse effects in the general US population even not in sensitive subpopulations (Caldwell et al. 2010).

For most emerging contaminants, however, toxicological data are incomplete and therefore benchmark values are not available (e.g. Webb et al. 2003). To deal with this problem, the TTC approach took as starting point that even for compounds for which toxicity is not known in detail a safe exposure could be estimated. The TTC distinguishes between classes of compounds, such as genotoxic compounds (TTC = 0.15 $\mu\text{g}/\text{person}/\text{day}$) and several groups of non-genotoxic compounds (with 1.5 $\mu\text{g}/\text{person}/\text{day}$ as most strict TTC within the latter class.) Assuming a daily drinking water consumption of 2 l and a contribution of 10% of the exposure by drinking water, Van der Hoek et al. (2008) derived drinking water guidance limits from the TTC values of 10 ng/l for genotoxic compounds and 0.1 $\mu\text{g}/\text{l}$ for non-genotoxic compounds.

Although our toxicological knowledge keeps growing, the aspects mentioned show the complexities we are confronted with and describe the uncertainties that still exist regarding the assessment of potential health risks of emerging contaminants.

5. Dealing with emerging contaminants in drinking water sources

Surface waters have multiple stakeholders: industries, governments, drinking water companies, and consumers. The quality of surface waters has to be protected to safeguard the sustained use for all functions. This section discusses how governments and drinking water companies deal with emerging contaminants in drinking water sources and shows the necessity of involvement of various stakeholders.

5.1. *The role of governments*

Public water supply is regulated by international and national legislation. In Europe, legislation given by the European Committee is becoming increasingly important. On the one hand this is a positive development; emerging contaminants cross national borders and so should measures to regulate them. On the other hand, international legislation implies a time-consuming process and dealing with compromises. As a consequence, lists of regulated compounds do not represent adequately the emerging contaminants we are faced with these days, as many of the listed compounds are no longer in use or only in limited quantities as soon as an act becomes operative.

Nowadays national legislation is often an implementation or a sharpening of the European legislation. Concerning emerging substances, several European acts are of concern.

The Drinking Water Act 98/83/EEC describes the minimum quality requirements that apply to drinking water. A number of substances are given specified requirements. Unfortunately, concerning the previously mentioned substances hardly any of the emerging contaminants is mentioned in this act.

The Water Framework Directive 2000/60/EC aims to safeguard the quality of European surface and ground waters. It has as a general principle that standards for compounds should be related to their eco(toxico)logical effects. Article 7 of the Directive explicitly links improvement of water quality to drinking water aims. The protection level of surface and ground water should be such that reliable drinking water can be prepared sustainably and that it is aimed to enable reduction of the

required level of purification treatment required in time. A number of priority compounds are named, but in this list none of the here named emerging substances is present.

From section 4, it is clear that numerous emerging contaminants have been produced and applied in Europe for many years and sometimes in very high amounts. Yet there is insufficient information on the hazards that they pose to human health and the environment. To improve the protection of the human health and the environment, the European Commission enforced the *REACH Regulation (Registration, Evaluation, Authorization of Chemicals; EC 1907/2006)* in 2007. REACH gives a greater responsibility to manufacturers to better and earlier assess hazards and risks of their produced compounds, and to identify and implement measures to protect the humans and the environment. REACH thus provides a legislative basis to investigate toxic properties of compounds before they are applied or emitted into the environment instead of after their emerge as contaminants (Field et al. 2006), however the potential of compounds to end up in drinking water is not considered in the investigations.

Besides legislation, also collaboration and discussion initiatives such as the International Commission for the Protection of the Rhine (ICPR) and the International Meuse Commission (ICM) aim to protect the sustainable use of surface waters. They provide a platform to discuss and solve disputes between polluters upstream and users downstream a river.

5.2. The position of drinking water companies

Drinking water companies aim to produce safe and irreproachable drinking water at reasonable costs. Application of the precautionary principle requires that, as long as health risks related to long-term exposure to mixtures of low concentrations of all kinds of emerging contaminants cannot fully be excluded, the produced drinking water should contain as less as possible contaminants. Moreover, compounds (like MTBE), which are currently considered not very toxic, are considered unwanted in principle.

Drinking water companies intensively monitor the quality of their sources and the performance of the treatment processes. It appears that conventional treatment steps, suitable for the removal of “conventional” contaminants, do not completely remove the often less lipophilic and less environmentally persistent emerging contaminants. Drinking water companies develop and introduce expensive and advanced treatment technologies to achieve maximum purification of drinking water. Treatment and purification techniques have, however, their technical limitations. Removal is not always 100%, is selective in nature and advanced treatment methods may lead to the creation of other unwanted chemical compounds. Therefore, preparation of chemically safe and irreproachable drinking water should preferably be enabled by prevention of the emission of emerging contaminants in the environment instead by technological improvements. To this aim, drinking water companies endorse political measures to prevent pollution at the source and to counteract the current shifting of responsibility for surface water quality from polluters to users like themselves. This is done by the publication of the Danube, Meuse and Rhine Memorandum 2008, collectively formulated by drinking water companies using these rivers as their sources (International Association of Waterworks in the Danube Catchment Area et al. 2008). It formulates the most important principles of sustainable use of surface waters necessary for drinking

water production and provides maximum concentrations of emerging contaminants in surface waters that should not be exceeded. It was composed as aid and orientation for politicians, governments, and policymakers in industry and water management.

6. Outlook

Rapid improvements in chemical analysis techniques during the last decades have led to the discovery of all kinds of emerging compounds in surface waters at concentrations that could not be observed earlier. The detection of those compounds demonstrates the impact that the widespread use of chemicals in our modern society has on the environment and casts on us the responsibility to seek for ways to deal with their presence in the environment and in the present and future drinking water sources. This requires prolonged and joint efforts of the scientific community and water sector.

Further developments in chemical screening techniques will definitely lead to the discovery of still other classes of compounds in the environment (Sumpter 2009). For newly discovered compounds, assessing possible health risks is a first priority.

In addition, innovative biological test methods (e.g. bioassays and genomics techniques) enable the measurement of biological (mixture) effects even of unknown compounds in water samples. These methods can be used to detect the presence of compounds with a wide scope of specific effects, such as genotoxicity or hormone-like activity, even if these compounds yet cannot be detected with chemical techniques. Furthermore, these tools provide a means to find answers to the important issue of relevance of exposure to mixtures and as such help to better investigate possible risks of low concentrations of emerging contaminants in drinking water sources.

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References

- Adler P, Steger-Hartmann T, Kalbfus W. 2001. Distribution of natural and synthetic estrogenic steroid hormones in water samples from Southern and Middle Germany. *Acta Hydrochimica et Hydrobiologica*. 29:227–241.
- Ahrens L, Felizeter S, Ebinghaus R. 2009. Spatial distribution of polyfluoroalkyl compounds in seawater of the German Bight. *Chemosphere*. 76:179–184.
- Allen Y, Matthiessen P, Scott AP, Haworth S, Feist S, Thain JE. 1999a. The extent of oestrogenic contamination in the UK estuarine and marine environments – further surveys of flounder. *Sci Total Environ*. 233:5–20.
- Allen Y, Scott AP, Matthiessen P, Haworth S, Thain JE, Feist S. 1999b. Survey of estrogenic activity in United Kingdom estuarine and coastal waters and its effects on gonadal development of the flounder *Platichthys flesus*. *Environ Toxicol Chem*. 18:1791–1800.
- Andresen JA, Muir D, Ueno D, Darling C, Theobald N, Bester K. 2007. Emerging pollutants in the north sea in comparison to Lake Ontario, Canada. *Environ Toxicol Chem*. 26:1081–1089.

- Barnhoorn IEJ, Bornman MS, Pieterse GM, van Vuren JHJ. 2004. Histological evidence of intersex in feral sharptooth catfish (*Clarias gariepinus*) from an estrogen-polluted water source in Gauteng, South Africa. *Environ Toxicol.* 19:603–608.
- Batt AL, Kostich MS, Lazorchak JM. 2008. Analysis of ecologically relevant pharmaceuticals in wastewater and surface water using selective solid-phase extraction and UPLC-MS/MS. *Anal Chem.* 80:5021–5030.
- Belfroid AC, van der Horst A, Vethaak AD, Schäfer AJ, Rijs GBJ, Wegener J, Cofino WP. 1999. Analysis and occurrence of estrogenic hormones and their glucuronides in surface water and waste water in The Netherlands. *Sci Total Environ.* 225:101–108.
- Benotti MJ, Trenholm RA, Vanderford BJ, Holady JC, Stanford BD, Snyder SA. 2009. Pharmaceuticals and endocrine disrupting compounds in US drinking water. *Environ Sci Technol.* 43:597–603.
- Bjerregaard LB, Korsgaard B, Bjerregaard P. 2006. Intersex in wild roach (*Rutilus rutilus*) from Danish sewage effluent-receiving streams. *Ecotoxicol Environ Safety.* 64:321–328.
- Blair RM, Fang H, Branham WS, Hass BS, Dial SL, Moland CL, Tong W, Shi L, Perkins R, Sheehan DM. 2000. The estrogen receptor relative binding affinities of 188 natural and xenochemicals: structural diversity of ligands. *Toxicol Sci.* 54:138–153.
- Bolz U, Hagenmaier H, Korner W. 2001. Phenolic xenoestrogens in surface water, sediments, and sewage sludge from Baden-Württemberg, south-west Germany. *Environ Pollut.* 115:291–301.
- Brian JV, Harris CA, Scholze M, Backhaus T, Booy P, Lamoree M, Pojana G, Jonkers N, Runnalls T, Bonfá A. 2005. Accurate prediction of the response of freshwater fish to a mixture of estrogenic chemicals. *Environ Health Perspect.* 113:721.
- Brooks BW, Huggett DB, Boxall AB. 2009. Pharmaceuticals and personal care products: research needs for the next decade. *Environ Toxicol Chem.* 28:2469–2472.
- Caldwell DJ, Mastrocco F, Nowak E, Johnston J, Yekel H, Pfeiffer D, Hoyt M, DuPlessie BM, Anderson PD. 2010. An assessment of potential exposure and risk from estrogens in drinking water. *Environ Health Perspect.* 118:338–344.
- Carson R. 1962. *Silent spring*. Boston (MA): Houghton Mifflin Company.
- Castiglioni S, Zuccato E, Chiabrando C, Fanelli R, Bagnati R. 2008. Mass spectrometric analysis of illicit drugs in wastewater and surface water. *Mass Spectrometry Rev.* 27:378–394.
- Céspedes R, Lacorte S, Raldua D, Ginebreda A, Barcelo D, Pina B. 2005. Distribution of endocrine disruptors in the Llobregat River basin (Catalonia, NE Spain.). *Chemosphere.* 61:1710–1719.
- Céspedes R, Petrovic M, Raldua D, Saura U, Pina B, Lacorte S, Viana P, Barcelo D. 2004. Integrated procedure for determination of endocrine-disrupting activity in surface waters and sediments by use of the biological technique recombinant yeast assay and chemical analysis by LC-ESI-MS. *Anal Bioanal Chem.* 378:697–708.
- Chang H, Wan Y, Hu J. 2009. Determination and source apportionment of five classes of steroid hormones in urban rivers. *Environ Sci Technol.* 43:7691–7698.
- Colborn T, Vom Saal FS, Soto AM. 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environ Health Perspect.* 101:378–384.
- Colwell RR. 1996. Global climate and infectious disease: the cholera paradigm. *Science.* 274:2025–2031.
- Cooney CM. 2009. Study detects trace levels of pharmaceuticals in US drinking water. *Environ Sci Technol.* 43:551.
- Daston GP, Cook JC, Kavlock RJ. 2003. Uncertainties for endocrine disrupters: our view on progress. *Toxicol Sci.* 74:245–252.
- Daughton CG, Ternes TA. 1999. Pharmaceuticals and personal care products in the environment: agents of subtle change? *Environ Health Perspect.* 107(Suppl 6):907–938.
- de Alda MJL, Barcelo D. 2001. Use of solid-phase extraction in various of its modalities for sample preparation in the determination of estrogens and progestogens in sediment and water. *J Chromatogr A.* 938:145–153.
- de Boer J. 2010. Persistent organic pollutant analysis – what level of sensitivity and selectivity do we need? *EnviroAnalysis 2010*, Toronto, Canada.
- De Moel PJ, Verberk JQJC, Van Dijk JC. 2004. *Drinkwater – principes en praktijk*. The Hague, the Netherlands: Delft Technical University/SDU Publishers B.V.

- Desbrow C, Routledge EJ, Brighty GC, Sumpter JP, Waldock M. 1998. Identification of estrogenic chemicals in STW effluent. 1. Chemical fractionation and in vitro biological screening. *Environ Sci Technol.* 32:1549–1558.
- Ellis JB. 2006. Pharmaceutical and personal care products (PPCPs) in urban receiving waters. *Environ Pollut.* 144:184–189.
- European Environment Agency. 1997. European workshop on the impact of endocrine disruptors on human health and wildlife, 2–4 December 1996, Weybridge, UK. Report of the Proceedings. Report EU 17549. 1997. Copenhagen: European Commission DG XII.
- Fairley P, Colborn T, Myers JP. 1996. Our stolen future: what pointers for industry? *Chem Week.* 158:55–56.
- Farre M, Gros M, Hernandez B, Petrovic M, Hancock P, Barcelo D. 2008. Analysis of biologically active compounds in water by ultra-performance liquid chromatography quadrupole time-of-flight mass spectrometry. *Rapid Commun Mass Spectrometry.* 22:41–51.
- Fawell JK, Sheahan D, James HA, Hurst M, Scott S. 2001. Oestrogens and oestrogenic activity in raw and treated water in Severn trent water. *Water Res.* 35:1240–1244.
- Fenet H, Gomez E, Pillon A, Rosain D, Nicolas JC, Casellas, Balaguer P. 2003. Estrogenic activity in water and sediments of a French river: contribution of alkylphenols. *Arch Environ Contam Toxicol.* 44:1–6.
- Ferrer I, Thurman EM. 2003. Liquid chromatography/time-of-flight/mass spectrometry (LC/TOF/MS) for the analysis of emerging contaminants. *Trac-Trends Anal Chem.* 22:750–756.
- Field JA, Johnson CA, Rose JB. 2006. What is “emerging”? *Environ Sci Technol.* 40:7105.
- Fischer A, Oehm C, Selle M, Werner P. 2005. Biotic and abiotic transformations of methyl tertiary butyl ether (MTBE). *Environ Sci Pollut Res Int.* 12:381–386.
- Focazio MJ, Kolpin DW, Barnes KK, Furlong ET, Meyer MT, Zaugg SD, Barber LB, Thurman ME. 2008. A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States – II) untreated drinking water sources. *Sci Total Environ.* 402:201–216.
- Fromme H, Tittlemier SA, Volkel W, Wilhelm M, Twardella D. 2009. Perfluorinated compounds – exposure assessment for the general population in Western countries. *Int J Hygiene Environ Health.* 212:239–270.
- Gagne F, Blaise C, Andre C. 2006. Occurrence of pharmaceutical products in a municipal effluent and toxicity to rainbow trout (*Oncorhynchus mykiss*) hepatocytes. *Ecotoxicol Environ Safety.* 64:329–336.
- Gibson R, Becerril-Bravo E, Silva-Castro V, Jimenez B. 2007. Determination of acidic pharmaceuticals and potential endocrine, disrupting compounds in wastewaters and spring waters by selective elution and analysis by gas chromatography-mass spectrometry. *J Chromatogr A.* 1169:31–39.
- Gibson R, Smith MD, Spary CJ, Tyler CR, Hill EM. 2005. Mixtures of estrogenic contaminants in bile of fish exposed to wastewater treatment works effluents. *Environ Sci Technol.* 39:2461–2471.
- Giger W. 2009. Hydrophilic and amphiphilic water pollutants: using advanced analytical methods for classic and emerging contaminants. *Analy Bioanal Chem.* 393:37–44.
- Gomez MJ, Petrovic M, Fernandez-Alba AR, Barcelo D. 2006. Determination of pharmaceuticals of various therapeutic classes by solid-phase extraction and liquid chromatography-tandem mass spectrometry analysis in hospital effluent wastewaters. *J Chromatogr A.* 1114:224–233.
- Gros M, Petrovic M, Barcelo D. 2009. Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/quadrupole-linear ion trap mass spectrometry and automated library searching. *Anal Chem.* 81:898–912.
- Hernando MD, Heath E, Petrovic M, Barcelo D. 2006a. Trace-level determination of pharmaceutical residues by LC-MS/MS in natural and treated waters. A pilot-survey study. *Anal Bioanal Chem.* 385:985–991.
- Hernando MD, Mezcua M, Fernandez-Alba AR, Barcelo D. 2006b. Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. *Talanta.* 69:334–342.

- Hilton MJ, Thomas KV. 2003. Determination of selected human pharmaceutical compounds in effluent and surface water samples by high-performance liquid chromatography–electrospray tandem mass spectrometry. *J Chromatogr A*. 1015:129–141.
- Hilton MJ, Thomas KV, Ashton D. 2003. Targeted monitoring programme for pharmaceuticals in the aquatic environment (Environment Agency). Report number P6-012/06/TR. Bristol (UK): Environment Agency. 57 p.
- Hogenboom AC, van Leerdam JA, de Voogt R. 2009. Accurate mass screening and identification of emerging contaminants in environmental samples by liquid chromatography–hybrid linear ion trap orbitrap mass spectrometry. *J Chromatogr A*. 1216:510–519.
- Houtman CJ, Booij P, Jover E, Pascual del RD, Swart K, van VM, Vreuls R, Legler J, Brouwer A, Lamoree MH. 2006a. Estrogenic and dioxin-like compounds in sediment from Zierikzee harbour identified with CALUX assay-directed fractionation combined with one and two dimensional gas chromatography analyses. *Chemosphere*. 65:2244–2252.
- Houtman CJ, Booij P, van der Valk KM, van Bodegom PM, van den Ende F, Gerritsen AA, Lamoree MH, Legler J, Brouwer A. 2007. Biomonitoring of estrogenic exposure and identification of responsible compounds in bream from Dutch surface waters. *Environ Toxicol Chem*. 26:898–907.
- Houtman CJ, Cenijn PH, Hamers T, Lamoree MH, Legler J, Murk AJ, Brouwer A. 2004a. Toxicological profiling of sediments using in vitro bioassays, with emphasis on endocrine disruption. *Environ Toxicol Chem*. 23:32–40.
- Houtman CJ, Van Houten YK, Leonards PE, Brouwer A, Lamoree MH, Legler J. 2006b. Biological validation of a sample preparation method for ER-CALUX bioanalysis of estrogenic activity in sediment using mixtures of xeno-estrogens. *Environ Sci Technol*. 40:2455–2461.
- Houtman CJ, Van Oostveen AM, Brouwer A, Lamoree MH, Legler J. 2004b. Identification of estrogenic compounds in fish bile using bioassay-directed fractionation. *Environ Sci Technol*. 38:6415–6423.
- Huerta-Fontela M, Galceran MT, Ventura F. 2008. Stimulatory drugs of abuse in surface waters and their removal in a conventional drinking water treatment plant. *Environ Sci Technol*. 42:6809–6816.
- International Association of Waterworks in the Danube Catchment Area, Association of River waterworks in the Meuse Catchment Area, and International Association of Waterworks in the Rhine Catchment Area. 2008. Danube, Meuse and Rhine Memorandum 2008:1–20.
- Isaacson CW, Kleber M, Field JA. 2009. Quantitative analysis of fullerene nanomaterials in environmental systems: a critical review. *Environ Sci Technol*. 43:6463–6474.
- Jemba PK. 2006. Excretion and ecotoxicity of pharmaceutical and personal care products in the environment. *Ecotoxicol Environ Safety*. 63:113–130.
- Jobling S, Nolan M, Tyler CR, Brighty G, Sumpter JP. 1998. Widespread sexual disruption in wild fish. *Environ Sci Technol*. 32:2498–2506.
- Johnson AC, Juergens MD, Williams RJ, Kümmerer K, Kortenkamp A, Sumpter JP. 2008. Do cytotoxic chemotherapy drugs discharged into rivers pose a risk to the environment and human health? An overview and UK case study. *J Hydrol*. 348:167–175.
- Johnson AC, Williams RJ, Matthiessen P. 2006. The potential steroid hormone contribution of farm animals to freshwaters, the United Kingdom as a case study. *Sci Total Environ*. 362:166–178.
- Jones OA, Lester JN, Voulvoulis N. 2005. Pharmaceuticals: a threat to drinking water? *Trends Biotechnol*. 23:163–167.
- Jugan ML, Oziol L, Bimbot M, Huteau V, Tamisier-Karolak S, Blondeau JP, Lévi Y. 2009. In vitro assessment of thyroid and estrogenic endocrine disruptors in wastewater treatment plants, rivers and drinking water supplies in the greater Paris area (France). *Sci Total Environ*. 407:3579–3587.
- Kasprzyk-Hordern B, Dinsdale RM, Guwy AJ. 2007. Multi-residue method for the determination of basic/neutral pharmaceuticals and illicit drugs in surface water by solid-phase extraction and ultra performance liquid chromatography–positive electrospray ionisation tandem mass spectrometry. *J Chromatogr A*. 1161:132–145.
- Kasprzyk-Hordern B, Dinsdale RM, Guwy AJ. 2008. The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK. *Water Res*. 42:3498–3518.

- Kasprzyk-Hordern B, Dinsdale RM, Guwy AJ. 2009. The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. *Water Res.* 43:363–380.
- Kirby MF, Allen YT, Dyer RA, Feist SW, Katsiadaki I, Matthiessen P, Scott AP, Smith A, Stentiford GD, Thain JE, et al. 2004. Surveys of plasma vitellogenin and intersex in male flounder (*Platichthys flesus*) as measures of endocrine disruption by estrogenic contamination in United Kingdom estuaries: Temporal trends, 1996 to 2001. *Environ Toxicol Chem.* 23:748–758.
- Kolb A, Puttmann W. 2006. Methyl tert-butyl ether (MTBE) in finished drinking water in Germany. *Environ Pollut.* 140:294–303.
- Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: a national reconnaissance. *Environ Sci Technol.* 36:1202–1211.
- Kroes R, Galli C, Munro I, Schilter B, Tran LA, Walker R, Würtzen G. 2000. Threshold of toxicological concern for chemical substances present in the diet: a practical tool for assessing the need for toxicity testing. *Food Chem Toxicol.* 38:255–312.
- Kroes R, Renwick AG, Cheeseman M, Kleiner J, Mangelsdorf I, Piersma A, Schilter B, Schlatter J, Van Schothorst F, Vos JG. 2004. Structure-based thresholds of toxicological concern (TTC): guidance for application to substances present at low levels in the diet. *Food Chem Toxicol.* 42:65–83.
- Kuch HM, Ballschmiter K. 2001. Determination of endocrine-disrupting phenolic compounds and estrogens in surface and drinking water by HRGC-(NCI)-MS in the picogram per liter range. *Environ Sci Technol.* 35:3201–3206.
- Kuster M, de Alda MJ, Hernando MD, Petrovic M, Martin-Alonso J, Barcelo D. 2008. Analysis and occurrence of pharmaceuticals, estrogens, progestogens and polar pesticides in sewage treatment plant effluents, river water and drinking water in the Llobregat river basin (Barcelona, Spain). *J Hydrol.* 358:112–123.
- Kuster M, Lopez de AM, Barcelo D. 2009. Liquid chromatography-tandem mass spectrometric analysis and regulatory issues of polar pesticides in natural and treated waters. *J Chromatogr A.* 1216:520–529.
- Kwadijk CJ, Korytar P, Koelmans AA. 2010. Distribution of perfluorinated compounds in aquatic systems in the Netherlands. *Environ Sci Technol.* 44:3746–3751.
- Lange IG, Daxenberger A, Schiffer B, Witters H, Ibarreta D, Meyer HHD. 2002. Sex hormones originating from different livestock production systems: fate and potential disrupting activity in the environment. *Anal Chim Acta.* 473:27–37.
- Legler J. 2008. New insights into the endocrine disrupting effects of brominated flame retardants. *Chemosphere.* 73:216–222.
- Legler J, Broekhof JLM, Brouwer A, Lanser PH, Murk AJ, van der Saag PT, Vethaak AD, Wester P, Zivkovic D, van der Burg B. 2000. A novel in vivo bioassay for (Xeno-)estrogens using transgenic zebrafish. *Environ Sci Technol.* 34:4439–4444.
- Legler J, Zeinstra LM, Schuitemaker F, Lanser PH, Bogerd J, Brouwer A, Vethaak AD, de Voogt P, Murk AJ, van der Burg B. 2002. Comparison of in vivo and in vitro reporter gene assays for short-term screening of estrogenic activity. *Environ Sci Technol.* 36:4410–4415.
- Loos R, Gawlik BM, Locoro G, Rimaviciute E, Contini S, Bidoglio G. 2009. EU-wide survey of polar organic persistent pollutants in European river waters. *Environ Pollut.* 157:561–568.
- Lopez-Roldan P, de Alda MJL, Barcelo D. 2004. Simultaneous determination of selected endocrine disruptors (pesticides, phenols and phthalates) in water by in-field solid-phase extraction (SPE) using the prototype PROFEXS followed by on-line SPE (PROSPEKT) and analysis by liquid chromatography-atmospheric pressure chemical ionisation-mass spectrometry. *Anal Bioanal Chem.* 378:599–609.
- Matamoros V, Jover E, Bayona JM. 2010. Part-per-trillion determination of pharmaceuticals, pesticides, and related organic contaminants in river water by solid-phase extraction followed by comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry. *Anal Chem.* 82:699–706.
- Matthiessen P, Arnold D, Johnson AC, Pepper TJ, Pottinger TG, Pulman KG. 2006. Contamination of headwater streams in the United Kingdom by oestrogenic hormones from livestock farms. *Sci Total Environ.* 367:616–630.

- McLachlan MS, Holmstrom KE, Reth M, Berger U. 2007. Riverine discharge of perfluorinated carboxylates from the European continent. *Environ Sci Technol.* 41:7260–7265.
- Meng CK. 2009. Identifying pharmaceuticals in surface water using LC-MS/MS in both positive and negative ion modes. *Am Lab.* 41:11–13.
- Morgenstern P, Versteegh AF, de Korte GA, Hoogerbrugge R, Mooibroek D, Bannink A, Hogendoorn EA. 2003. Survey of the occurrence of residues of methyl tertiary butyl ether (MTBE) in Dutch drinking water sources and drinking water. *J Environ Monitor.* 5:885–890.
- Morteani G, Moller P, Fuganti A, Paces T. 2006. Input and fate of anthropogenic estrogens and gadolinium in surface water and sewage plants in the hydrological basin of Prague (Czech Republic). *Environ Geochem Health.* 28:257–264.
- Nishihara T, Nishikawa J, Kanayama T, Dakeyama F, Saito K, Imagawa M, Takatori S, Kitagawa Y, Hori S, Utsumi H. 2000. Estrogenic activities of 517 chemicals by yeast two-hybrid assay. *J Health Sci.* 46:282–298.
- Palma P, Kuster M, Alvarenga P, Palma VL, Fernandes RM, Soares AM, Lopez de Alda MJ, Barcelo D, Barbosa IR. 2009. Risk assessment of representative and priority pesticides, in surface water of the Alqueva reservoir (South of Portugal) using on-line solid phase extraction-liquid chromatography-tandem mass spectrometry. *Environ Int.* 35:545–551.
- Peck M, Gibson RW, Kortenkamp A, Hill EM. 2004. Sediments are major sinks of steroidal estrogens in two United Kingdom rivers. *Environ Toxicol Chem.* 23:945–952.
- Petrovic M, Barcelo D. 2006. Liquid chromatography-mass spectrometry in the analysis of emerging environmental contaminants. *Anal Bioanal Chem.* 385:422–424.
- Petrovic M, Gonzalez S, Barcelo D. 2003. Analysis and removal of emerging contaminants in wastewater and drinking water. *Trac-Trends Anal Chem.* 22:685–696.
- Petrovic M, Sole M, de Alda MJL, Barcelo D. 2002. Endocrine disruptors in sewage treatment plants, receiving river waters, and sediments: integration of chemical analysis and biological effects on feral carp. *Environ Toxicol Chem.* 21:2146–2156.
- Prevedouros K, Cousins IT, Buck RC, Korzeniowski SH. 2006. Sources, fate and transport of perfluorocarboxylates. *Environ Sci Technol.* 40:32–44.
- Quiros L, Cespedes R, Lacorte S, Viana P, Raldua D, Barcelo D, Pina B. 2005. Detection and evaluation of endocrine-disruption activity in water samples from Portuguese rivers. *Environ Toxicol Chem.* 24:389–395.
- Rahman F, Langford KH, Scrimshaw MD, Lester JN. 2001. Polybrominated diphenyl ether (PBDE) flame retardants. *Sci Total Environ.* 275:1–17.
- Rahman MF, Yanful EK, Jasim SY. 2009. Endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) in the aquatic environment: implications for the drinking water industry and global environmental health. *J Water Health.* 7:224–243.
- Reemtsma T, Quintana JB, Rodil R, Garcia-Lopez M, Rodriguez I. 2008. Organophosphorus flame retardants and plasticizers in water and air I. Occurrence and fate. *Trac-Trends Anal Chem.* 27:727–737.
- Richardson SD. 2008. Environmental mass spectrometry: emerging contaminants and current issues. *Anal Chem.* 80:4373–4402.
- Richardson SD. 2009. Water analysis: emerging contaminants and current issues. *Anal Chem.* 81:4645–4677.
- RIWA Vereniging van Rivierwaterbedrijven. 2003. Annual Report 2001–2002. The Rhine. 2003. Nieuwegein: Association of River Waterworks RIWA.
- RIWA Vereniging van Rivierwaterbedrijven. 2008. Annual Report 2007 The Rhine. 2008. Nieuwegein: Association of River Waterworks RIWA.
- Rodrigues AM, Ferreira V, Cardoso VV, Ferreira E, Benoliel MJ. 2007. Determination of several pesticides in water by solid-phase extraction, liquid chromatography and electrospray tandem mass spectrometry. *J Chromatogr A.* 1150:267–278.
- Ruhoy IS, Daughton CG. 2008. Beyond the medicine cabinet: an analysis of where and why medications accumulate. *Environ Int.* 34:1157–1169.
- Sacher F, Ehmann M, Gabriel S, Graf C, Brauch HJ. 2008. Pharmaceutical residues in the river Rhine – results of a one-decade monitoring programme. *J Environ Monitor.* 10:664–670.

- Safe SH. 1995. Environmental and dietary estrogens and human health – is there a problem. *Environ Health Perspect.* 103:346–351.
- Safe SH. 2000. Endocrine disruptors and human health – is there a problem? An update. *Environ Health Perspect.* 108:487–493.
- Scheurer M, Brauch HJ, Lange FT. 2009. Analysis and occurrence of seven artificial sweeteners in German waste water and surface water and in soil aquifer treatment (SAT). *Anal Bio Anal Chem.* 394:1585–1594.
- Schriks M, Heringa MB, van der Kooi MM, de VP, van Wezel AP. 2009. Toxicological relevance of emerging contaminants for drinking water quality. *Water Res.* 44:461–476.
- Sharpe RM, Skakkebaek NE. 1993. Are estrogens involved in falling sperm counts and disorders of the male reproductive-tract. *Lancet.* 341:1392–1395.
- Sheahan DA, Brighty GC, Daniel M, Jobling S, Harries JE, Hurst MR, Kennedy J, Kirby SJ, Morris S, Routledge EJ, et al. 2002. Reduction in the estrogenic activity of a treated sewage effluent discharge to an English river as a result of a decrease in the concentration of industrially derived surfactants. *Environ Toxicol Chem.* 21:515–519.
- Shore LS, Shemesh M. 2003. Naturally produced steroid hormones and their release into the environment. *Pure Appl Chem.* 75:1859–1871.
- Skutlarek D, Exner M, Farber H. 2006. Perfluorinated surfactants in surface and drinking water. *Environ Sci Pollut Res.* 13:299–307.
- Snyder SA, Westerhoff P, Yoon Y, Sedlak DL. 2003. Pharmaceuticals, personal care products, and endocrine disruptors in water: implications for the water industry. *Environ Eng Sci.* 20:449–469.
- Sole M, Raldúa D, Piferrer F, Barcelo D, Porte C. 2003. Feminization of wild carp, *Cyprinus carpio*, in a polluted environment: plasma steroid hormones, gonadal morphology and xenobiotic metabolizing system. *Comp Biochem Physiol C-Toxicol Pharmacol.* 136:145–156.
- Stackelberg PE, Gibs J, Furlong ET, Meyer MT, Zaugg SD, Lippincott RL. 2007. Efficiency of conventional drinking-water-treatment processes in removal of pharmaceuticals and other organic compounds. *Sci Total Environ.* 377:255–272.
- Stolker AA, Niesing W, Hogendoorn EA, Versteegh JF, Fuchs R, Brinkman UA. 2004. Liquid chromatography with triple-quadrupole or quadrupole-time of flight mass spectrometry for screening and confirmation of residues of pharmaceuticals in water. *Anal Bioanal Chem.* 378:955–963.
- Sumpter JP. 2005. Endocrine disrupters in the aquatic environment: an overview. *Acta Hydrochimica et Hydrobiologica.* 33:9–16.
- Sumpter JP. 2009. Protecting aquatic organisms from chemicals: the harsh realities. *Philos Trans A Math Phys Eng Sci.* 367:3877–3894.
- Sumpter JP, Johnson AC. 2008. 10th anniversary perspective: reflections on endocrine disruption in the aquatic environment: from known knowns to unknown unknowns (and many things in between). *J Environ Monitor.* 10:1476–1485.
- Swartjes FA, Baars AJ, Fleuren RHLJ, Otte PF. 2004. Risicogrenzen voor MTBE (Methyl *tertiair*-butyl ether) in bodem, sediment, grondwater, oppervlaktewater, drinkwater en voor drinkwaterbereiding. RIVM Report 711701039/2004. National Institute for Public Health and the Environment.
- Ter Laak TL, van der Aa M, Houtman CJ, Stoks PG, van Wezel AP. 2010. Relating environmental concentrations of pharmaceuticals to consumption: a mass balance approach for the river Rhine. *Environ Int.* 36:403–409.
- Terzic S, Senta I, Ahel M, Gros M, Petrovic M, Barcelo D, Muller J, Knepper T, Marti I, Ventura F, et al. 2008. Occurrence and fate of emerging wastewater contaminants in Western Balkan Region. *Sci Total Environ.* 399:66–77.
- Van der Aa NGFM, Kommer GJ, Versteegh JFM. 2009. Huidig en toekomstig gebruik van geneesmiddelen. *H2O.* 2009:33–35.
- Van der Hoek JP, Mons MN, Stoks P, Van der Kooij D. 2008. Vision on and guideline values for xenobiotic substances in drinking water. *H2O.* 2008:33–35.
- Van der Linden SC, Heringa MB, Man HY, Sonneveld E, Puijker LM, Brouwer A, Van Der Burg B. 2008. Detection of multiple hormonal activities in wastewater effluents and surface water, using a panel of steroid receptor CALUX bioassays. *Environ Sci Technol.* 42:5814–5820.

- Van Wezel A, Puijker L, Vink C, Versteegh A, De Voogt P. 2009. Odour and flavour thresholds of gasoline additives (MTBE, ETBE and TAME) and their occurrence in Dutch drinking water collection areas. *Chemosphere*. 76:672–676.
- Versteegh JFM, Van der Aa NGFM, Dijkman E. 2007. Geneesmiddelen in drinkwater en drinkwaterbronnen. Resultaten van het meetprogramma 2005/2006. RIVM Report 703719016/2007, 1–53. 2007. Bilthoven: Dutch Ministry for Public Health and the Environment.
- Vethaak AD, Lahr J, Schrap SM, Belfroid AC, Rijs GBJ, Gerritsen A, de Boer J, Bulder AS, Grinwis GCM, Kuiper RV, et al. 2005. An integrated assessment of estrogenic contamination and biological effects in the aquatic environment of The Netherlands. *Chemosphere*. 59:511–524.
- Vryzas Z, Vassiliou G, Alexoudis C, Papadopoulou-Mourkidou E. 2009. Spatial and temporal distribution of pesticide residues in surface waters in northeastern Greece. *Water Res*. 43:1–10.
- Webb S, Ternes T, Gibert M, Olejniczak K. 2003. Indirect human exposure to pharmaceuticals via drinking water. *Toxicol Lett*. 142:157–167.
- Weiss JM, Hamers T, Thomas KV, Van Der Linden S, Leonards PE, Lamoree MH. 2009. Masking effect of anti-androgens on androgenic activity in European river sediment unveiled by effect-directed analysis. *Anal Bioanal Chem*. 394:1385–1397.
- Weiss S, Jakobs J, Reemtsma T. 2006. Discharge of three benzotriazole corrosion inhibitors with municipal wastewater and improvements by membrane bioreactor treatment and ozonation. *Environ Sci Technol*. 40:7193–7199.
- Wiesner MR, Lowry GV, Jones KL, Hochella MF, Jr, Di Giulio RT, Casman E, Bernhardt ES. 2009. Decreasing uncertainties in assessing environmental exposure, risk, and ecological implications of nanomaterials. *Environ Sci Technol*. 43:6458–6462.
- Wolff MS, Toniolo PG, Lee EW, Rivera M, Dubin N. 1993. Blood-levels of organochlorine residues and risk of breast-cancer. *J Natl Cancer Inst*. 85:648–652.
- World Health Organisation. 2006. Guidelines for drinking-water quality. Vol. 1. 3rd ed, incorporating first and second addenda. Geneva, Switzerland: World Health Organisation.
- Wuijts S, Van Rijswijk HFMW. 2008. Drinkwateraspecten en de Kaderrichtlijn Water. Criteria voor de bescherming van drinkwaterbronnen en kwaliteitsdoelstellingen. RIVM Report 734301 028, 1–86. Bilthoven, The Netherlands: National Institute for Health and the Environment.
- Zuccato E, Castiglioni S, Bagnati R, Chiabrando C, Grassi P, Fanelli R. 2008. Illicit drugs, a novel group of environmental contaminants. *Water Res*. 42:961–968.
- Zuccato E, Chiabrando C, Castiglioni S, Calamari D, Bagnati R, Schiarea S, Fanelli R. 2005. Cocaine in surface waters: a new evidence-based tool to monitor community drug abuse. *Environ Health*. 4:14.