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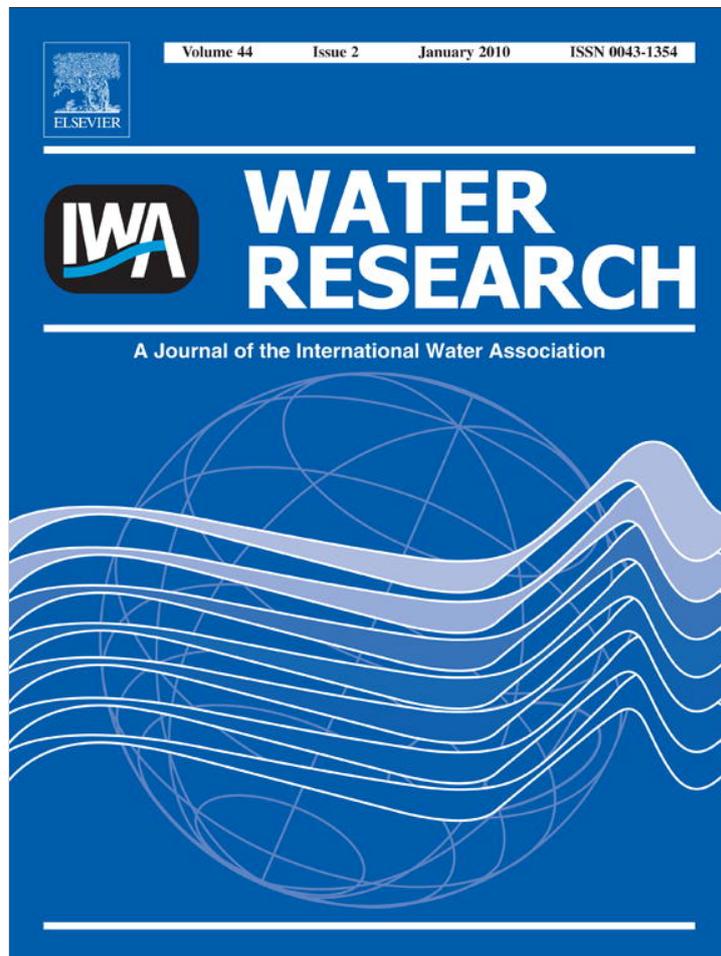
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Toxicological relevance of emerging contaminants for drinking water quality

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ABSTRACT

The detection of many new compounds in surface water, groundwater and drinking water raises considerable public concern, especially when human health based guideline values are not available it is questioned if detected concentrations affect human health. In an attempt to address this question, we derived provisional drinking water guideline values for a selection of 50 emerging contaminants relevant for drinking water and the water cycle. For only 10 contaminants, statutory guideline values were available. Provisional drinking water guideline values were based upon toxicological literature data. The maximum concentration levels reported in surface waters, groundwater and/or drinking water were compared to the (provisional) guideline values of the contaminants thus obtained, and expressed as Benchmark Quotient (BQ) values. We focused on occurrence data in the downstream parts of the Rhine and Meuse river basins. The results show that for the majority of compounds a substantial margin of safety exists between the maximum concentration in surface water, groundwater and/or drinking water and the (provisional) guideline value. The present assessment therefore supports the conclusion that the majority of the compounds evaluated pose individually no appreciable concern to human health.

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1. Introduction

Due to anthropogenic activities, freshwater systems worldwide are confronted with thousands of compounds. In the European Union, for example, there are more than 100 000 registered chemicals (EINECS), of which 30 000–70 000 are in daily use. About 300 million tons of synthetic compounds annually used in industrial and consumer products, partially find their way to natural waters (Schwarzenbach et al., 2006). A major contribution to chemical contamination originates from wastewater discharges that impact surface water quality

with incompletely removed organic contaminants (Kolpin et al., 2004; Snyder et al., 2001). Additional contamination comes from diffuse agricultural activities, in which over 140 million tons of fertilizers and several million tons of pesticides are applied each year, and from atmospheric deposition. Such contamination can become an increasing problem for drinking water supplies, especially since the European REACH legislation may drive producers to develop newly designed less lipophilic/bioaccumulative chemicals that will be inherently more difficult to remove by traditional drinking water treatment techniques.

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Recently, Loos et al. (2009) presented an EU-wide monitoring study on 35 organic compounds in European river waters in concentrations up to 40 µg/L. In addition, we have shown the occurrence of emerging polar contaminants, such as benzotriazoles and metabolites of illicit drugs (e.g. benzoylecgonine, desalkylflurazepam and 9-carbonic acid- δ -9-THC) in groundwaters and surface waters in the Netherlands (Hogenboom et al., 2009; Van Leerdam et al., 2009).

Many of these emerging contaminants raise considerable toxicological and public concern, especially when human health based guideline values are unavailable. At present, the World Health Organization (WHO) and the US Environmental Protection Agency (US EPA) have derived approximately 125 statutory guideline values for contaminants in drinking water (Cotruvo, 1988; US EPA, 2006; WHO, 2006). However, the potential health effects of many emerging contaminants present in the water cycle and the potential human health concern associated with direct water ingestion have not been evaluated and statutory standards are not available. Therefore, we proposed earlier to assess the potential human health concern of unknown non-genotoxic compounds (lacking structural alerts that raise concern for potential genotoxicity) by comparing the environmental or drinking water concentration to a TTC (Threshold of Toxicological Concern) derived target value (Mons et al., 2008). The TTC concept was developed in the context of food safety to obtain a first clue on risks of unregulated chemicals present at low levels. The TTC thus derived is based on the molecular structure of the chemical involved and its related mode of toxic action (Munro et al., 1996). Assuming a daily intake of 2 l/day of drinking water, and a maximum contribution of 10% from drinking water to the total exposure – both of which are standard assumptions for deriving drinking water-quality guidelines (WHO, 2006) – TTC based target values proposed for drinking water are 0.1 µg/L for non-genotoxic compounds and 0.01 µg/L for genotoxicants (Mons et al., 2008). This value is based on a TTC level of 1.5 µg/person/d (0.15 µg/person/d for substances containing structural alerts that raise concern for potential genotoxicity with an acceptable lifetime cancer risk of 10^{-6}) for compounds in food (Kroes et al., 2004). Since the TTC based value is rather conservative, an over-estimation of the actual risk may be the result. For emerging contaminants, a more profound human health based assessment may therefore be very valuable. The objectives of the present study were twofold. The first objective was to collect existing drinking water guideline values for a selection of 50 emerging contaminants relevant for the water cycle. If existing guideline values were not available, provisional guideline values were derived with the aid of relevant toxicological literature data. The second aim was to compare the maximum concentration levels reported in surface water, groundwater and/or drinking water to the (provisional) guideline values of the contaminants thus obtained, and express this as a Benchmark Quotient (BQ) value (further abbreviated as “BQ value”). The present study does not attempt to quantify mixture interactions, since for compounds with an unknown mode of action there is no accepted methodology for such an assessment.

2. Materials and methods

The toxicological assessment of the compounds presented in this paper comprises of a tiered approach in five consecutive steps (Fig. 1). First, the compounds to be assessed were selected. Second, n-octanol-water partition coefficients ($\log K_{ow}$) were obtained and compounds with a $\log K_{ow} > 3$ were excluded from further assessment. This $\log K_{ow}$ cut off value is applied as a default threshold; for compounds with a $\log K_{ow}$ above 3 it is less likely that they pass drinking water treatment plants (Westerhoff et al., 2005). Third, if available, statutory drinking water guideline values were obtained from websites of competent authorities; else provisional guideline values were derived with the aid of toxicological data relevant for humans as reported in literature. Fourth, measured maximum surface water, groundwater and/or drinking water concentrations were obtained from various sources and compared to (provisional) guideline values. Finally, a BQ value was calculated from the maximum concentrations reported and the (provisional) drinking water guideline values obtained. These steps are described in more detail below.

2.1. Selection of compounds for assessment

A priority list representing a broad range of chemical classes was formulated with more than 100 compounds of interest. The arguments for inclusion were (i) questions related to toxicity posed by Dutch drinking water companies, (ii) potential low removal efficiency during drinking water production, (iii) appearance in recent literature and (iv) occurrence in surface waters, groundwaters and drinking water as determined by ourselves and others in various screening studies.

2.2. Collection of compound-specific data

2.2.1. n-Octanol-water partition coefficients ($\log K_{ow}$)

All $\log K_{ow}$ values were obtained with the aid of the estimation program KOWWIN (US EPA, v1.67). An exception was made for perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), for which accurate $\log K_{ow}$ values cannot be calculated with estimation software. For these compounds the $\log K_{ow}$ values were obtained from a database (Krop and de Voogt, 2008).

2.2.2. Toxicological data

As illustrated in Fig. 1 (step 3), the first step was to obtain existing statutory drinking water guideline values from e.g. the US EPA (URL1) and the WHO (URL2). If not available, the second step was to obtain an established (by an (inter)national organization) Tolerable Daily Intake (TDI), Acceptable Daily Intake (ADI) or Reference Dose (RfD) and subsequently a provisional drinking water guideline value was derived as further described in Section 2.3. If not available, in a third step toxicity data collection focused primarily on established (by an (inter)national organization) lowest/no observed (adverse) effect levels (LO/NO(A)ELs) and subsequently a TDI was calculated as further described in Section 2.3. Finally, in a fourth step, miscellaneous toxicological information was collected and a TDI was calculated accordingly. In the case of insufficient human relevant toxicological data the

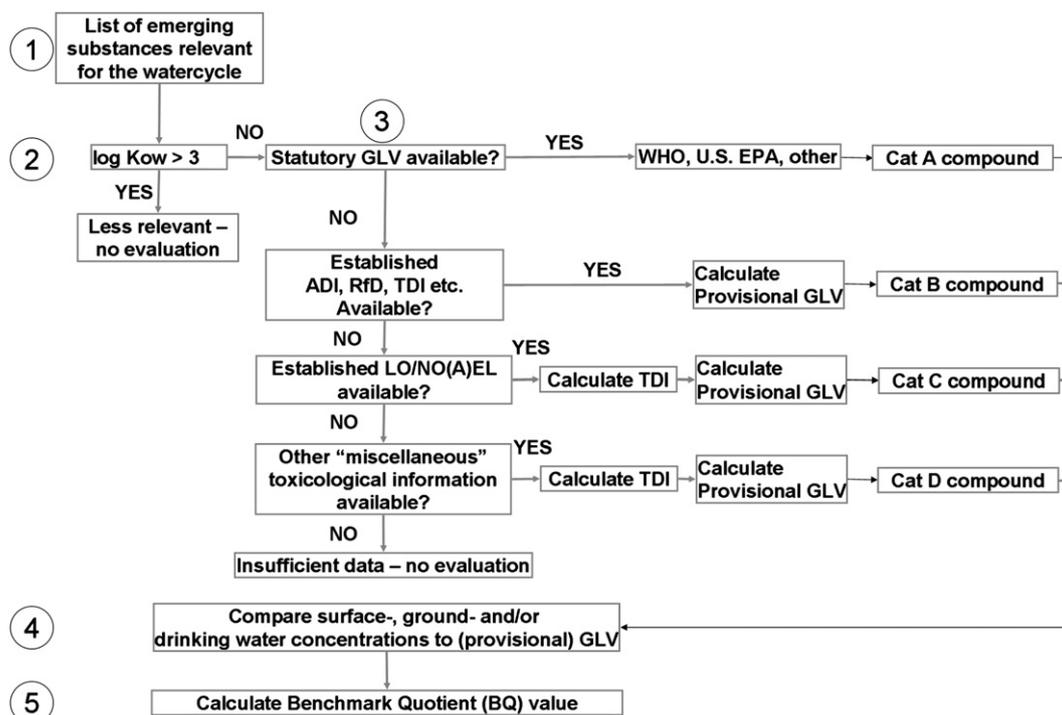


Fig. 1 – Flow diagram of the assessment conducted in the present study. Abbreviations: $\log K_{ow}$, n-octanol-water partition coefficient; GLV, drinking water guideline value; ADI, acceptable daily intake; RfD, reference dose; TDI, tolerable daily intake; LO/NO(A)EL, lowest/no observed (adverse) effect level; numbers correspond to consecutive steps as described Section 2. Compound categories: see Section 2.2.2.

compound of interest was not further evaluated and removed from the list. To facilitate the interpretation for which compounds the toxicity database is strong and less strong, all compounds were categorized (Table 2); (A) representing compounds with a statutory drinking water guideline value, (B) representing compounds with an established TDI, ADI or RfD, (C) representing compounds for which the TDI was calculated with an established LO(A)EL or NO(A)EL and (D) representing compounds for which the TDI was calculated with miscellaneous toxicological information.

TDIs, ADIs, RfDs and/or other chronic toxicity data were sourced from peer-reviewed scientific papers and from other sources such as “grey literature”. In addition, a literature search was performed on the internet and/or toxicological relevant data were obtained from the US EPA IRIS database, the European Chemicals Bureau (ECB), the Organization for Economic Cooperation and Development (OECD), the Dutch National Institute for Health and the Environment (RIVM), the US Food and Drug Administration (US FDA), the Joint Meeting FAO/WHO Meetings on Pesticide Residues (JMPR), the Dutch Expert Committee for Occupational Standards (DECOS), the Dutch board for authorization of plant protection products and biocides (CTGB), the Scientific Committee on Occupational Exposure Limits (SCOEL), the US National Toxicology Program (NTP), the Joint FAO/WHO Committee on Food Additives (JECFA), the Food and Agriculture Organization (FAO), the Danish veterinary and food administration, the European Union (EU), the US National Research Council (NRC), the EFSA scientific panel on contaminants in the food chain (CONTAM) and the Hazardous Substance Data Bank (HSDB).

2.2.3. Occurrence data

Collection of occurrence data focused primarily on maximum concentrations of compounds measured in the downstream parts of the Rhine and Meuse river basins during the past decade. If not available, maximum concentrations in other surface waters and/or groundwaters were sought. The primary source of occurrence data of compounds in surface waters were the annual reports of the Dutch Association of River Water Companies (RIWA) and the German Association of River Water Companies (ARW). Occurrence data of compounds in drinking water were obtained from the REWAB data set (restricted water-quality data from the Dutch water companies). If not available, alternative resources were searched such as “grey literature”, unpublished data, or publicly available sources such as RIVM, the Dutch ministry of transport, public works and water management (Rijkswaterstaat) and the WHO. Additional data on the occurrence of compounds was obtained from peer-reviewed scientific papers and an internet based literature search.

2.3. Derivation of provisional drinking water guideline values

A drinking water guideline value represents the concentration of a constituent that does not exceed tolerable risk to the health of the consumer over a lifetime (WHO, 2006). In some cases, an odour-threshold value may be much lower than the health based guideline value. To calculate a provisional health based guideline value, the general methodology was applied

Table 1 – List of compounds assessed in the present study.

| No. | Compound | CAS | log K _{ow} | No. | Compound | CAS | Log K _{ow} |
|-----|--|------------|---------------------|-----|---|-------------|---------------------|
| 1 | 1,4-Dioxane ² | 123-91-1 | −0.3 ^a | 26 | Ethylenediamine tetra acetic acid (EDTA) ² | 60-00-4 | −3.9 ^b |
| 2 | 2,6-Dichlorobenzamide (BAM) ³ | 2008-58-4 | 0.8 ^a | 27 | Glyphosate ³ | 1071-83-6 | −4.0 ^a |
| 3 | 4-Methylbenzenesulfonamide (p-toluenesulfonamide, 4-tolylsulfonamide) ² | 70-55-3 | 0.9 ^b | 28 | Imidacloprid ³ | 138261-41-3 | 0.6 ^a |
| 4 | Acetylsalicylate (aspirin, acetyl salicylic acid) ⁶ | 50-78-2 | 1.2 ^a | 29 | Iohexol ¹ | 66108-95-0 | −3.1 ^a |
| 5 | Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) ³ | 77521-29-0 | −2.2 ^b | 30 | Iomeprol (iomeron) ¹ | 78649-41-9 | −1.4 ^b |
| 6 | Amidotrizoic acid (diatrizoic acid) ¹ | 117-96-4 | 1.4 ^b | 31 | Iopamidol ¹ | 62883-00-5 | −2.4 ^a |
| 7 | Bentazone ³ | 25057-89-0 | 2.3 ^a | 32 | Iopromide ¹ | 73334-07-3 | −2.1 ^a |
| 8 | Benzene ² | 71-43-2 | 2.1 ^a | 33 | Isoproturon ³ | 34123-59-6 | 2.9 ^a |
| 9 | Benzothiazole ² | 95-16-9 | 2.0 ^a | 34 | Methyl tert-butyl ether (MTBE) ⁴ | 1634-04-4 | 0.9 ^a |
| 10 | Benzotriazole (1H-benzotriazole) ² | 95-14-7 | 1.4 ^a | 35 | Metoprolol ⁶ | 37350-58-6 | 1.9 ^a |
| 11 | Bis(2-chloroisopropyl)ether (BCIPE) ² | 108-60-1 | 2.5 ^a | 36 | n-Butylbenzenesulphonamide ² | 3622-84-2 | 2.3 ^b |
| 12 | Carbamazepine ⁶ | 298-46-4 | 2.5 ^a | 37 | Nicosulfuron ³ | 111991-09-4 | −1.2 ^b |
| 13 | Carbendazim ³ | 10605-21-7 | 1.5 ^a | 38 | n-Nitrosodimethylamine (NDMA) ² | 62-75-9 | −0.6 ^a |
| 14 | Chloridazon (pyrazon) ³ | 1698-60-8 | 1.1 ^a | 39 | p,p'-Sulfonyldiphenol ² | 80-09-1 | 1.7 ^b |
| 15 | Clofibrac acid ⁶ | 882-09-7 | 2.6 ^a | 40 | Perfluorooctanesulfonate (PFOS) (potassium-salt) ⁵ | 2795-39-3 | −1.08 ^c |
| 16 | Dichlorophenoxyacetic acid (2,4-D) ³ | 94-75-7 | 2.8 ^a | 41 | Perfluorooctanoic acid (PFOA) ⁵ | 335-67-1 | 2.8 ^c |
| 17 | Diethyl phthalate ² | 84-66-2 | 2.4 ^a | 42 | Phenazone ⁶ | 60-80-0 | 0.4 ^a |
| 18 | Diethyl toluamide (DEET) ³ | 134-62-3 | 2.2 ^a | 43 | Simazine ³ | 122-34-9 | 2.2 ^a |
| 19 | Diethylamine (DEA) ² | 109-89-7 | 0.6 ^a | 44 | Sulfamethoxazole ⁶ | 723-46-6 | 0.9 ^a |
| 20 | Diethylene glycol dimethyl ether (diglyme, bis(2-methoxy ethyl)ester) ² | 111-96-6 | −0.4 ^a | 45 | Tolyltriazole ² | 29385-43-1 | NA |
| 21 | Diethylene triamine penta acetic acid (DTPA) ² | 67-43-6 | −4.2 ^b | 46 | Trichloroethene ² | 79-01-6 | 2.4 ^a |
| 22 | Dimethenamid ³ | 87674-68-8 | 2.2 ^a | 47 | Triethylphosphate (ethylphosphate) (TEP) ² | 78-40-0 | 0.8 ^a |
| 23 | Dimethylamine (DMA) ² | 124-40-3 | −0.4 ^a | 48 | Triphenylphosphine oxide (TPPO) ² | 791-28-6 | 2.8 ^a |
| 24 | Diuron ³ | 330-54-1 | 2.7 ^a | 49 | Tris(2-chloroethyl) phosphate (TCEP) ² | 115-96-8 | 1.4 ^a |
| 25 | Ethyl tert-butyl ether (ETBE) ⁴ | 637-92-3 | 1.9 ^b | 50 | Urotropine (methenamine, hexamine) ² | 100-97-0 | −4.2 ^b |

NA not available. Chemical categories: ¹Iodinated contrast media; ²Miscellaneous organic compounds; ³Miscellaneous pesticides; ⁴Oxygenated gasoline additives; ⁵Perfluorinated organic compounds; ⁶Pharmaceuticals.

a log K_{ow} values were derived from US EPA's KOWWIN experimental database.

b log K_{ow} values were calculated with the aid of US EPA's KOWWIN.

c log K_{ow} values were obtained from Krop and de Voogt (2008).

as described by Van Leeuwen (2000) and the WHO (2006). For compounds without a statutory drinking water guideline value, first the Tolerable Daily Intake (TDI) was determined. The point of departure (POD) for calculating the TDI was mostly a chronic LO(A)EL, NO(A)EL, benchmark dose level, maximum tolerated dose (MTD) or lowest effective safe dose. In case only inhalatory toxicity data could be found, a route-to-route extrapolation was carried out according to toxicological methods as described by Stokinger and Woodward (1958). An appropriate safety factor to extrapolate between species (inter-species differences), inter-individual differences (intraspecies differences), exposure route/duration and quality of the data was utilized as part of the TDI calculation (Van Leeuwen and Vermeire, 2007). Secondly, a drinking water equivalent level (DWEL) was calculated by multiplying the TDI

by a typical average body weight of 70 kg and division by a daily water consumption of 2 l. Finally, to account for the fraction of the TDI allocated to drinking water, the DWEL was multiplied by an allocation factor to give the provisional guideline value. In most cases, when there was insufficient exposure information to derive chemical-specific allocation factors, a default allocation factor of 10% was used.

2.4. Evaluation of water-quality data in the context of human health

Of each compound the maximum concentration level reported in surface waters, groundwater and/or drinking water was compared to its (provisional) guideline value and was expressed as a BQ value (concentration in water divided by

Table 2 – Parameters used for derivation of (provisional) drinking water guideline values.

| Compound | Point of departure (POD) | Category ^a | ΣUF ^b | TDI, ADI or RfD (mg/kg bw/d) | (Provisional) guideline value (µg/L) |
|---|---|-----------------------|------------------|------------------------------|--------------------------------------|
| 1,4-Dioxane | POD is an oral slope factor as derived by US EPA (1988a) of 0.011 per mg/kg bw/d from a 110-week study in rats (NCI, 1978). | B | NA | NA | 30 ^d |
| 2,6-Dichlorobenzamide (BAM) | POD is a NOAEL of 4.5 mg/kg bw/d for decreased body weight in both sexes and increased liver weight in males as derived by the Danish EPA (2004) from a study in which dogs were fed BAM in the diet for 2 years (Wilson and Thorpe, 1971), with an uncertainty factor of 300 (100 for inter- and intraspecies variation and 3 for uncertainties in the dataset). | C | 300 | 0.015 | 52.5 |
| 4-Methylbenzenesulfonamide (p-toluenesulfonamide, 4-tolylsulfonamide) | POD is a NOAEL of 300 mg/kg bw/d for reproductive effects (decrease lactation index and litter weight at birth) as derived from a GLP compliant study in which rats were administered 4-methylbenzenesulfonamide via oral gavage for 42 days (OECD/SIDS, 1994), with an uncertainty factor of 400 (100 for inter- and intraspecies variation and 4 for extrapolation to chronic exposure). | D | 400 | 0.75 | 2600 |
| Acetylsalicylate (aspirin, acetylsalicylic acid) | POD is a LOEL of 10 mg/person from a human study as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 20 | 0.007 | 25 |
| Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) | POD is a NOAEL of 32 mg/kg bw/d as derived by the WHO (2005a) from a 26-month toxicity study in rats (study reference unknown). | A | 100 | 0.3 | 900 ^c |
| Amidotriazoic acid (diatrizoic acid) | POD is the highest therapeutic dose of 50 mg/person/d (0.71 mg/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 10 | NA | 250000 |
| Bentazone | POD is a NOAEL of 9 mg/kg bw/d as derived by the WHO (1998) from a 2-year dietary toxicity study in rats (study reference unknown). | A | 100 | 0.1 | 300 ^c |
| Benzene | POD is a risk estimate as derived by the WHO (2003a) from a 2-year gavage study in rats and mice (NTP, 1986). | A | NA | NA | 10 ^{c,d} |
| Benzothiazole | POD is a NOEL of 5.1 mg/kg bw/d as derived by the WHO/JECFA (2003) from a study in which rats were administered benzothiazole in the diet for 90 days (Morgareidge, 1971). Daily observations revealed no treatment related effects in histopathological/haematological parameters, body weight, food consumption and liver/kidney weights. An uncertainty factor of 200 was applied (100 for inter- and intraspecies variation and 2 for extrapolation to chronic exposure). | C | 200 | 0.026 | 90 |
| Benzotriazole (1H-benzotriazole) | POD is a LOAEL of 295 mg/kg bw/d for histological changes in the liver, decreased body weight gain and inflammation of the prostate/uterus as derived by the Dutch Expert Committee for Occupational Standards (DECOS, 2000) from a study in which rats were administered benzotriazole in the diet for 78 weeks (BIBRA Toxicology International, 1995), with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for extrapolation of a LOAEL to a NOAEL). | C | 1000 | 0.295 | 1000 |
| Bis(chloroisopropyl)ether (BCIPE) | POD is a NOAEL of 35.8 mg/kg bw/d as derived by the US EPA (1989) from a 24-month chronic toxicity study in mice (Mitsumori et al., 1979). | B | 1000 | 0.04 | 140 |
| Carbamazepine | POD is a maximum tolerated dose (MTD) of 250 mg/kg bw/d as derived by Snyder et al. (2008) from a 2-year study in rats showing evidence of carcinogenicity (Singh et al., 2005). | B | NA | 0.00034 | 1 |
| Carbendazim | POD is a NOAEL of 2.5 mg/kg bw/d as derived by the WHO/JECFA (1995) from a 2-year study in dogs (Sherman, 1972). | B | 100 | 0.03 | 105 |
| Chloridazon (pyrazon) | POD is a NOAEL of 5.4 mg/kg bw/d for adverse histopathological/haematological changes, decreased food intake, lower body weight gain and higher organ weights (liver, kidney, thyroid gland) as derived from a study in which rats were orally administered chloridazon (method of administration unspecified) for 7 weeks (ECB, 2000b), with an uncertainty factor of 100 (inter- and intraspecies variation). | D | 100 | 0.054 | 189 |
| Clofibric acid | POD is a LOEL of 1 mg/kg bw/d as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007) from an 8-week oral study in humans (Larsen et al., 1994). | B | 100 | 0.01 | 30 |

(continued on next page)

Table 2 (continued)

| Compound | Point of departure (POD) | Category ^a | ΣUF ^b | TDI, ADI or RfD (mg/kg bw/d) | Provisional guideline value (µg/L) |
|---|---|-----------------------|------------------|------------------------------|------------------------------------|
| Dichlorophenoxyacetic acid (2,4-D) | POD is a NOAEL of 1 mg/kg bw/d as derived by the WHO (2003b) from a 1-year study of toxicity in dogs and a 2-year study of toxicity and carcinogenicity in rats (study reference unknown). | A | 100 | 0.01 | 30 ^c |
| Diethyl phthalate | POD is a NOAEL of 750 mg/kg bw/d as derived by US EPA (1988b) from a 16-week toxicity study in rats (Brown et al., 1978). | B | 1000 | 0.8 | 2800 |
| Diethyl toluamide (DEET) | POD is a NOEL of 100 mg/kg bw/d based on clinical signs, reduced haemoglobin/haematocrit levels and histological changes in liver, lymph nodes and uterus as derived by the California Environmental Protection Agency (California EPA, 2000) from a study in which beagle dogs were orally administered DEET (gelatin capsules) for 1 year (Goldenthal, 1994), with an uncertainty factor of 56 (14 for inter- and intraspecies variation and 4 for extrapolation to chronic exposure). | C | 56 | 1.8 | 6250 |
| Diethylamine (DEA) | POD is a LOAEL of 75 mg/m ³ for reduced mean body weights and adverse histopathological effects (lesions of the nasal mucosa) as derived by the scientific committee on occupational exposure limits (SCOEL, 2002) from a study in which rats were exposed to DEA via the inhalatory route for 24 weeks (6.5 h/d, 5d/wk) (Lynch et al., 1986), with an uncertainty factor of 50 (5 for the absence of human data and a NOAEL and 10 for route-to-route extrapolation uncertainties). | C | 50 | 2.14 ^f | 750 |
| Diethylene glycol dimethyl ether (diglyme, bis(2-methoxy ethyl)ester) | POD is a NOAEL 25 mg/kg bw/d for developmental effects (adversely affected implants per liter and decreased weight gain) as derived by the WHO (2002) from a study in which rabbits were administered diglyme via oral gavage for 13 days (NTP, 1987), with an uncertainty factor of 500 (100 for inter- and intraspecies variation and 5 for uncertainties in the dataset). | C | 500 | 0.05 | 175 |
| Diethylene triamine penta acetic acid (DTPA) | POD is a NOAEL of 100 mg/kg bw/d for developmental effects (increased fetal deformations) as derived from a study according to OECD guideline 414 in which rats were administered DTPA (in its sodium form) via oral gavage during day 6–15 of pregnancy (ECB, 2000c), with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for extrapolation to chronic exposure). | D | 1000 | 0.1 | 350 |
| Dimethenamid | POD is a NOAEL of 7 mg/kg bw/d as derived by the WHO/IMPR (2005) from a 24-month study in rats given diets containing racemic dimethenamid (study reference unknown). | B | 100 | 0.07 | 245 |
| Dimethylamine (DMA) | POD is a LOAEL of 19 mg/m ³ for concentration-related lesions in the respiratory/olfactory mucosa as derived by the scientific committee on occupational exposure limits (SCOEL, 1991) from a study in which rats and mice were exposed to DMA via the inhalatory route for 2 years (6 h/d, 5d/wk) (CIIT, 1990), with an uncertainty factor of 50 (5 for the absence of human data and a NOAEL and 10 for route-to-route extrapolation uncertainties). | C | 50 | 0.54 ^g | 190 |
| Diuron | POD is a NOEL of 0.625 mg/kg bw/d as derived by US EPA (1988c) from a 2-year feeding study in dogs (DuPont, 1964). | B | 300 | 0.002 | 7 |
| Ethyl tert-butyl ether (ETBE) | POD is a NOAEL of 500 ppm (29.1 mg/kg bw/d ^h) for testes degeneration as derived from a study in which rats were exposed to ETBE via the inhalatory route for 13 weeks (Medinsky et al., 1999), with an uncertainty factor of 200 (100 for inter- and intraspecies variation and 2 for extrapolation to chronic exposure). | D | 200 | 0.15 | 525 ^e |
| Ethylenediamine tetra acetic Acid (EDTA) | POD is a NOAEL of 250 mg/kg bw/d (190 mg/kg bw/d as the free acid) as derived by the WHO/JECFA (1973) from a 2-year toxicity study in rats (study reference unknown). | A | 100 | 1.9 | 600 ^{b,c} |
| Glyphosate | POD is a NOAEL of 32 mg/kg bw/d as derived by the WHO (2005a) from a 26-month study of toxicity in rats fed technical-grade glyphosate (study reference unknown). | A | 100 | 0.3 | 900 ^c |
| Imidacloprid | POD is a NOAEL of 5.7 mg/kg bw/d as derived by the WHO/IMPR (2001) from a 2-year study of toxicity and carcinogenicity in rats (study reference unknown). | B | 100 | 0.06 | 210 |
| Iohexol | POD is a safe dose of 75 g/person/d (1.07 g/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 10 | NA | 375 000 |

| Chemical Name | Study Description | D | 2100 | 1.9 | 6700 |
|----------------------------------|--|---|------|---------|--------------------|
| Iomeprol (iomeron) | POD is a NOEL of 2 g Iodine/kg bw/d (equal to 4 g iomeprol/kg bw/d) for adverse effects on liver and kidney (non-lipid cytoplasmic vacuolization of hepatocytes and renal tubular epithelium cells) as derived from a study in which dogs were intravenously exposed to iomeprol for 28 days (Morisetti et al., 1994), with an uncertainty factor of 2100 (35 for inter- and intraspecies, 10 for route-to-route extrapolation and 6 for extrapolation to chronic exposure). | D | 2100 | 1.9 | 6700 |
| Iopamidol | POD is a safe dose of 83 g/person/d (1.19 g/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 10 | NA | 415 000 |
| Iopromide | POD is a safe dose of 50 g/person/d (0.71 g/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 10 | NA | 250 000 |
| Isoprotruron | POD is a NOAEL of 3 mg/kg bw/d as derived by the WHO (2003c) from a 90-day study in dogs and a 2-year feeding study in rats (study reference unknown). | A | 1000 | 0.003 | 9 ^c |
| Methyl tert-butyl ether (MTBE) | POD is a NOAEL of 300 mg/kg bw/d as derived by the Dutch National Institute for Health and the Environment (RIVM) (Swarthjes et al., 2004) from a 90-day oral toxicity study in rats (Robinson et al., 1990). | B | 1000 | 0.3 | 9400 ^e |
| Metoprolol | POD is a LOEL of 100 mg/person/d (1.42 mg/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 100 | 0.014 | 50 |
| n-Butylbenzenesulphonamide | POD is a NOAEL of 50 mg/kg bw/d for adverse treatment related macro- or microscopic effects (liver enlargement, hepatocyte hypertrophy, thymic atrophy and lymphocytolysis) as derived from a study according to OECD guideline 407 (GLP compliant) in which rats were administered n-butylbenzenesulphonamide via oral gavage for 28 days (Proviron Fine Chemicals, 2003), with an uncertainty factor of 600 (100 for inter- and intraspecies differences, 6 for extrapolation to chronic exposure). | D | 600 | 0.083 | 292 |
| Nicosulfuron | POD is a NOAEL of 199 mg/kg bw/d as derived from a 2-year study in rats (URL3). | B | 1000 | 0.2 | 700 |
| n-Nitrosodimethylamine (NDMA) | POD is a tumor dose (TD ₀₅ , dose level that causes 5% increase in tumour incidence over the background) of 18 µg/kg bw/d as derived by the WHO (2008) from a detailed 2-year cancer dose-response study in rats (Peto et al., 1991a,b). | A | NA | NA | 0.1 ^{c,d} |
| p,p'-Sulfonyldiphenol | POD is a NOEL of 10 mg/kg bw/d for histopathological effects (hyperplasia of the mucosal epithelium, hypertrophy of hepatocytes), decreased food consumption/body weight gain and increased liver weights as derived from a study according to OECD guideline 421 in which male and female rats were administered p,p'-sulfonyldiphenol via oral gavage for respectively 45 days and from 14 days before mating to day 3 of lactation (Mitsubishi Chemical Safety Institute Ltd, date of study unknown), with an uncertainty factor of 600 (100 for inter- and intraspecies differences, 6 for extrapolation to chronic exposure). | D | 600 | 0.017 | 60 |
| Perfluorooctane sulfonate (PFOS) | POD is a NOAEL of 0.03 mg/kg bw/d as derived by the Scientific Panel on Contaminants in the Food Chain (CONTAM) (EFSA, 2008) from a 182-day study in Cynomolgus monkeys (Seacat et al., 2002). | B | 200 | 0.00015 | 0.5 |
| Perfluorooctanoic acid (PFOA) | POD is a benchmark dose level (BMDL10) of 0.3 mg/kg bw/d as derived by the Scientific Panel on Contaminants in the Food Chain (CONTAM) (EFSA, 2008) from a number of studies in mice and male rats (study references unknown). | B | 200 | 0.0015 | 5.3 |
| Phenazone | POD is a LOEL of 250 mg/person/day (3.57 mg/kg bw/d) as derived by the Dutch National Institute for Health and the Environment (RIVM) (Versteegh et al., 2007). | B | 100 | 0.036 | 125 |
| Simazine | POD is a NOAEL of 0.52 mg/kg bw/d as derived by the WHO (1996) from a 2-year combined chronic toxicity/oncogenicity study in rats (Ciba-Geigy, 1988; unpublished study submitted to WHO). | A | 1000 | 0.52 | 2 ^c |
| Sulfamethoxazole | POD is a NOAEL of 25 mg/kg/d as derived by Schwab et al. (2005) from a 60-week study in rats (Swarm et al., 1973). | B | 200 | 0.13 | 440 |
| Tolytriazole | POD is a NOAEL of 150 mg/kg bw/d for observed mild apathy as derived from a study in which rats were administered tolytriazole via oral gavage for 29 days (Benzotriazoles Coalition, 2001; ECB, 2000a), with an uncertainty factor of 600 (100 for inter- and intraspecies variation and 6 for extrapolation to chronic exposure). | D | 600 | 0.25 | 875 |

(continued on next page)

Table 2 (continued)

| Compound | Point of departure (POD) | Category ^a | ΣUF ^b | TDI, ADI or RfD (mg/kg bw/d) | TDI, ADI or RfD (Provisional) guideline value (µg/L) |
|--|--|-----------------------|------------------|------------------------------|--|
| Trichloroethene | POD is a benchmark dose level (BMDL10) of 0.146 mg/kg bw/d as derived by the WHO (2005b)/Health Canada (2003) from a developmental toxicity study in rats (Dawson et al., 1993). | A | 100 | 0.0015 | 20 ^c |
| Triethylphosphate (ethylphosphate) (TEP) | POD is a NOEL of 335 mg/kg bw/d for fertility effects (effects on litter size) as derived from a study in which rats were administered TEP via the food for a unknown period (OECD/SIDS, 1998), with an uncertainty factor of 600 (100 for inter- and intraspecies variation and 6 for extrapolation to chronic exposure). | D | 600 | 0.56 | 1950 |
| Triphenylphosphine oxide (TPPO) | POD is a NOAEL of 8 mg/kg bw/d for salivation, vomiting, diarrhea, histopathological (liver damage and skeletal muscle atrophy/haematological (elevated GPT, GOT and alkaline phosphatase activities, reduced haemoglobin/haematocrit levels) parameters as derived from a study in which dogs were administered TPPO via the food for 3 months (ECB, 2000d), with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for extrapolation to chronic exposure). | D | 1000 | 0.008 | 28 |
| Tris(2-chloroethyl)phosphate (TCEP) | POD is a NOAEL of 22 mg/kg bw/d for increased relative liver and kidney weights as derived from a study in which rats were administered TCEP via oral gavage for 16 weeks (NTP, 1991), with an uncertainty factor of 1000 (10 for inter- and intraspecies variation and 10 for extrapolation to chronic exposure and uncertainty in genotoxic potential). | D | 1000 | 0.022 | 77 |
| Urotropine (methenamine, hexamine) | POD is a NOAEL of 15 mg/kg bw/d as derived by the WHO/JECFA (1974) from a teratogenicity study (exposure from the fourth to fifty-sixth day after mating) in dogs (Hurni and Ohder, 1973). | B | 100 | 0.15 | 500 |

NA not available.

a Categories: A) statutory drinking water guideline value available; B) established TDI, ADI or RfD available; C) TDI calculated with a established LO(A)EL or NO(A)EL; D) TDI calculated with miscellaneous toxicological information.

b Uncertainty factors.

c WHO drinking water guidelines (WHO, 2006).

d Based on a specific cancer risk level of 10^{-5} .

e The odour-threshold value for drinking water preparation is 15 µg/L for MTBE and ~1 µg/L for ETBE (Swarjes et al., 2004; Van Wezel et al., 2009).

f Using the Stokinger-Woodward approach (Stokinger and Woodward, 1958), a TDI of 150 mg/person/d (2.14 mg/kg bw/d) can be calculated from the 8-h threshold limit value (15 mg/m³) assuming 100% oral/inhalatory absorption and a 8-h total workshift ventilation of 10 m³.

g Using the Stokinger-Woodward approach (Stokinger and Woodward, 1958), a TDI of 40 mg/kg/person/d (0.54 mg/kg bw/d) can be calculated from the 8-hour threshold limit value (3.8 mg/m³) assuming 100% oral/inhalatory absorption and a 8-h total workshift ventilation of 10 m³.

h A TDI of 0.15 mg/kg bw/day can be calculated from the NOAEL (500 ppm = 29.1 mg/kg bw/d) assuming 100% oral/inhalatory absorption, a specific lung retention of 25% and a minute ventilation volume for rat of 45 mL.

guideline value) in order (i) to provide perspective on what the occurrence of emerging contaminants might signify to human health and (ii) to help prioritize further investigations. A BQ value of 1 represents a (drinking) water concentration equal to the (provisional) guideline value. Compounds with a BQ value of ≥ 1 in drinking water may be of potential human health concern if the water were to be consumed over a lifetime period. Compounds with a BQ value ≥ 0.1 in drinking water were identified as those that may warrant further investigation; this is consistent with various US State and Federal practices (Toccalino, 2007). For compounds found in surface waters and groundwater the BQ value threshold to carry out an additional assessment was set at an arbitrary value of ≥ 0.2 , since these source waters are purified in drinking water treatment plants which provides extra safety. Compounds in surface waters/groundwater or drinking water with a BQ value of ≤ 0.2 or 0.1 respectively, are presumed to present no appreciable concern to human health.

3. Results

3.1. Selection of compounds

For only 50 compounds out of the original list, statutory guideline values or useful toxicity and occurrence data could be found. These compounds constitute the final list, which includes compounds from various groups such as iodinated contrast media, pharmaceuticals, oxygenated gasoline additives, perfluorinated organic compounds, miscellaneous organic compounds and pesticides (Table 1). Natural and synthetic steroid hormones such as 17β -estradiol, 17α -ethynylestradiol and estrone were not included in this assessment, as they are removed relatively easily in drinking water purification processes (Nghiem et al., 2004).

3.2. (Provisional) drinking water guideline values

For 10 compounds WHO statutory drinking water guideline values were available and these compounds were classified as category A. For the remaining 40 compounds a provisional guideline value was established with the aid of toxicological data. An established TDI, ADI or RfD was available for 22 compounds (category B). In 7 cases when there was no TDI, ADI or RfD available, an established NO(A)EL or LO(A)EL was used to calculate a TDI and subsequently a provisional drinking water guideline value (category C). For the remaining 11 compounds, miscellaneous toxicological data was used to calculate a TDI and subsequently a provisional drinking water guideline value (category D). As tabulated in Table 2, (provisional) guideline values ranged from 0.0001 mg/L for NDMA to 415 mg/L for the iodinated contrast medium iopamidol. All iodinated contrast media had relatively high provisional guideline values, ranging from 6.7 mg/L (iomeprol) to 415 mg/L (iopamidol). In the cases of MTBE and ETBE, the human health based guideline values were at least one order of magnitude higher than the corresponding odour-threshold based guideline values of respectively 15 $\mu\text{g/L}$ and $\sim 1 \mu\text{g/L}$ (Swartjes et al., 2004; Van Wezel et al., 2009). For two compounds (DMA and DEA) the provisional guideline

values were established by route-to-route extrapolation of inhalatory LOAELs to oral LOAELs. Since benzene was evaluated to be genotoxic/carcinogenic (IARC group I) and NDMA (IARC group 2A) and 1,4-dioxane (IARC group 2B) are respectively suspected non-genotoxic and genotoxic carcinogens, their corresponding (provisional) guideline values are provided as an upper bound lifetime cancer risk to an individual of 10^{-5} , or the odds that one case of cancer would result for every 100 000 persons subjected to continuous exposure over a 70-year lifetime.

3.3. Concentration of compounds in surface waters, groundwaters and drinking water

The maximum concentrations of compounds reported in surface waters and/or groundwaters are summarized in Table 3. Measured maximum surface water concentrations were available for 37 of the 50 compounds in the annual reports of RIWA and ARW. For two compounds (MTBE and clofibric acid) maximum concentrations in Dutch groundwater are reported. For the remaining compounds, the maximum concentration reported in surface waters was taken from other sources (see Section 2.2.3).

The six compounds with the highest reported maximum concentrations in surface waters were EDTA (29 $\mu\text{g/L}$), DTPA (12.2 $\mu\text{g/L}$), p,p'-sulfonyldiphenol (10 $\mu\text{g/L}$), urotropine (10 $\mu\text{g/L}$), 1,4-dioxane (10 $\mu\text{g/L}$) and AMPA (5 $\mu\text{g/L}$), whereas in groundwater a relatively high concentration was found for MTBE (27.3 $\mu\text{g/L}$) showing the environmental relevance of this compound. The highest maximum concentration of iodinated contrast media in surface waters was reported for iomeprol (0.97 $\mu\text{g/L}$).

Table 3 also summarizes the maximum concentrations of compounds reported in drinking water. Data on the occurrence of compounds in drinking water were relatively scarce, and limited to 35 compounds. For 18 compounds, drinking water concentrations were obtained from the Dutch REWAB database and for 17 compounds drinking water concentrations were taken from reports by others. Drinking water concentrations for the remaining compounds could not be found. The highest maximum concentration reported was for EDTA (13.6 $\mu\text{g/L}$), followed by DTPA (9 $\mu\text{g/L}$), metoprolol (2.1 $\mu\text{g/L}$) and BCIPE (1.9 $\mu\text{g/L}$).

3.4. Comparison of compound concentrations to (provisional) guideline values (BQ value)

For all compounds found in surface waters, groundwaters and drinking water the calculated BQ value was < 1 (Table 3). The three compounds exhibiting the highest BQ values (i.e. posing the highest potential human health concern) in surface water are 1,4-dioxane, carbamazepine and PFOS (Fig. 2A). For MBTE and ETBE BQ values of respectively 1.8 and 1.2 can be calculated, when comparing their maximum concentrations reported in surface water to the odour-threshold based guideline values of 15 $\mu\text{g/L}$ and $\sim 1 \mu\text{g/L}$ (not shown in Fig. 2). These BQ values do not indicate a concern for human health per se, but rather indicate that the maximum environmental concentration reported exceeds the odour-threshold. This implies that for MTBE and ETBE

Table 3 – Reported concentrations in surface waters, groundwaters and drinking water and comparison to (provisional) drinking water guideline values expressed as Benchmark Quotient (BQ) values.

| Compound | Surface waters and groundwaters | | | | | Drinking water | | | | |
|---|--|----------|------|---------------------------|--|----------------|------|-----------------------------|--|--|
| | Max conc (µg/L) (number of measurements, year) | Source | Ref | BQ value ^a | Max conc (µg/L) (number of measurements, year) | Source | Ref | BQ value ^a | | |
| 1,4-Dioxane | 10 (NA, 1997) | SW, NL | (4) | 0.3 | 0.5 (NA) | UDW, NL | (4) | 0.02 | | |
| 2,6-Dichlorobenzamide (BAM) | 0.05 (40, 2002-2006) | SW, NL | (11) | 0.001 | 0.23 (14, 2002) | FDW, USA | (10) | 0.004 | | |
| 4-Methylbenzenesulfonamide (p-toluenesulfonamide, 4-tolylsulfonamide) | 0.06 (20, 2005) | SW, NL | (13) | 0.00002 | NA | | | | | |
| Acetylsalicylate (aspirin, acetyl salicylic acid) | 0.065 (NA, 2007) | SW, NL | (15) | 0.003 | 0.12 (12, 2007) | FDW, NL | (15) | 0.005 | | |
| Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) | 5 (499, 2005) | SW, NL | (11) | 0.006 | 1.1 (6, 2001) | FDW, NL | (10) | 0.001 | | |
| Amidotrizoic acid (diatrizoic acid) | 0.63 (189, 2006) | SW, GER | (2) | 0.000003 | 0.25 (6, 2006) | FDW, NL | (10) | 0.000001 | | |
| Bentazone | 0.1 (126, 2007) | SW, NL | (11) | 0.0003 | 0.28 (11, 2006) | FDW, NL | (10) | 0.0009 | | |
| Benzene | 0.74 (116, 2001) | SW, NL | (11) | 0.07 | 0.96 (12, 2005) | TW, NL | (10) | 0.1 | | |
| Benzothiazole | 0.03 (3, 2008) | SW, NL | (6) | 0.0003 | 0.01 (10, 2007) | FDW, NL | (14) | 0.0001 | | |
| Benzotriazole (1H-benzotriazole) | 0.54 (11, 2007) | SW, NL | (11) | 0.0005 | 0.2 (10, 2007) | FDW, NL | (14) | 0.0002 | | |
| Bis(chloroisopropyl)ether (BCIPE) | 2.9 (15, 1984-1985) | GW, NL | (6) | 0.02 | 1.9 (9, 1982-1984) | FDW, NL | (6) | 0.01 | | |
| Carbamazepine | 0.227 (263, 2003) | SW, NL | (11) | 0.2 | 0.03 (2, 2007) | FDW, NL | (15) | 0.03 | | |
| Carbendazim | 1.5 (111, 2006) | SW, BE | (11) | 0.01 | NA | | | | | |
| Chloridazon (pyrazon) | 0.3 (68, 2002) | SW, BE | (11) | 0.002 | NA | | | | | |
| Clofibrac acid | 0.091 (NA, 2007) | BFGW, NL | (15) | 0.003 | 0.14 (2, 2007) | FDW, NL | (15) | 0.005 | | |
| Dichlorophenoxyacetic acid (2,4-D) | 0.2 (34, 2006) | SW, NL | (11) | 0.007 | 0.11 (5, 2002) | TW, NL | (10) | 0.004 | | |
| Diethyl phthalate | 0.9 (8, 2005) | SW, NL | (11) | 0.0003 | NA | | | | | |
| Diethyl toluamide (DEET) | 0.06 (36, 2005) | SW, NL | (11) | 0.00001 | 0.03 (1, 2005) | TW, NL | (10) | 0.000005 | | |
| Diethylamine (DEA) | 0.29 (38, 2007) | SW, NL | (11) | 0.0004 | NA | | | | | |
| Diethylene glycol dimethyl ether (diglyme, bis(2-methoxy ethyl)ester) | 3.64 (11, 2007) | SW, NL | (11) | 0.02 | 0.15 (13, 2007) | UDW, NL | (1) | 0.0009 | | |
| Diethylene triamine penta acetic acid (DTPA) | 12.2 (53, 2005) | SW, NL | (11) | 0.03 | 9 (2, 2001) | FDW, NL | (10) | 0.03 | | |
| Dimethenamid | 0.12 (4, 2005) | SW, NL | (9) | 0.0005 | NA | | | | | |
| Dimethylamine (DMA) | 0.34 (42, 2005) | SW, NL | (11) | 0.002 | NA | | | | | |
| Diuron | 0.68 (386, 2002) | SW, BE | (11) | 0.1 | 0.08 (2, 2005) | TW, NL | (10) | 0.01 | | |
| Ethyl tert-butyl ether (ETBE) | 1.2 (97, 2006) | SW, GER | (2) | 0.002 (1.2 ^b) | NA | | | | | |
| Ethylenediamine tetra acetic Acid (EDTA) | 29 (192, 2005) | SW, NL | (11) | 0.05 | 13.6 (7, 2001) | FDW, NL | (10) | 0.02 | | |
| Glyphosate | 1.2 (291, 2006) | SW, NL | (11) | 0.001 | 0.46 (3, 2006) | TW, NL | (10) | 0.0005 | | |
| Imidacloprid | 0.06 (1, 2007) | SW, NL | (11) | 0.0003 | NA | | | | | |
| Iohexol | 0.5 (180, 2005) | SW, NL | (11) | 0.000001 | 0.06 (1, 2007) | FDW, NL | (15) | 0.000002 | | |
| Iomeprol (iomeron) | 0.97 (172, 2007) | SW, NL | (11) | 0.0001 | 0.01 (1, 2006) | FDW, NL | (10) | 0.000001 | | |
| Iopamidol | 0.714 (188, 2006) | SW, NL | (11) | 0.000002 | 0.1 (6, 2006) | FDW, NL | (10) | 0.000002 | | |
| Iopromide | 0.56 (186, 2004) | SW, NL | (11) | 0.000002 | 0.04 (2, 2007) | FDW, NL | (15) | 0.000002 | | |
| Isoprotruron | 0.31 (256, 2002) | SW, NL | (11) | 0.03 | 0.02 (1, 2004) | TW, NL | (10) | 0.002 | | |
| Methyl tert-butyl ether (MTBE) | 27.3 (14, 2003-2005) | GW, NL | (7) | 0.003 (1.8 ^b) | 1.25 (27, 2006) | FDW, NL | (10) | 0.0001 (0.08 ^b) | | |
| Metoprolol | 0.2 (114, 2006) | SW, NL | (11) | 0.004 | 2.1 (2, 2005) | FDW, NL | (10) | 0.04 | | |
| n-Butylbenzenesulphonamide | 0.78 (300-400, 2004-2006) | SW, NL | (6) | 0.003 | 0.05 (2, 2004) | TW, NL | (13) | 0.0002 | | |
| Nicosulfuron | 0.17 (5, 2007) | SW, NL | (11) | 0.0002 | NA | | | | | |
| n-Nitrosodimethylamine (NDMA) | 0.0071 (38, 2006) | SW, NL | (11) | 0.07 | 0.002 (21, 2007) | UDW, NL | (5) | 0.02 | | |

| | | | | | | | | |
|--|-----------------------|---------|------|--------|----------------------|---------|------|---------|
| p,p'-Sulfonyldiphenol | 10 (300, 2005-2006) | SW, BE | (6) | 0.1 | NA | TW, GER | (12) | 0.04 |
| Perfluorooctane sulfonate (PFOS) | 0.11 (NA, 2008) | SW, NL | (8) | 0.2 | 0.02 (NA, 2005/2006) | TW, GER | (12) | 0.1 |
| Perfluorooctanoic acid (PFOA) | 0.647 (NA, 2005/2006) | SW, GER | (13) | 0.1 | 0.52 (NA, 2005/2006) | FDW, NL | (15) | 0.0002 |
| Phenazone | 0.11 (26, 2005) | SW, NL | (12) | 0.0009 | 0.03 (8, 2005) | FDW, NL | (10) | 0.03 |
| Simazine | 0.13 (124, 2006) | SW, BE | (11) | 0.07 | 0.06 (4, 2004) | FDW, NL | (15) | 0.00007 |
| Sulfamethoxazole | 0.11 (170, 2005) | SW, NL | (11) | 0.0003 | 0.03 (4, 2007) | FDW, NL | (10) | 0.09 |
| Tolyltriazole | 0.29 (11, 2007) | SW, NL | (11) | 0.0003 | NA | FDW, NL | (6) | 0.005 |
| Trichloroethene | 1.35 (206, 2006) | SW, NL | (11) | 0.07 | 1.75 (8, 2005) | FDW, NL | (6) | 0.005 |
| Triethylphosphate (ethylphosphate) (TEP) | 0.189 (25, 2007) | SW, NL | (11) | 0.0001 | NA | FDW, NL | (6) | 0.005 |
| Triphenylphosphine oxide (TPPO) | 0.344 (88, 2003) | SW, NL | (11) | 0.01 | 0.13 (6, 2007) | FDW, NL | (6) | 0.005 |
| Tris(2-chloroethyl)phosphate (TCEP) | 0.29 (8, 2006) | SW, NL | (11) | 0.004 | NA | FDW, NL | (6) | 0.005 |
| Urotropine (methenamine, hexamine) | 10 (NA, 1997-1998) | SW, GER | (3) | 0.02 | NA | FDW, NL | (6) | 0.005 |

Sources: bank-filtrated groundwater (BFGW); groundwater (GW); surface water (SW); finished drinking water (FDW); tap water (TW); unspecified drinking water (UDW). Locations: Belgium (BE); Germany (GER), the Netherlands (NL); United States of America (USA). References: (1) Anonymous data Dutch drinking water companies; URL4; (3) Brauch et al., 2000; (4) ECB, 2002; (5) Kleinneijhuis and Puijker, 2008; (6) KWR internal data (KWR, 2009); (7) De Voogt et al., 2008; (8) Loos et al., 2009; (9) Mout et al., 2007; (10) REWAB database, 2009; (11) RIWA database; URL5 (12) Skutlarek et al., 2006; (13) van Beelen, E.S.E. (HWL, the Netherlands), personal communication; (14) Van Leerdam et al., 2009; (15) Versteegh et al., 2007. NA: Not available; an absence of measured concentrations above the detection limit.

a BQ value: ratio of reported maximum concentration to the (provisional) guideline value (cf. Table 2).

b Based on an odour-threshold value (cf. Table 2).

there is a concern for drinking water production, because consumers will not accept odorous drinking water. The BQ values of the remaining compounds calculated for surface waters and groundwater ranged between 0.1 (p,p'-sulphonylphenol, diuron) and 0.000001 (iohexol). For all iodinated contrast media the concentration in surface waters was at least three orders of magnitude less than the (provisional) guideline value. For drinking water, the BQ values of these compounds were even lower (Fig. 2B). For two compounds (benzene and PFOA) found in drinking water, the BQ value was equal to 0.1 indicating that additional assessments such as establishing trends may be warranted. However, for 15 compounds occurrence data in drinking water were not available and therefore the human health concern associated with drinking water consumption due to presence of any of these compounds remains unknown.

4. Discussion

Rapid new developments in analytical chemistry lead to the detection and quantification of many emerging contaminants in drinking water and its environmental sources (surface water and groundwater). Since toxicological information is often absent, such compounds are a growing concern for drinking water companies and their customers.

The present study attempts to address potential human health concern associated with water containing emerging contaminants. The 50 compounds included in this study represent a broad range of chemical classes for which maximum concentrations in surface waters, groundwater and/or drinking water were obtained in the downstream parts of the Rhine and Meuse basins. The results as presented in Fig. 2 indicate that a substantial margin exists between the (provisional) guideline value and the maximum concentrations of most compounds reported in surface waters, groundwaters and/or drinking water.

The compounds evaluated with a relatively high BQ value (i.e. a high potential human health concern) and a known carcinogenic action are 1,4-dioxane, benzene and NDMA. The (provisional) guideline values for 1,4-dioxane (30 µg/L), benzene (10 µg/L) and NDMA (0.1 µg/L) used in the present study are based on a specific cancer risk level of 10^{-5} . However, when applying a specific risk level of 10^{-6} , as is common practice in the Netherlands, the provisional guidelines value would be 3 µg/L, 1 µg/L and 0.01 µg/L, respectively. This would result in BQ values much higher than the arbitrary thresholds for surface waters and drinking water employed in the present study. This indicates that very low concentrations of these compounds in drinking water could lead to a potential carcinogenic effect, and we conclude that for these compounds it is important to monitor trends in their (environmental) occurrence.

Furthermore, Fig. 2 illustrates that the (provisional) guideline values of the majority of non-genotoxic compounds are at least two orders of magnitude above the Threshold of Toxicological Concern (TTC)-based drinking water target value for non-genotoxic compounds (0.1 µg/L). In addition, the (provisional) guideline values (expressed as a specific risk level of 10^{-6}) of the three compounds with known carcinogenic action (1,4-dioxane, benzene and NDMA) are equal (NDMA) or much higher (1,4-

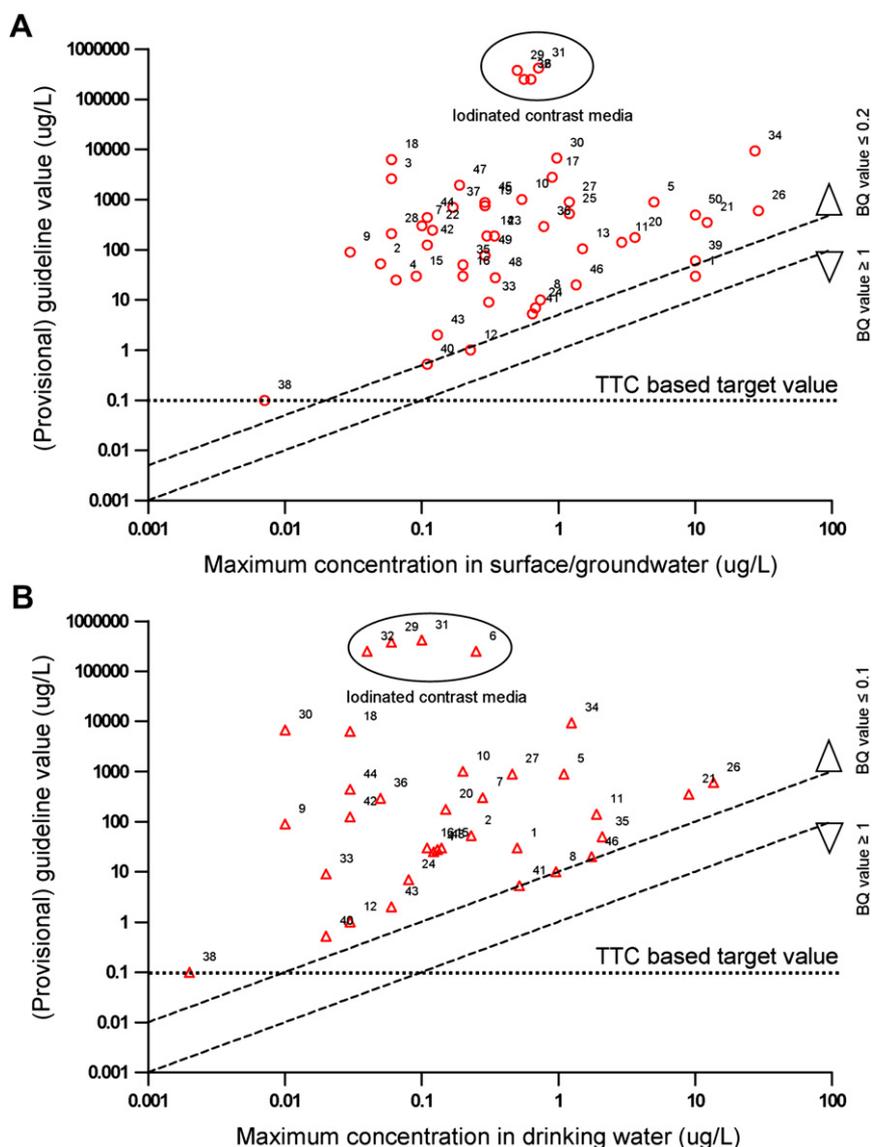


Fig. 2 – Comparison of compound concentrations in (A) surface/groundwaters and (B) drinking water to (provisional) guideline values. Benchmark Quotient (BQ) thresholds are indicated with dashed lines. Threshold of Toxicological Concern (TTC) based target value for non-genotoxic compounds (0.1 $\mu\text{g/L}$) is indicated with a dotted line. Numbers correspond to compounds as tabulated in Table 1.

dioxane and benzene) than the TTC derived target value of 0.01 $\mu\text{g/L}$ for genotoxic compounds. This illustrates that the TTC based drinking water target value may be a conservative value ideally suited for exposure based waiving of compounds for which there is no sufficient toxicological information, which can be followed up by a more data-intensive evaluation.

Two perfluorinated organic compounds were evaluated in the present study. For PFOA in drinking water a BQ value equal to the arbitrary threshold of 0.1 was calculated, whereas for PFOS in surface waters a BQ value of 0.2 was calculated. These persistent compounds are becoming a global problem, and PFOA and PFOS have already been detected in the ng/L range in, e.g. European and Japanese tapwaters (Ericson et al., 2007; Loos et al., 2007; Norimitsu et al., 2004). Recently, Skutlarek et al. (2006) observed at sampling site Neheim (river Ruhr catchment, a tributary of the river Rhine, Germany)

concentrations of PFOA of 0.65 $\mu\text{g/L}$ in Lake Moehne, and 0.53 $\mu\text{g/L}$ in corresponding drinking water, respectively. The authors concluded that water treatment steps may not effectively eliminate perfluorinated compounds to a sufficient extent, although approximately 50% of the waterworks at the Ruhr river are equipped with activated carbon filters. Hence, more research should be devoted to the behavior of perfluorinated organic compounds in drinking water treatment processes.

Several structurally related iodinated contrast media (iopamidol, iohexol, iomeprol and iopromide) were evaluated in the present research. However, their calculated BQ values are much lower than the BQ threshold above which further investigations would be warranted. Iopromide, for example, is a relatively non-toxic compound with a reported safe dose (intravenous) of 50 g/person/d (Versteegh et al., 2007). Despite

the absence of human health effects, these compounds may deserve further attention from an environmental impact point of view. Since environmental sublethal effects of iodinated contrast media to organisms are largely unknown, taken together with high persistence and environmental presence at relatively high concentrations, additional environmental assessments may be necessary.

For compounds with a low (provisional) guideline value as identified in the present study (e.g. carbamazepine), additional environmental monitoring may be warranted to characterize concentrations and to establish trends in their occurrence. As shown by Walraven and Laane (2009), river flow rates may influence contaminant concentrations seasonally, thus resulting in substantially varying BQ values. For example, it can be observed that the riverine concentration of the fuel oxygenate MTBE is highly dependent on the flow of the river Meuse. Similar patterns may occur for other compounds, resulting in (temporarily) exceedance of the BQ threshold.

The evaluation as presented here supports the conclusion that the majority of the selected compounds as found in surface waters, groundwater and drinking water do not pose an appreciable concern to human health. This finding of no adverse effect to human health from exposure to trace quantities of compounds (e.g. pharmaceuticals) in surface waters and/or drinking water is supported by other results reported in the literature. Kingsbury et al. (2008) recently evaluated the potential health effects of 148 organic compounds in source water and finished water. The authors showed that the annual mean concentration of all compounds detected in finished water was less than the established human health benchmarks. Furthermore, Snyder et al. (2008) arrived at the same findings after evaluating human health effects associated with potential drinking water exposure of a suite of 62 indicator pharmaceuticals and potential endocrine disrupting compounds.

Despite the absence of any concern to human health, drinking water remains a major point of consumer concern and some residual uncertainties need further exploration. For example, drinking water guideline values are developed using toxicity information for single compounds. Hence, the long-term cumulative dose-additive or synergistic effects of low concentrations of contaminants co-occurring as mixtures on human health and potentially sensitive sub-populations remain currently unknown. Understanding and implementing of such information is important for the development of future (enforceable) guideline values. Finally, the relatively large data gap on occurrence of compounds in drinking water should compel further research and assessment, especially for those compounds with a low (provisional) guideline value.

5. Major conclusions

- For most compounds evaluated in the present assessment, a substantial margin exists between the (provisional) guideline value and the maximum concentrations in surface waters, groundwaters and/or drinking water.
- The TTC based drinking water target values (0.1 µg/L and 0.01 µg/L for non-carcinogenic compounds, respectively) as proposed earlier are the conservative values they are meant

to be. They are optimally suited to provide exposure based waiving.

- The concentrations in drinking water of compounds such as MTBE, ETBE, 1,4-dioxane, NDMA and benzene should be monitored closely, since their guideline values are easily exceeded.
- Alkylated perfluorinated compounds such as PFOA and PFOS are environmentally persistent compounds and their increasing occurrence in (the sources of) drinking water should be monitored closely.
- For compounds with a very low (provisional) guideline value (e.g. mutagenic and carcinogenic compounds) it is important to better establish trends in their environmental occurrence.
- From a toxicological point of view iodinated contrast media as present in drinking water, such as amidotrizoic acid iopamidol, iohexol and iopromide, are not a direct concern for human health. However, further environmental assessment may be necessary, especially since the sublethal (ecological) effects of these compounds are largely unknown.
- Better understanding of the potential mixture effects of emerging compounds present in drinking water is important for the development of future guideline values.

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