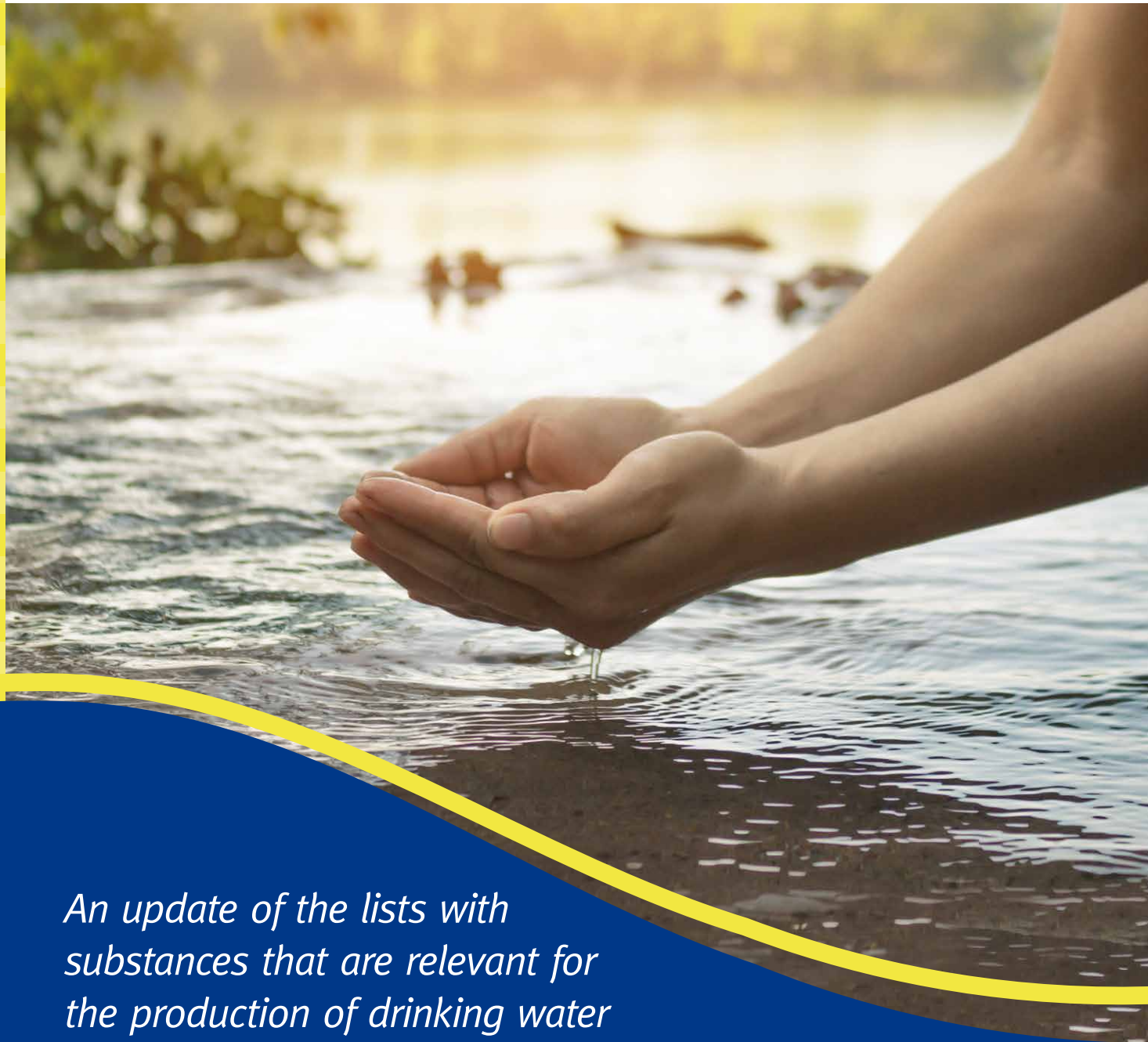
RIWA-Meuse

Drinking water relevant substances in the Meuse



An update of the lists with substances that are relevant for the production of drinking water from the river Meuse

RIWA - Vereniging van Rivierwaterbedrijven

Colophon

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Design	Make My Day, Wormer
Photo	Shutterstock.com Het Waterlaboratorium
Infographics	Studio Ilva, Angeren
ISBN/EAN	9789083075952
Publication date	March 2022

Summary

RIWA-Meuse is the Association of river water works along the Meuse. RIWA-Meuse represents the interests of the drinking water companies in Belgium and the Netherlands that use the River Meuse as a source for their drinking water production. RIWA-Meuse aims for clean water in the river Meuse to guarantee the sustainable supply of impeccable drinking water. For this reason, RIWA-Meuse closely monitors the quality of the Meuse water and, where necessary, advocates improvement of the water quality. In 2007 RIWA-Meuse began to focus on specific substances which are relevant for the production of drinking water.

The goal of this study is to evaluate and update the current lists of (1) drinking water relevant and (2) candidate drinking water relevant substances. Substances are considered as relevant if they fulfil a fixed set of criteria concerning i.e. their detection frequency, occurrence in concentrations above the ERM target value, (potential) removal by water treatment, toxicity, odour/taste threshold and public perception. To check if a substance fulfils the criteria monitoring data has to be available. Substances that are expected to be present in the Meuse, but are not monitored yet, are marked as candidate relevant substances. The criteria used for determining the relevance of substances for drinking water production have evolved over the years.

One of the adaptations in this evaluation is the splitting of the candidate list in A) a list of substances that a are known to be present in the Meuse and are recommended for monitoring with a target analysis and B) a list that contains the substances that will first be monitored with a screening method (since this is more practical quickly screen if a substance is present or not). This means the following lists are now used:

- **List 1** - Drinking water relevant compounds
- **List 2** - Candidate drinking water relevant compounds
  - **A** - Recommended for monitoring with a target analysis
  - **B** - Recommended for monitoring with a screening technique
- **List 3** - No longer drinking water relevant compounds

The evaluation was performed based on measurement data from the monitoring stations and intake points along the Meuse in the period 2016-2020. New candidate drinking water relevant compounds are identified based on a literature study and screening data. This results in the proposal of the lists in **Table S1**.

All associated drinking water companies are recommended to monitor the selected compounds on List 1, 2A and 2B in order to have a detailed insight in the water quality of the river Meuse.

Table S1 – Lists with (candidate) relevant substances (for the Meuse)

List 1	Score	List 2A	Score	List 2B	Score
valsartan	25	dichloromethane sulfonic acid	26	cyanopropanal	26
valsartanic acid	25	ritalinic acid	26	4-amino-3-hydroxybenzoic acid	25
metformin	14	candesartan	24	ethyldimethylcarbamate	25
guanylurea	20	chlorate	21	levothyroxine	25
lamotrigine	20	fluconazole	20	toluenesulfonamide (ortho)	25
dibromoacetic acid	19	oxipurinol	20	10-hydroxy-amitriptyline	24
1,4-dioxane	18	1,2,4-triazole	14	β-asarone	24
hydrochlorothiazide	15	fexofenadine	14	kojic acid	20
melamine	14	N-acetyl-4-aminoantipyrine	14	adamantan-1-amine	19
tramadol	14	4-aminophenol	13	gliclazide	19
cyanuric acid	14	4-mesyl-2-nitrotoluene	13	gamma-cyhalothrin	15
metolachlor	14	bisphenol-F	13	benzovindiflupyr10	
diethylenetriaminepentaacetic acid (DTPA)	13	methylglycindi acedic acid (MGDA)	13	isofetamid	10
ethylenediaminetetraacetic acid (EDTA)	13	1,3-di-o-tolylguanidine	12	mefentrifluconazole	10
N-formyl-4-aminoantipyrine	13			oxathiapiprolin	10
nitriloacetic acid (NTA)	13			pyriofenone	10
terbuthylazine	13			toluenesulfonamide (para)	10
benzothiazole	13			cyanoguanidine	8
bromate	12			p-toluenesulfonic acid	8
di-n-butyltin	12				
ketoprofen	12				
monobromoacetic acid	12				
naproxen	12				
prosulfocarb	12				
glyphosate	11				
aminomethylphosphonic acid (AMPA)	11				
chloridazone-desphenyl	11				
diisopropyl ether (DIPE)	10				
trifluoroacetic acid	10				
sulfamic acid	10				
fluoride	N/A				
PFAS (group of 20 individual substances)	N/A				

Abbreviatons

4-AAA 4-Acetylaminoantipyrine
4-FAA 4-Formylaminopyrine
ADI Acceptable daily intake
AMPA Aminomethylphosphonic acid
AQZ Aqualab Zuid

BPA Bisphenol A
BPF Bisphenol F
BQ Benchmark Quotient
BTO Bedrijfstakonderzoek (Joint Research)

CALUX Chemical Activated Luciferase gene eXpression
CTGB Dutch Board for the Authorisation of Plant Protection Products and Biocides

DDD Daily Defined Dose
DIPE Diisopropylether
DNEL Derived no effect level
DTPA Diethylenetriaminepentaacetic acid
DWB Drinkwaterbesluit

EC European Commission
ECHA European Chemicals Agency
EDMC Ethyl dimethyl carbamate
EDTA Ethylenediaminetetraacetic acid
EFSA European Food Saftey Authorization
ERM European River Memorandum

HWL Het Waterlaboratorium

Kow Octanol/water partition coefficient
KWR KWR Watercycle Research Institute

LC Liquid chromatography
LOD Limit of detection
LOQ Limit of quantification
LOTD Lowest oral therapeutic dose

Max Maximum concentration in the Meuse in 2016-2020

NOAEL No observable adverse effect level
NSAID Nonsteroidal anti-inflammatory drug
NTA Nitrilotriacetic acid

OEHHA Office of Environmental Health Hazard Assessment

PFAS Poly- and perfluoroalkyl substances
PFOA Perfluorooctanoic acid
pGLV Provisional drinking water guideline value
PMOC Polar mobile organic compounds
PMT Persistent, mobile and toxic

REACH Registration, Evaluation, Authorisation and Restriction of Chemicals
RIVM Rijksinstituut voor Volksgezondheid en Milieu (Dutch Institute for Health and Environment)
RIWA Association of River Waterworks
RWS Rijkswaterstaat (Dutch Directorate-General for Public Works and Water Management)

SVHC Substance of very high concern

TDI Tolerable daily intake
TFA Trifluoroacetic acid
TTC Threshold of Toxicological Concern
TWI Tolerable weeky intake

UBA Umweltbundesamt (German Environment Agency)
US EPA United States Environmental Protection Agency

VP Vapour pressure
vPvM Very persistent, very mobile

WFD Water Framwork Directive
WHO World Health Organization

Contents

1

Background

In 2007 RIWA-Meuse began to focus on specific substances which are relevant for the production of drinking water. Relevant in the sense that these substances have the potential of ending up in drinking water after going through a natural treatment process; a situation which is clearly undesirable. The reason behind this approach was article 7.3 of the Water Framework Directive 2000/60/EC (WFD), which states:

"Member States shall ensure the necessary protection for the bodies of water identified with the aim of avoiding deterioration in their quality in order to reduce the level of purification treatment required in the production of drinking water. Member States may establish safeguard zones for those bodies of water."

The WFD sets European environmental quality standards (EQS) for Priority Substances and Priority Hazardous Substances in order to achieve good chemical status of water bodies. For each river basin additional standards can be set for specific substances which hinder reaching good chemical and good ecological status. As RIWA-Meuse felt this was insufficient, it started looking for a framework that helps setting the target on reducing the level of purification treatment required in the production of drinking water. River water companies had already published several memoranda in which they published target values that permit sustainable production of drinking water with basic natural treatment methods. By determining which substances disallow this benchmark, RIWA-Meuse thereby focused on their emissions. In the beginning these substances were called 'threatening the drinking water function of the river Meuse'.

In 2007 a total number of 16 substances were classified as 'threatening' and 34 as 'potentially threatening' (Van den Berg et al., 2007). After an update in 2009, a number of 19 substances were classified as 'threatening' and again 34 as 'potentially threatening' (Van den Berg, 2009). Due to the term 'threatening' being deemed as having a severe connotation, in particular by several parties in the International Meuse Commission, as of 2011 the classification was renamed 'substances which are relevant for the production of drinking water from the river Meuse' or 'drinking water relevant substances' for short. In 2011 a total number of 19 substances were classified as 'drinking water relevant' and this was also the first time they were ranked by relevance (Fischer et al., 2011). Likewise, 23 substances were classified as 'potential drinking water relevant' based on 13 measurements per year. Another 30 substances were also classified as 'potential drinking water relevant' based on 4 measurements per year.

During an evaluation in 2015, a number of 28 substances were classified as 'drinking water relevant' and 34 as 'candidate drinking water relevant' which is the new name for what previously was called 'potential drinking water relevant' (Van der Hoek et al., 2015). For the first time also, a list was drawn of 53 'no longer drinking water relevant substances'. After the previous evaluation in 2018, the list of drinking water relevant substances now consists of 33 chemical substances (Van der Velden-Slootweg and Bannink, 2018). A number of 15 substances were classified as 'candidate drinking water relevant' and the list of 'no longer drinking water relevant substances' contains 82 chemical substances.

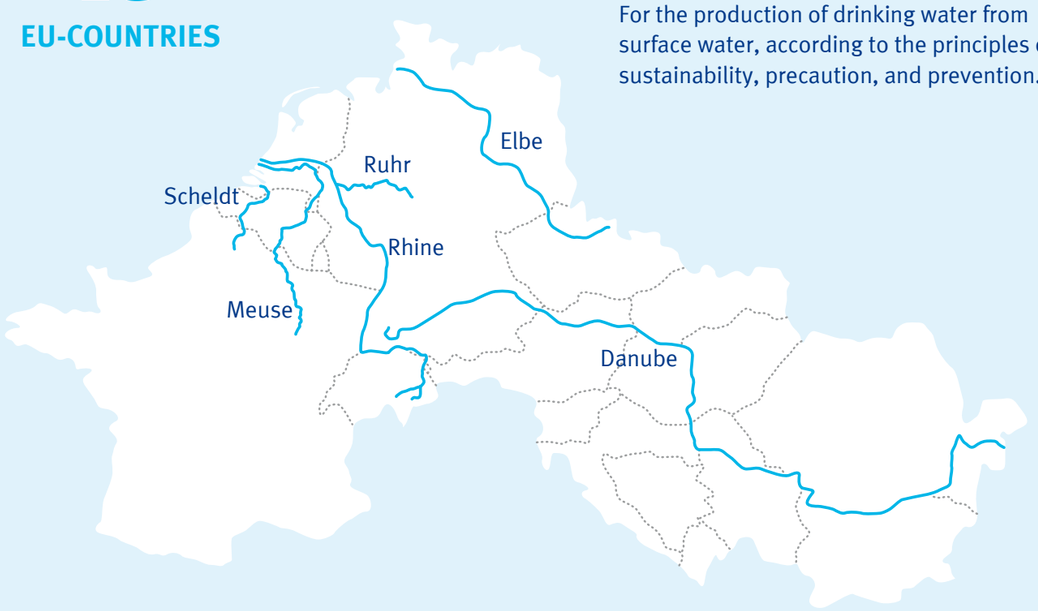
The criteria used for determining the relevance of substances for drinking water production have evolved over the years. The selection criteria are described in paragraph 2.1.

Target Values of the European River Memorandum

Drinking water companies from the river basins of the Meuse, Rhine, Danube, Elbe, Ruhr and Scheldt have the European River Memorandum (ERM) drawn up in order to use surface water for the production drinking water. Surface water that meets the ERM Target Values can be used sustainably to produce drinking water, which can be prepared using natural purification methods.

EUROPEAN RIVER MEMORANDUM

18
EU-COUNTRIES

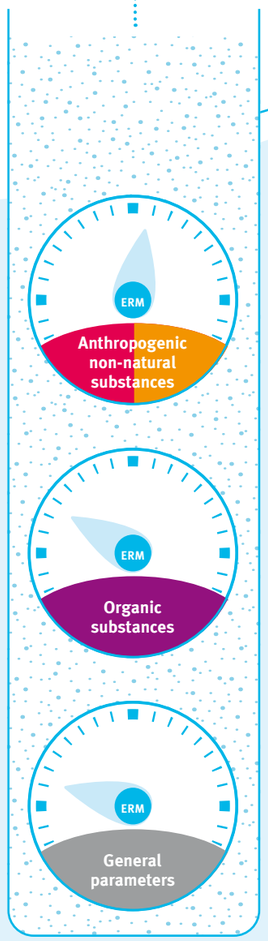


COMMON STRATEGY AND VISION

For the production of drinking water from surface water, according to the principles of sustainability, precaution, and prevention.

Important principles

- Drinking water supply has a priority above other uses
- Sustainable management of water resources
- Emphasis on the prevention and protection of water bodies
- Enforcing responsibility for the discharge of substances
- Provide insight into (potentially) harmful substances



TARGET VALUES

- Anthropogenic non-natural substances
- Organic substances
- General parameters

RIWA-Meuse

WATER QUALITY ASSESSMENT

Water quality indicators for

170
DRINKING WATER COMPANIES

188
MILLION CUSTOMERS

2

Methodology

2.1 Ranking methodology

To define whether a substance is relevant to produce drinking water using the Meuse as a source, a set of criteria was defined which the substance should meet. These criteria make it possible to determine objectively whether a component is relevant. However, it should be stated that in exceptional cases a substance can be added or removed based on well founded arguments (expert judgement) since it is impossible to capture all arguments to indicate a substance as "relevant" in criteria.

The defined criteria have the following characteristics:

- The measured concentrations
- The frequency of detection
- The distribution of the substance in the Meuse catchment area
- Recent occurrence
- The toxicological properties of the substance
- The (potential) degree of removal of the substance during the water treatment process
  The last two characteristics are used to calculate an individual substance score
  (see Appendix REF _Ref80608293 \r \h I.1)

Figure 1 on page 16-17 shows a schematic representation of the flow scheme that was followed for the evaluation of the substances.

It is only possible to include substances on List 1 in case monitoring data for the Meuse is sufficiently available. This is the reason that List 2 was introduced in 2015: on this list all substances could be placed that, based on various sources (literature, screening data, monitoring data from other parties, data on usage), are expected to be a drinking water relevant substance for the Meuse. When enough monitoring data is collected, it can be evaluated if the substances should be placed on List 1.

One of the issues encountered in practice is that analytical techniques are not always available to monitor the candidate substances. Developing a new method can be costly in terms of money and time. Especially when the concentration range of a candidate substance is uncertain, it is a difficult decision whether it is worth the effort to develop an analytical method.

The relatively new implementation of (target) screening techniques based on liquid chromatography (LC) provides a practical solution to this issue: these substances are expected to be present in the river Meuse, but in an unknown concentration range, can initially be added to the target screening database. In this way it is possible to follow whether these substances may or may not be detected in the surface water and drinking water. If the screening data shows that the substance might be relevant, a target analyse can be developed subsequently. The substance can then be monitored in a quantitative manner, which makes it possible to determine if the substance should be included on List 1.

The methodology has therefore been adapted by adding an additional list for candidate substances for which it is recommended to follow them with a screening technique.

It can happen that the parent substance as well as (one of) its metabolite(s) are placed on List 1 and/or 2. As a rule the parent substance and the metabolite will be coupled together and placed on one list. Having both the monitoring data of the parent substance and its relevant metabolite available helps to demonstrate that the use of a certain parent substance causes problems when it degrades in a persistent metabolite (Van der Hoek et al., 2015).

For the lists the following monitoring frequencies are maintained:
List 1: **13 times** a year for **5 years**
List 2a: **13 times** a year for **1 year**
List 2b: **13 times a year** via **targeted screening**
List 3: need for monitoring decided by drinking water companies individually

Since the last update in 2018, some adaptations have been made to ranking methodology. For the calculation of the substance score the criterion "public perception" was taken into account (Fischer et al., 2011; Van der Hoek et al., 2015; Van der Velden-Slootweg and Bannink, 2018). If the substance belonged to one of the specific categories "pharmaceutical", "pesticide", "hormone", or "hormone disruptor", it was considered harmful to the public perception of the drinking water consumers and 3 points were awarded. The idea behind this criterion was that consumers would be extra concerned about the presence of substances that are designed to be biologically active and therefore, their presence is even more undesirable compared to other less toxic substances. In practice this however, resulted in a bias towards these categories, because they were already given a higher score based on their toxicity. In addition, industrial substances are also seen as undesirable substances, especially if they have harmful characteristics like the perfluorinated substances (PFAS). Therefore, substances no longer receive a score for public perception.

On the other hand, substances that are detected in concentrations that are not relevant based on the benchmark quotient (BQ)[1], can still be relevant for drinking water companies since the concentrations exceed the legal drinking water standard. This is for example the case for AMPA and glyphosate. For these substances the drinking water companies need an exemption to use the surface water as source for the production of drinking water. Therefore, it remains important to keep drawing attention to the undesirability of the presence of these substances in sources of drinking water. Substances that exceed a legal drinking water standard are allocated 3 points in their score.

Another issue that was encountered in the last updates was that there was no measured concentration available for the candidate substances, which made it difficult to calculate a score for toxicity. In this update estimated concentrations of 1 or 10 µg/L are used to calculate a BQ and score for toxicity. These estimated concentrations are based on literature or monitoring data and give an indication if the substance could form a risk based on the BQ based on its (provisional) drinking water guideline value (pGLV) and the estimated virtual concentration.

Listing drinking water relevant substances

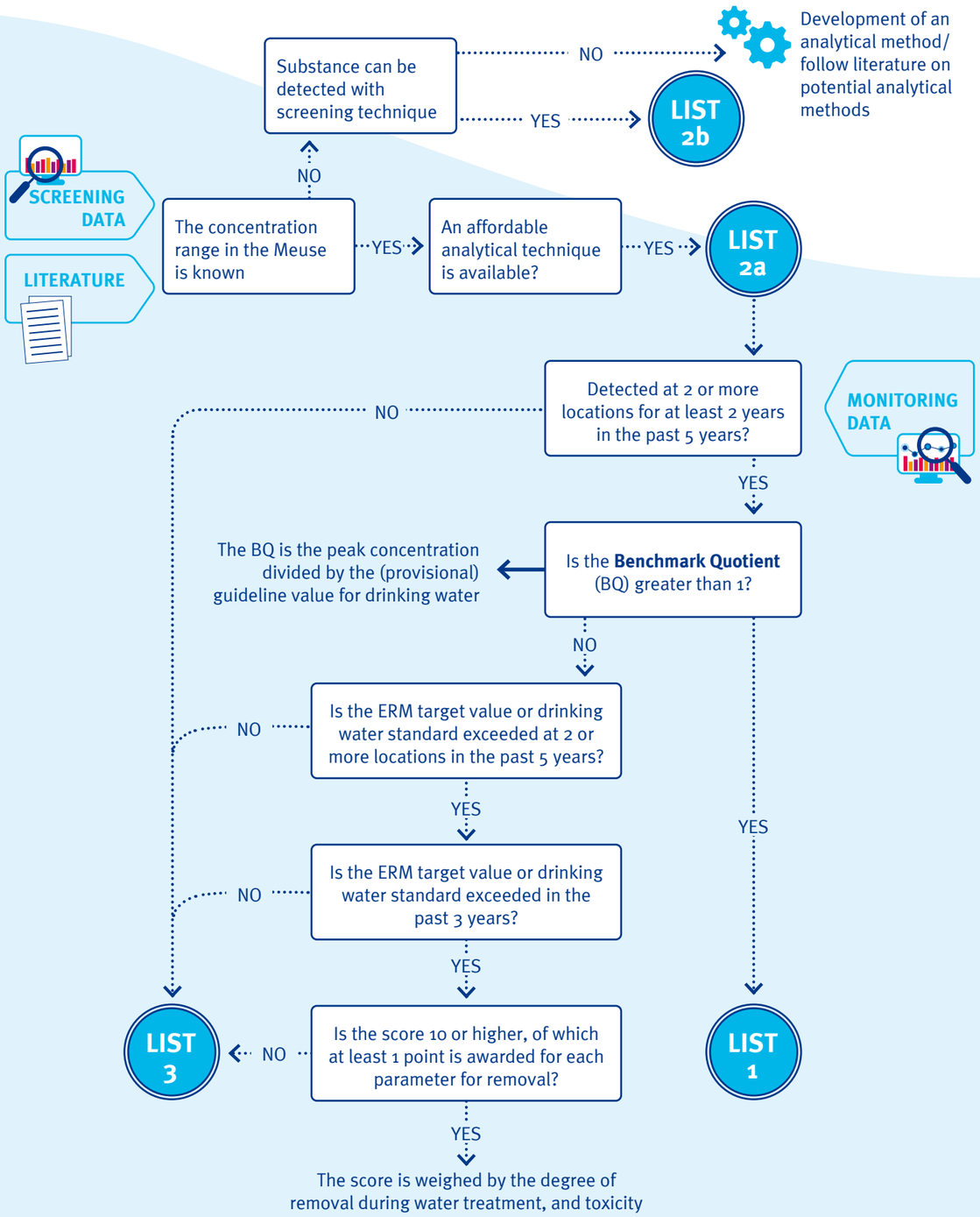


Figure 1 A schematic overview of the ranking scheme used to establish the list of drinking water relevant substances

The specific criteria for each list:

LIST 1 DRINKING WATER RELEVANT SUBSTANCES

1. The substance was detected at two or more RIWA Meuse monitoring stations or intake points in the last 5 years (for a minimum of two years), with a frequency of at least 7% of the measurements[1] *and*
2. The substance was found to exceed ERM target values or the Drinking Water Standards from the Dutch Drinking Water Regulation on at least two different RIWA Meuse monitoring stations or intake points in the past 5 years (taking into account possible removal by conventional treatment), with a frequency of at least 1% of the measurements *and*
3. The substance was found to exceed the drinking water standard or the ERM target value used by the drinking water companies, at least once in the past 3 years *and*
4. The total score of the substance has to be 10 or higher, of which at least 1 point is awarded for each parameter defining the substance removal (polarity, volatility, and biodegradability) (the exact calculation of the score is explained in Appendix I.1).

If the benchmark quotient of the substance is 1 or higher, the substance is considered drinking water relevant and criteria 2, 3, and 4 can be neglected.

LIST 2a CANDIDATE SUBSTANCES FOR QUANTITATIVE MONITORING

1. The substance is present in the river Meuse at concentrations well above the ERM target value *or*
2. The concentration of the substance is expected to increase due to increased use in the catchment area in the near future (e.g. due to a change in usage of pesticides) (based on expert judgement) *and*
3. The substance can be monitored with an affordable measuring technique with a reasonable limit of detection.

LIST 2b CANDIDATE SUBSTANCES FOR SCREENING

1. The substance has undesirable properties for the production of drinking water and is expected to be present in the river Meuse (based on research), but the concentrations are unknown *and*
2. The substance can be detected with an available targeted screening technique and can be added to the database.

List 3 contains all substances that are completely evaluated, but do not or no longer fulfil the criteria. This list is kept in order to secure the information with regard to the evaluation of these substances and to avoid duplication of efforts during a following evaluation.

LIST 3 NEED FOR MONITORING DECIDED BY DRINKING WATER COMPANIES INDIVIDUALLY

Former List 1 and 2 substances which do not meet the criteria of List 1 in the past 5 years.

*1 If the substance is monitored more than 13 times per year, it has to be detected at two or more RIWA Meuse monitoring stations with a frequency of at least 7% of the measurements per year. This criterion is equivalent to the criterion requiring that the substance with a monitoring frequency of 13 times a year, is detected at least once a year.

Drinking water relevant substances

200.482
measurements

screening

1.356
substances

literature review

30
substances*

selection based on

- Concentration
- Frequency of Detection
- Toxicity
- Purification Requirement
- Expert judgement

evaluation + recommendations

LIST 1 **DRINKING WATER RELEVANT SUBSTANCES**

Industrial compounds and consumer products

- 1,4-Dioxane
- Melamine
- Cyanuric acid
- Diethylenetriaminepentaacetic acid (DTPA)
- Ethylenediaminetetraacetic acid (EDTA)
- Nitriloacetic acid (NTA)
- Benzothiazole
- Bromate
- Di-N-butyltin
- Aminomethylphosphonic acid (AMPA)
- Diisopropyl ether (DIPE)
- Trifluoroacetic acid
- Sulfamic acid
- Fluoride
- PFAS*

Pharmaceuticals and endocrine disrupting chemicals (EDC's)

- Valsartan
- Valsartanic acid
- Metformin
- Guanylurea
- Lamotrigine
- Hydrochlorothiazide
- Tramadol
- N-Formyl-4-aminoantipyrine
- Ketoprofen
- Naproxen

Pesticides, biocides and their metabolites

- Dibromoacetic acid
- Metolachlor
- Terbuthylazine
- Monobromoacetic acid
- Prosulfocarb
- Glyphosate
- Aminomethylphosphonic acid (AMPA)
- Chloridazone-desphenyl

* PFAS is a group of substances

For the lists the following monitoring frequencies are maintained:

LIST 1 **13x a year for 5 years**

LIST 2a **13x a year for 1 year**

LIST 2b **13x a year via targeted screening**

LIST 3 **need for monitoring decided by drinking water companies individually**

+

evaluated every 3 years

LIST 2a — CANDIDATE SUBSTANCES FOR QUANTITATIVE MONITORING

Industrial compounds and consumer products

- Dichloromethane sulfonic acid
- 1,2,4-Triazole
- 4-Aminophenol
- 4-Mesyl-2-nitrotoluene
- Bisphenol-F
- Methylglycindi acedic acid (α-ADA, MGDA)
- 1,3-Di-o-tolylguanidine

Pharmaceuticals and endocrine disrupting chemicals (EDC's)

- Ritalinic acid
- Candesartan
- Fluconazole
- Oxipurinol
- Fexofenadine
- N-acetyl-4-aminoantipyrine

Biocide

- Chlorate

LIST 2b — CANDIDATE SUBSTANCES FOR SCREENING

Industrial compounds and consumer products

- Ccyanopropanal
- 4-Amino-3-hydroxybenzoic acid
- Ethyldimethylcarbamate
- Toluenesulfonamide (ortho)
- Kojic acid
- Adamantan-1-amine
- Toluenesulfonamide (para)
- Cyanoguanidine
- P-toluenesulfonic acid

Pharmaceuticals and endocrine disrupting chemicals (EDC's)

- Levothyroxine
- 10-Hydroxy-amitriptyline
- β-asarone
- Adamantan-1-amine
- Gliclazide

Pesticides

- Gamma-cyhalothrin
- Benzovindiflupyr
- Isofetamid
- Mefentrifluconazole
- Oxathiapiprolin
- Pyriofenone

LIST 3 — NEED FOR MONITORING DECIDED BY DRINKING WATER COMPANIES INDIVIDUALLY

Industrial compounds and consumer products

- 1,2-Benzisothiazol-3(2H)-one
- 1,3-Diphenylguanidine
- 1H-Benzotriazole
- 2,2,6,6-Tetramethyl-4-oxopiperidinonoxy
- 2,3,3,3-Tetrafluoro-2-(heptafluorpropoxy) propanoate (GenX substance)
- 2'-Aminoacetophenone
- 3,5,6-Trichloro-2-pyridinol (TCP)
- 4-Methylbenzotriazole
- 4-n-Nonyl phenol
- Acesulfame-K
- Acetone
- AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline)
- Benzo(a)pyrene
- Bis(2-chloroisopropyl) ether
- BPS (4,4'-sulfonyldiphenol)
- Caffeine
- Diglyme (bis(2-methoxyethyl)ether)
- Dimethyldisulfide
- ETBE (ethyl-tertiairy-butyl-ether)
- Ethyl sulphate
- Galaxolide (HHCB)
- Hexa(methoxymethyl)melamine
- Methenamine/urotropine/hexamine
- Methoxymethyltriphenylphosphonium
- MTBE (methyl-tert-butylether)
- Musk (ketone)
- Musk (xylene)
- NDMA (nitrosodimethylamine)
- O-desmethylvenlafaxine
- Phenanthrene
- Pyrazole
- Sucralose
- Surfynol 104
- TBP (tributylphosphate)
- TCEP (tris(2-chloroethyl) phosphate)
- TCPP (tri-(2-chloroisopropyl) phosphate)
- Tetrachloroethene
- Tetrahydrofuran
- Tolyltriazole
- Tribromomethane
- Trichloroacetic acid (TCA)
- Trichloroethene
- Trichloromethane
- Trifluoromethanesulfonic acid (F3-MSA)
- Triisobutyl phosphate
- Triphenylphosphine oxide (TPPO)
- Vinylchloride

Pharmaceuticals and endocrine disrupting chemicals (EDC's)

- 1,3-Diethyldiphenylurea
- 10,11-Dihydro-10,11-dihydroxycarbamazepine
- Acetaminophen (paracetamol)
- Amidotrizoic acid
- Amoxicillin
- Anti-androgenic activity (expressed in flutamide-equivalents)
- Aspirin (acetylsalicylic acid)
- Azelaic acid
- Barbital
- BBP (butylbenzylphtalate)
- Bisphenol A
- Carbamazepine
- Cetirizine
- Ciprofloxacin
- Citalopram
- Clarithromycin
- Clindamycin
- DBP (dibutyl phthalate)
- DEP (diethyl phthalate)
- DIBP (di-(2-methyl-propyl)phthalate)
- Diclofenac
- Erythromycin
- Estrogenic activity (expressed in 17β-estradiolequivalents)
- Estrone
- Gabapentin
- Glucocorticoid activity (expressed in dexamethasone-equivalents)
- Ibuprofen
- Iohexol
- Iomeprol
- Iopamidol
- Iopromide
- Ioxaglic acid
- Ioxitalamic acid
- Irbesartan
- Lincomycin
- N-butylbenzenesulphonamide
- Pentobarbital
- Phenazone
- Phenobarbital
- Salicylic Acid
- Sotalol
- Sulfamethoxazole
- Telmisartan
- Triamcinolonehexacetonide
- Venlafaxine
- Vigabatrin

Pesticides, biocides and their metabolites

- 2-(Methylthio)benzothiazole
- 2,4-D (2,4-dichlorophenoxyacetic Acid)
- BAM (2,6-dichlorobenzamide)
- Carbendazim
- Chloridazon
- Chlorotoluron
- Dimethenamid
- Diuron (DMCU)
- DMSA (N,Ndimethylaminosulfanilide)
- Isoproturon
- MCPA (4-chloro-2-methylphenoxyacetic acid)
- Mecoprop (MCPP)
- Metazachlor
- Metazachlor-ethane sulfonic acid
- Metazachlor-oxanilic acid
- Methyl-desfenylchloridazon
- Metolachlor-ethane sulfonic acid
- N,N-dimethylsulfamid (DMS)
- Nicosulfuron
- Oxadiazon
- Sebuthylazine
- Thiabendazole
- Triflusulfuron-methyl

2.2 Data collection

2.2.1 Monitoring data

The monitoring data of substances was obtained from the RIWA Meuse database. This database is assembled using data provided by drinking water companies and water management agencies located near the Meuse (Figure 2). The monitoring stations are shown in Table 1. For this evaluation data is used from the period 2016-2020.

Table 1 - RIWA monitoring stations located near the Meuse, in order of downstream appearance

	Monitoring station/intake point	Abbreviation	Drinking water company / water management agency
1	Tailfer	TAI	Vivaqua
2	Namêche	NAM	Water-link
3	Liège/Luik	LUI	Water-link
4	Eijsden	EYS	Rijkswaterstaat Water, Verkeer en Leefomgeving
5	Roosteren	ROO	NV Waterleiding Maatschappij Limburg
6	Heel	HEE	NV Waterleiding Maatschappij Limburg
7	Brakel	BRA	Dunea
8	Heusden	HEU	Dunea
9	Keizersveer	KEI	Evides NV/WBB
10	Haringvliet/Stellendam (combined)	HAV/STE	Evides NV

2.2.2 Substance information

To rank substances in order of increasing relevance for the drinking water function of the river Meuse, the substances were scored based on following properties:

- Toxicity (benchmark quotient)
- Removal by water treatment (polarity, volatility, biodegradability)
- Odour/taste threshold

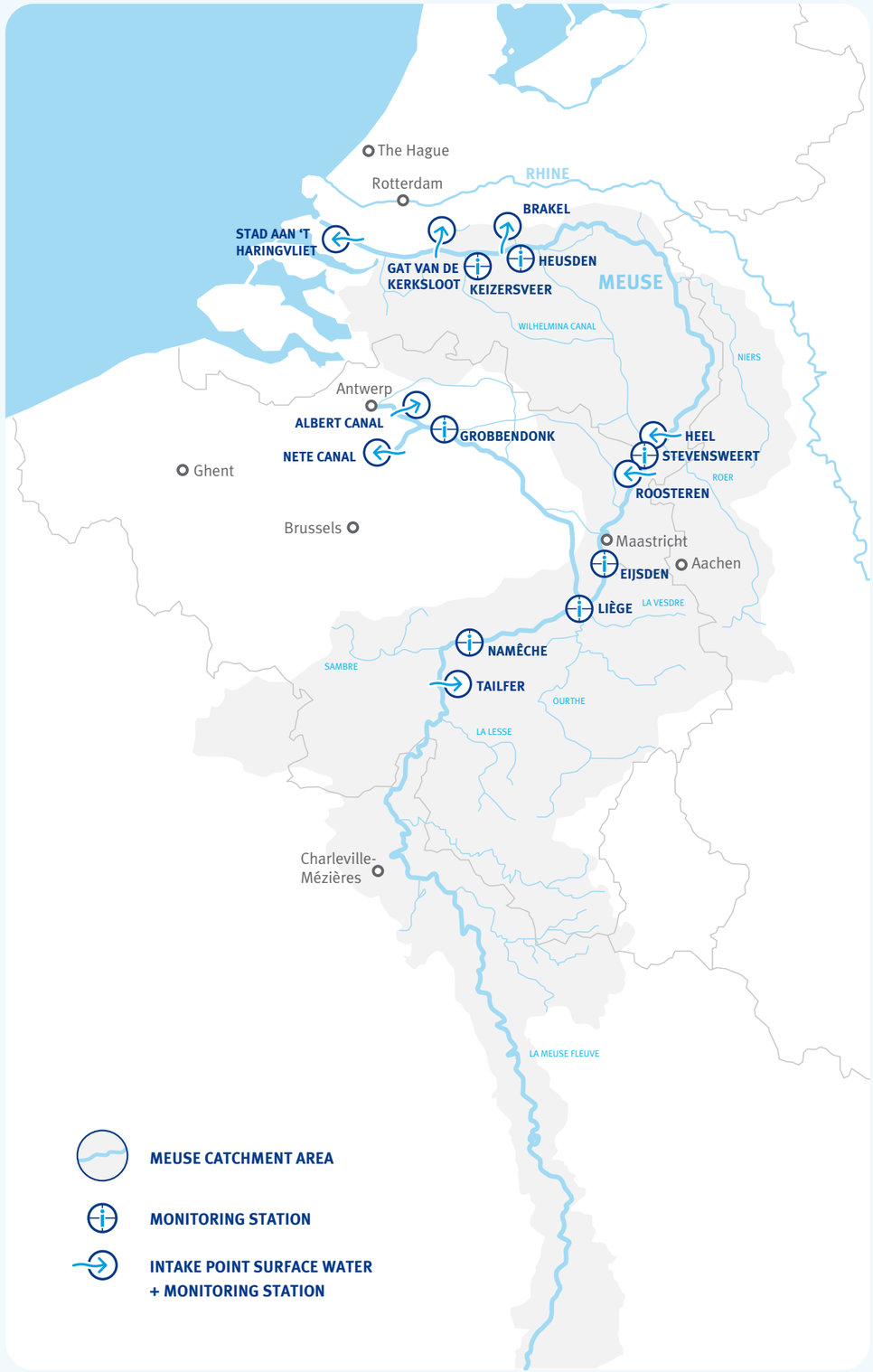
The scoring system is described in Appendix I.1, and explained in detail in the 2011 RIWA Meuse report (Fischer et al., 2011).

For the calculation of a benchmark quotient the maximum concentration in the surface water is compared to a (provisional) drinking water guideline value (pGLV) that is based on toxicity data. Most pGLVs were taken or calculated from the following sources:

- Indicative pGLV's derived by the Dutch National Institute for Public Health and the Environment (RIVM). These pGLV's can be found on the RIVM website https://rvszoeksysteem.rivm.nl/
- Guidelines for Drinking-water Quality, Fourth Edition (WHO, 2017)

For substances that did not have a pGLV yet, toxicity data was collected from risk assessment reports prepared by official institutes like the European Food Safety Authority (EFSA), Joint Expert Committee on Food Additives (JECFA), United States Environmental Protection Agency (US EPA) and Canada Health (Canadian federal institute of Health). If an official risk assessment was not found, toxicity data were collected from the REACH registration files (https://www.echa.europa.eu/nl) or from literature.

Figure 2



For pharmaceutical residues the defined daily dose (DDD) was used to calculate a pGLV in case toxicity data were not available. Based on these toxicity data, a pGLV was calculated as described in Appendix I.1.

If neither toxicity data or a DDD were available the threshold of toxicological concern (TTC) was used (Kroes et al., 2004). De TTC-value is a threshold value for the exposure level of all chemicals below which an adverse effect to human health is not expected. For most substances the TTC-value is 0.1 µg/L.

Information needed to estimate the removal by water treatment was either collected from the REACH registration files; the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) or from the program EPI Suite™, v4.11 (https://www.epa.gov/tsca-screening-tools). It concerns these parameters:

- The octanol/water partition coefficient (Log K_{ow}) as an indicator of polarity. The log K_{ow} was obtained as an experimental value or estimated using “KOWWIN v1.68 Log Kow estimate” in EPI SuiteTM.
- The vapor pressure of the substance as an indicator of volatility. The vapor pressure was obtained as an experimental value or estimated using the “mean vapor pressure of Antoine & Grain methods” in EPI Suite™.
- The biodegradability was derived from estimations using the “BioWIN3 Ultimate Survey Model” in the EPI Suite™.

2.3 Literature review

To select candidate drinking water relevant substances (List 2a and 2b) various sources of information were used, namely: scientific literature studies, reports published by KWR Watercycle Research Institute (KWR) -that performs joint research studies for the Dutch drinking water companies (bedrijfstakonderzoek - BTO) -, RIVM reports, measurement data from RIWA and Rijkswaterstaat (RWS), and screening data from Aqualab Zuid (AQZ), Het Waterlaboratorium (HWL) and Water-link. For scientific literature, Web of Science and the website https://www.sciencedirect.com has been used. BTO reports have been requested via www.btonet.nl. Information was collected from the years 2019 - 2021. Hereby the following search terms were used (in various combinations):

- substance / pollutant
- emerging
- water (drinking, surface, waste)
- screening (non-target, suspect, target)

3

Results

3.1 Proposal for the new monitoring program for the Meuse

3.3.1 Drinking water relevant substances

The criteria 1, 2 and 3 as described in **Figure 1** of paragraph 2.1 were used to select parameters from the RIWA-Meuse database respectively. This database contains all monitoring results from the members of RIWA-Meuse at intake points or main monitoring stations along the river Meuse. These stations are listed in **Table 1**. From the parameters that met all the criteria 1, 2 and 3 respectively several were unselected, because:

- The parameter is not a substance, such as temperature and electric conductivity. Bioassays like the CALUX tests are also not included. Although these effect parameters are considered to possess valuable water quality information, it is recommended to firstly attempt to identify the substance(s) responsible for the measured activity if the ERM target value is exceeded.
- The parameter is not an individual substance, such as the sum of polycyclic aromatic hydrocarbons (PAHs).

Oxygen and acidity (pH) were excluded as for these parameters a minimal value, or a bandwidth, apply as ERM target value. The selection of parameters after these steps were then tested and ranked on criterion 4, explained in paragraph 2.2.2 and appendix I.1.

The resulting proposal for the novel List 1 is shown in **Table 2**. Compared to the former List 1, ten substances are included for the first time, one substance originates from List 2 and three substances do originate from List 3.

Three compounds do not (yet) fulfill the criteria, but are included based on other arguments. This concerns bromate, fluoride and PFAS (see paragraph 3.2.4).

3.1.2 Candidates for the list

To compile new candidate lists, a literature review was conducted on emerging substances. Besides, monitoring- and screening data from water companies were evaluated to investigate whether potentially relevant substances to the drinking water function of the Meuse were detected. Details on this study are described in paragraph 3.2. The study results in the proposal of 6 new substances on List 2a (**Table 3**) and 19 new substances on List 2b (**Table 4**). Eight substances that were proposed for List 2 in 2018 remain on List 2a, because they were not yet sufficiently monitored,

It was proposed to add the 14 substances on List 2a to the joint monitoring program of the Meuse and follow them with a quantitative analytical method. After one year the substances that have been monitored can be evaluated according to the methodology mentioned in paragraph 2.1 and it can be decided to either add the substances to List 1 or List 3.

Furthermore, it was suggested to follow the 19 substances on List 2b in the Meuse with targeted screening in first instance. Depending on their detection rate it can be decided if these substances should subsequently be monitored with a quantitative method.

Table 2 - Proposed list of drinking water relevant substances for the river Meuse (List 1)

#	Substance	CAS RN	Category	Score[1]	Previous List
1a	valsartan	137862-53-4	pharmaceutical	25	List 1
1b	valsartanic acid	164265-78-5	pharmaceutical	25	List 1
2a	metformin	657-24-9	pharmaceutical	14	List 1
2b	guanylurea	141-83-3	pharmaceutical	20	List 1
3	lamotrigine	84057-84-1	pharmaceutical	20	List 1
4	dibromoacetic acid	631-64-1	biocide (desinfection)	19	New
5	1,4-dioxane	123-91-1	industrial	18	List 1
6	hydrochlorothiazide	58-93-5	pharmaceutical	15	List 1
7	melamine	108-78-1	industrial	14	List 1
8	tramadol	27203-92-5	pharmaceutical	14	List 1
9	cyanuric acid	108-80-5	industrial	14	New
10	metolachlor	51218-45-2	pesticide	14	List 3
11	diethylenetriaminepentaacetic acid (DTPA)	67-43-6	industrial	13	List 1
12	ethylenediaminetetraacetic acid (EDTA)	60-00-4	industrial	13	List 1
13	N-formyl-4-aminoantipyrine	1672-58-8	pharmaceutical	13	List 2
14	nitriloacetic acid (NTA)	139-13-9	industrial	13	List 1
15	terbuthylazine	5915-41-3	pesticide	13	List 1
16	benzothiazole	95-16-9	industrial	13	New
17	bromate[3]	15541-45-4	industrial	12	New
18	di-n-butyltin	1002-53-5	industrial	12	New
19	ketoprofen	22071-15-4	pharmaceutical	12	New
20	monobromoacetic acid	79-08-3	biocide (desinfection)	12	New
21	naproxen	22204-53-1	pharmaceutical	12	List 3
22	prosulfocarb	52888-80-9	pesticide	12	New
23	glyphosate	1071-83-6	pesticide	11	List 1
24	aminomethylphosphonic acid (AMPA)	1066-51-9	pesticide/industrial (metabolite)	11	List 1
25	chloridazone-desphenyl	6339-19-1	pesticide (metabolite)	11	List 1
26	diisopropyl ether (DIPE)[2]	108-20-3	industrial	10	List 1
27	trifluoroacetic acid	76-05-1	industrial	10	List 3
28	sulfamic acid	5329-14-6	industrial	10	New
29	fluoride[3]	16984-48-8	industrial	N/A	List 1
30	PFAS[4]	N/A	industrial	N/A	New

1 The score of substances was calculated using the scoring system described in Appendix I.1. See Appendix I.2 for details.
2 DIPE has a clear emitting source (Société de Prayon, Engis) and it is proposed to monitor the substance only at the monitoring stations downstream from this source.
3 For bromate and fluoride it is not possible to calculate a score based on the EPI SuiteTM models because these are not suitable for this substance. Fluoride remains on the list based on expert judgement.
4 PFAS are included based on their toxicological relevance. This parameter includes the following individual PFAS mentioned in the European Drinking Water Directive (https://eur-lex.europa.eu/eli/dir/2020/2184/oj): Perfluorobutanoic acid (PFBA); Perfluoropentanoic acid (PFPA); Perfluorohexanoic acid (PFHxA); Perfluoroheptanoic acid (PFHpA); Perfluorooctanoic acid (PFOA); Perfluorononanoic acid (PFNA); Perfluorodecanoic acid (PFDA); Perfluoroundecanoic acid (PFUnDA); Perfluorododecanoic acid (PFDoDA); Perfluorotridecanoic acid (PFTrDA); Perfluorobutane sulfonic acid (PFBS); Perfluoropentane sulfonic acid (PFPS); Perfluorohexane sulfonic acid (PFHxS); Perfluoroheptane sulfonic acid (PFHpS); Perfluorooctane sulfonic acid (PFOS); Perfluorononane sulfonic acid (PFNS); Perfluorodecane sulfonic acid (PFDS); Perfluoroundecane sulfonic acid; Perfluorododecane sulfonic acid; Perfluorotridecane sulfonic acid

Table 3 - Proposed candidate drinking water relevant substances for monitoring in the river Meuse (List 2a)

#	Substance	CAS RN	Category	Score[1]	Previous List
1	dichloromethane sulfonic acid	53638-45-2	industrial	26	New
2	ritalinic acid	19395-41-6	pharmaceutical	26	List 2
3	candesartan	139481-59-7	pharmaceutical	24	New
4	chlorate	14866-68-3	biocide	21	New
5	fluconazole	86386-73-4	pharmaceutical	20	List 2
6	oxipurinol	2465-59-0	pharmaceutical	20	List 2
7	1,2,4-triazole	288-88-0	industrial	14	List 2
8	fexofenadine	83799-24-0	pharmaceutical	14	List 2
9	N-acetyl-4-aminoantipyrine	83-15-8	pharmaceutical	14	List 2
10	4-aminophenol	123-30-8	industrial	13	List 2
11	4-mesyl-2-nitrotoluene	1671-49-4	industrial	13	List 2
12	bisphenol-F	620-92-8	industrial	13	New
13	methylglycindi acedic acid (α-ADA, MGDA)	164462-16-2	industrial	13	New
14	1,3-di-o-tolylguanidine	97-39-2	industrial	12	New

1 The score of substances was calculated using the scoring system described in Appendix I.1. See Appendix I.2 for details.

Table 4 - Proposed candidate drinking water relevant substances for screening in the river Meuse (List 2b)

#	Substance	CAS RN	Category	Score[1]	Previous List
1	cyanopropanal	3515-93-3	industrial	26	New
2	4-amino-3-hydroxybenzoic acid	2374-03-0	industrial	25	New
3	ethyldimethylcarbamate	687-48-9	industrial	25	New
4	levothyroxine	51-48-9	pharmaceutical (thyroid hormone)	25	New
5	toluenesulfonamide (ortho)	88-19-7	industrial	25	New
6	10-hydroxy-amitriptyline	1246833-15-7	pharmaceutical (antidepressant)	24	New
7	β-asarone	5273-86-9	pharmaceutical (insect repellant) /flavouring agent	24	New
8	kojic acid	501-30-4	food additive	20	New
9	adamantan-1-amine	768-94-5	industrial/pharmaceutical	19	New
10	gliclazide	21187-98-4	pharmaceutical (antidiabeticum)	19	New
11	gamma-cyhalothrin	76703-62-3	pesticide	15	New
12	benzovindiflupyr	1072957-71-1	pesticide	10	New
13	isofetamid	875915-78-9	pesticide	10	New
14	mefentrifluconazole	1417782-03-6	pesticide	10	New
15	oxathiapiprolin	1003318-67-9	pesticide	10	New
16	pyriofenone	688046-61-9	pesticide	10	New
17	toluenesulfonamide (para)	70-55-3	industrial	10	New
18	cyanoguanidine	461-58-5	industrial	8	New
19	p-toluenesulfonic acid	104-15-4	industrial	8	New

1 The score of substances was calculated using the scoring system described in Appendix I.1. See Appendix I.2 for details.

3.1.3 No longer drinking water relevant substances

Twelve substances from the 2018-list will be removed and added to List 3. Amongst these are six x-ray contrasting agents. These substances are present in the Meuse with concentrations up to 1 µg/l, but their toxicity is very low. Benzo(a)pyrene was not found in the last three years. The other substances are removed as well because of low toxicity.

3.2 Compiling the candidate list

3.2.1 Literature

A complete list of the literature that was included in this study is shown in Appendix I.8.

A trainee at Evides performed a search for novel pesticides at the European market. This resulted in six novel pesticides that were added to the suspect screening at AQZ in January 2021. Since no monitoring data was available yet, the six substances were added to List 2b, as candidates for screening. It concerns **benzovindiflupyr**, **gamma-cyhalothrin**, **isofetamid**, **mefentrifluconazole**, **oxathiapiprolin** and **pyriofenone**.

A relevant paper was written by Schultze et al. (2019), with the aim to investigate the presence of persistent and mobile organic chemicals in surface and groundwater in Europe. Five chromatographically different targeted methods were developed to analyse a total of 57 polar mobile organic compounds (PMOC) in 14 water samples. The samples came from Germany, Spain and The Netherlands. Detected substances were classified in a range of six priorities, depending on their novelty and frequency of detection in the 14 samples. 15 substances were added to the shortlist, the majority of which was removed because of low toxicity values. **1,3-Di-o-tolylguanidine** is added to List 2a. Five substances were added to List 2b to be investigated by suspect screening.

Bisphenols were mentioned in multiple papers; three analogs (AP, P and Z) were found in surface water in Slovenia and Croatia, in submicromolar concentration (Cesen et al., 2019). Bisphenol-S was found in surface water by Schultze et al. (2019). KWR published a paper about regrettable substitutions for BPA (Steenbeek et al., 2020). Nine substitutes were described. Since no monitoring data is available for these substances, it is unknown if these substitutes are now present in surface water. Therefore, the most important substitute, **bisphenol-F**, was added to List 2a.

In two different papers the presence of parabens was mentioned (Bazin et al., 2020; Cesen et al., 2019). These substances are estrogenic, although at least 8000-fold less than estradiol. **Benzylparaben**, as the most toxic one, was added to the shortlist, but not to List 2 because of low toxicity. Nevertheless, it could be interesting to add benzylparaben to the suspect library, to get insight in its presence in the Meuse. The risk of hormone disrupting substances is in mixtures of all kind of estrogenic chemicals.

Several papers desribe the results of a suspect screening using liquid chromatography with high resolution mass spectrometry on water samples. Angeles et al. (2021) performed a suspect screening on wastewater and surface water samples from a.o. Sweden and Switzerland. The substance that was detected in the highest concentrations in surface water was **4-amino-3-hydroxybenzoic acid**. This is an industrial substance which was detected with an average concentration of 2.8 µg/L, and a maximum concentration of 54 µg/L. 4-amino-3-hydroxybenzoic acid is added to List 2b. Picardo et al. (2020) performed a suspect screening on natural toxins in surface water and drinking water in the Ter River in Spain. The natural substances -asarone and kojic acid were detected in concentrations in the range of 0.1 – 4.3 µg/L, and therefore added to List 2b.

Two substances were added because they are in the top 25 most prescribed pharmaceuticals in the Netherlands (based on the amount of defined daily doses). This concerns the anti-diabetic **gliclazide** and **levothyroxine**, which is used to treat thyroid hormone deficiency.

In 2020, Waterschap Limburg (the Water Board of the province Limburg) issued a new permit for Sitech for the discharge of waste water from the factories on the Chemelot industrial area in Sittard-Geleen. The water is discharged into the Ur, a tributary of the Meuse. Sitech has composed a list of substances that may be present in the surface water of the Meuse in concentrations above 1 µg/L. From these industrial substances, **cyanopropanal** was added to List 2b. No toxicity data was available for cyanopropanal, making it a potentially relevant substance.

Ethyl dimethyl carbamate (EDMC or N'N-dimethyl urethane) is an industrial substances that was detected in the surface water of the Rhine near Basel in concentrations of 100-200 ng/L (Scheurer and Fleig 2020). Since these concentrations are above the ERM target value, and the substance is classified as potentially carcinogenic and mutagenic, it was added to List 2b.

3.2.2 Screening

In autumn 2019, the regular intake monitoring by AQZ revealed an unknown substance in relatively high intensity, which was rapidly identified as prosulfocarb. A couple of days after the identification, approximately 12 µg/l prosulfocarb was measured in the Meuse at Roosteren. The consequence of this discharge was the exceedance of the ERM target value at five locations and stops at the different intake points of the drinking water companies. In 2020, prosulfocarb was not detected above the ERM target value, however, autumn 2021 again multiple increases in concentrations were observed. Therefore, prosulfocarb is added to List 1 to be monitored for the next five years.

Multiple pharmaceuticals were detected with the suspect screening which is frequently performed at AQZ and HWL for intake water of WML, Dunea and Evides. Amongst these are amantadine, fexofenadine, fluconazole, oxipurinol, N-acetyl-4-aminoantipyrine and ritalinic acid which were added to List 2.

3.2.3 Monitoring

The monitoring programs of the drinking water companies change over time, for example due to the development of new analytical methods or because new substances are added to existing methods. In recent years, risk-based monitoring was introduced in the Netherlands, which was initiated in response to amended regulations of the European Drinking Water Directive (van der Aa et al. 2017). The drinking water companies base their monitoring programs on a risk analysis. Part of this risk analysis is an inventory of new chemical threats, similar as the inventory that is performed in this study. Not all substances are relevant for each drinking water company, and it may also be the case that a substance is included in one monitoring program based on the risk analysis, but not yet everywhere. The substances that are not monitored at multiple locations cannot meet the criteria for List 1. For this reason, in this study the substances that have exceeded the ERM target value, but are only monitored at a few locations, are also taken into account. These substances are expected to meet the criteria of List 1 if they would have been monitored at more locations have been placed on List 2. This concerns **candesartan**, **chlorate**, **dichloromethane sulfonic acid**, **N-acetyl-4-aminoantipyrine** and **oxipurinol**. The last two substances are also detected in multiple locations with suspect screening (see paragraph 3.2.2).

3.2.4 Current developments

In 2021, the media regularly covered PFAS because recent scientific insights indicate that the levels of PFAS Dutch people ingest via food and drinking are potentially relevant for the human health. The European Food Safety Authority (EFSA) issued a new scientific opinion on the health risks associated with the presence of PFAS in food (EFSA, 2020) EFSA derived a health based tolerable weekly intake (TWI) of 4.4 ng/kg/week for the sum of four PFAS[2]. Based on this TWI, RIVM derived a pGLV of 4 ng PFOA-equivalents/liter (Van der Aa et al., 2021). The pGLV is not yet formally implemented by the Dutch Ministry of Infrastructure and Water because there are still discussions going on (see paragraph 3.3.4.for more information).

New risk limits were also proposed by RIVM for **bromate**: Smit (2021) derived new ecological risk limits for surface water. This new limit is relevant since Water boards consider ozonation as an additional treatment step to remove micropollutants in their wastewater treatment plants. Bromate can be formed from the reaction of ozone with bromide. It is expected that the Dutch Ministry of Infrastructure and Water Management will establish a new discharge standard for bromate in the end of 2021. Besides the ecological risk limits, Smit (2021) also mentions a negligible risk level of 0.005 µg/kg bw/day for human health. If this risk level would be used to derive a drinking water guideline (pGLV), this value would be lower than the current legal drinking water standard of 1 µg/L. RIVM therefore recommends to evaluate the drinking water standard (Smit, 2021).

If a pGLV for bromate will be derived based on the negligible risk level and the proposed pGLV for PFAS is adopted, bromate and several PFAS would both fulfill the criteria to be included on List 1 since the benchmark quotient for these compounds will be › 1 (**Figure 1**). Since it is clear that these (group of) compounds are potentially relevant for the human health at the present concentrations in the Meuse, it was decided to include them on List 1 in advance of the new drinking water guideline values.

Fluoride is included based on expert judgement: this compound is emitted by Société de Prayon in Engis as an impurity in the process in which they upgrade technical phosphoric acid to phosphoric acid with food quality. The process was optimized in 2014 resulting in a reduction of the fluoride emission, but the substance remains on List 1 to verify that the concentrations will go downward.

3.2.5 PMT substances

During the last decade scientific developments have allowed new ways to identify and categorize substances that generate problems for drinking water production, especially from surface water, as they are persistent, mobile and toxic (PMT) or very persistent and very mobile (vPvM) (Neumann et al., 2019; Arp & Hale, 2019). As a result of their physical-chemical properties, these substances are difficult to remove in the current drinking water purification systems and therefore might end up in drinking water in higher concentrations than acceptable (Reemtsma et al., 2016; Albergamo et al., 2019; Schulze et al., 2019).

In 2017 the German Umweltbundesamt (UBA) has come up with a coherent vision based on the idea to prevent emissions into the environment of substances, registered under the EU's Registration, Evaluation, Authorization, and restriction of Chemicals (REACH), which have the intrinsic properties that indicate a hazard to the sources of our drinking water (Neumann, 2019). These properties are persistency, mobility, and toxicity (PMT) as well as being very persistent and very mobile (vPvM). UBA proposed criteria and an assessment procedure that can be used to identify these substances. The aim is to classify these substances as "substances of very high concern" (SVHC), and to minimize environmental emissions of PMT/vPvM substances by encouraging registrants to implement strict risk reduction measures.

2 The four PFAS include perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorononanoic acid (PFNA) and perfluorohexanesulfonic acid (PFHxS)

This will eventually avoid undue contamination of the sources of our drinking water and will protect these valuable resources for future generations. This idea is gradually getting accepted by regulatory agencies and can be recognized in the recently presented EU Chemical Strategy, as part of the EU's zero pollution ambition, which is a key commitment of the European Green Deal (European Commission, 2020).

Unlike the WFD, the added value of this concept is that it identifies problems **beforehand** at the source of the problem and prevents pollution. Within the WFD regulations there is a system of watch-lists and lists with priority substances that can identify problem causing substances **after** they have entered the environment. Which is putting the proverbial cart before the horse. The current problems with PFAS and similar substances proves again that the precautionary principle should prevail. Prevention is always better than the cure and should be the preferred option.

The proposed approach in which PMT/vPvM substances are classified as SVHC also offers solutions for other European environmental directives aiming to protect the water environment, like the Industrial Emissions Directive and the Urban Wastewater Treatment Directive.

Currently a Working Group is assessing PMT substances under the umbrella of a national Approach on Emerging Substances of the Dutch Ministry of Infrastructure and Water Management. In the remark columns in the tables in Appendix I.2, I.3, and I.4 is shown if the substances of List 1, 2a and 2b are classified as PMT/vPvM according to the methodology of UBA.

3.3 Background information on the new relevant and candidate substances

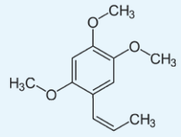
In this chapter background information is provided for the substances that are newly added to List 1, 2a or 2b. The substances are grouped to their use as either pharmaceutical, pesticide or in an industrial application.

3.3.1 Pharmaceutical residues and flavouring agents

β-Asarone is a constituent of oil of calamus, a flavouring agent derivedfrom Acorus calamus and Asarum european (**Figure 4**). β-Asarone is used as flavouring agent in alcoholic beverages (EC 2002). Based on toxicity data of β-asarone it was concluded that the substance is carcinogenic. Maximum levels for β -asarone in foodstuffs and beverages are 0.1 mg/kg in foodstuffs and beverages, with the exception of 1 mg/kg in alcoholic beverages and seasonings used in snack foods. β-Asarone as such may not be added to foodstuffs. In the US, calamus oil and its extracts are prohibited from use in food (EC 2002).

Candesartan is an angiotensin receptor blocker used mainly for the treatment of high blood pressure and heart failure. In 2020 candesartan was in the top 100 of most prescribed medicines in the Netherlands, with 64 million DDD (gipdatabank). The medicine was detected in concentrations above the ERM target value at Brakel three times in 2020. From 2021, the medicine is also part of the targeted method at AQZ and already exceeded the ERM target value twice at Haringvliet.

β-Asarone



Candesartan

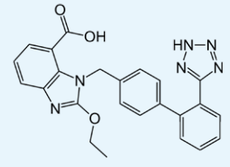


Figure 4

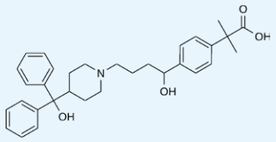
Acorus calamus

Photo by J.F. Gaffard, Autoreille, France, May 2004,, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=10296.

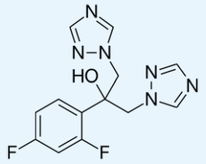
Asarum european

Photo by Bernd Haynold – own work, CC BY 2.5, https://commons.wikimedia.org/w/index.php?curid=715395

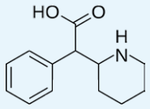
Fexofenadine



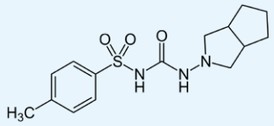
Fluconazole



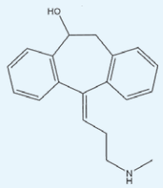
Ritalinic acid



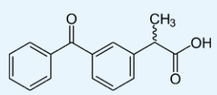
Gliclazide



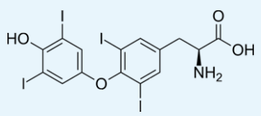
10-Hydroxy-amitriptyline



Ketoprofen



Levothyroxine



Fexofenadine, **fluconazole** and **ritalinic acid** are already on List 2 for years, but until this year no monitoring was available, except for the suspect screening. The three pharmaceuticals were added to the regular method at AQZ from 1-1-2021; they will be evaluated next year. The antihistamine drug **fexofenadine** was detected in the majority of the Meuse samples at Heel and Keizersveer with the suspect screening since 2019. Fexofenadine is often prescribed in the Netherlands with more than 20 million DDD in 2020 (gipdatabank). **Fluconazole** is an antifungal pharmaceutical used for a number of fungal infections. The substance is rarely found with the suspect screening. Fluconazole had 651.940 DDD in 2020 (gipdatabank). **Ritalinic acid** is the inactive metabolite of the psychostimulant drug methylphenidate (brand name concerta®). Methylphenidate improves the attention and mood and is used for people suffering from ADHD (attention deficit hyperactivity disorder) and narcolepsy (sleeping disease. Methyphenidate is also a widely used medicine with more than 48 million DDD in the Netherlands in 2020 (gipdatabank). Ritalinic acid is detected with the suspect screening in approximately half of the samples of the Meuse at Keizersveer, just above the detection limit.

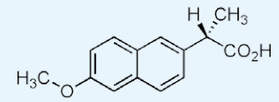
Gliclazide (brand name Diamicron®) is an often prescribed medicine against diabetes mellitus type 2. Gliclazide lowers the blood sugar by increasing the amount of insulin the body produces. With more than 118 million DDD it is 20th on the list of 100 most prescribed medication in the Netherlands (gipdatabank).

10-Hydroxy-amitriptyline is one of the metabolites of amitriptyline, a widely used tricyclic antidepressant. Amitriptyline is used against depressive disorder and (chronic) pain, e.g. fibromyalgia and migraine. Amitriptyline is in the top-100 of mostly described pharmaceuticals in the Netherlands with more than 20 million defined daily doses (DDD) in 2020 (gipdatabank). Its major metabolite is nortriptyline, an active metabolite, which has more than 9 million DDD. Nortriptyline is metabolized further into 10-hydroxynortriptyline. It is recommendable to investigate both 10-hydroxy-AT and 10-hydroxy-NT. In the Netherlands, amitriptyline was found in RWZI effluent, not yet in surface water.

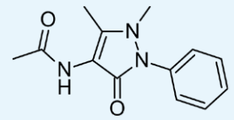
Ketoprofen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic effects. It acts by inhibiting the body's production of prostaglandin. Ketoprofen is generally prescribed for arthritis-related inflammatory pains or severe toothaches that result in the inflammation of the gums. Ketoprofen was detected in concentrations up to 0.18 µg/L in the Meuse.

Levothyroxine (brand name Euthyrox®) is a manufactured form of the thyroid hormone thyroxine. It is used to treat thyroid hormone deficiency (hypothyroidism). With more than 113 million DDD it is 21st on the list of 100 most prescribed medication in the Netherlands (gipdatabank).

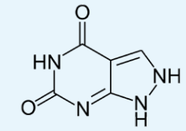
Naproxen



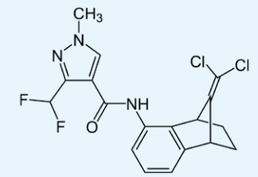
N-Acetyl-4-aminoantipyrine



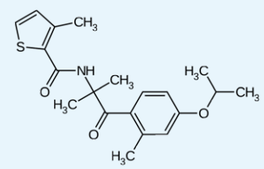
Oxipurinol



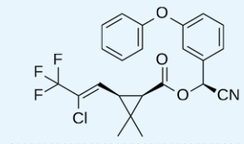
Benzovindiflupyr



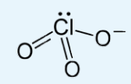
Isofetamid



Gamma-cyhalothrin



Chlorate



Naproxen, sold under the brand name Aleve® among others, is a NSAID used to treat pain, menstrual cramps, inflammatory diseases such as rheumatoid arthritis, gout and fever. It is available in immediate and delayed release formulations. Naproxen is on the international market since 1973 and with almost 37 million DDD it is 53rd on the list of 100 most prescribed medication in the Netherlands in 2020 (gipdatabank).

N-Acetyl-4-aminoantipyrine (AAA) is a metabolite of the medicine metamizole. Metamizole is a non-steroidal anti-inflammatory drug (also called a 'NSAID'). The drug has a strong analgesic, fever-reducing and anti-spasmodic effect. Metamizole is used for the short-term treatment of severe pain or high fever when the use of other medicines is not recommended (apotheek.nl). Metamizole is not often prescribed with only 1256 DDD in 2020 (gipdatabank). Metamizole is rapidly broken down in the environment into the stable substances AAA and FAA (ARW 2017).

Oxipurinol is the metabolite of allopurinol, a medicine used to decrease high blood uric acid levels. Allopurinol is often prescribed with almost 24 million DDD in the Netherlands in 2020 (gipdatabank). Oxipurinol was detected in the Meuse in concentrations up to 0.9 µg/L.

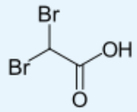
3.3.2 Pesticides and biocides

Benzovindiflupyr and **isofetamid** are both fungicides. Although structurally quite different, they are both succinate dehydrogenase inhibitors (SDHI). Benzovindiflupyr might be harmful to plants, animals and human. More research is ongoing; the currently calculated pGLV might be lowered in the future. The substance has low biodegradability. Benzovindiflupyr is allowed in the Netherlands; isofetamid not, both are allowed in Belgium and Germany.

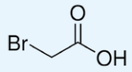
Gamma-cyhalothrin is a broad-spectrum pyrethroid insecticide; the synthetic pyrethroid mimics the structure and properties of the naturally occurring insecticide pyrethrin. It has a high mammalian toxicity and is potentially bioaccumulating. It is considered to be a neurotoxicant; highly toxic to honey bees, moderately toxic to birds and earthworms. The gamma-isomer is considered to be the most active against insects. In the Netherlands, gamma-cyhalothrin is not (yet) allowed, in contrast to Belgium and Germany. Its water solubility is low, therefore the chance is low that this pesticide ever becomes drinking water relevant.

Chlorate is an inorganic substance that is formed as a by-product of disinfection with chlorine dioxide or sodium hypochlorite (chlorine bleach) (Versteegh et al., 1993). Chlorine dioxide is a strong disinfectant applied during a.o. drinking water treatment, wastewater treatment, industrial process water treatment and cooling tower water disinfection. Chlorine dioxide prevents bacterial growth in the drinking water distribution system. In 2021, 119 biocidal products containing sodium hypochlorite are permitted in the Netherlands (www.ctgb.nl). Chlorate can end up in surface water as a by-product of chlorine dioxide and sodium hypochlorite through both domestic and industrial wastewater treatment plants.

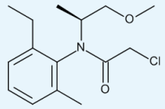
Dibromoacetic acid



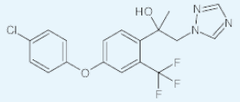
Monobromoacetic acid



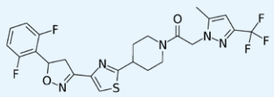
S-metolachlor



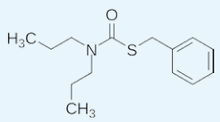
Mefentrifluconazole



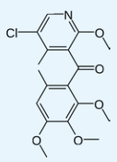
Oxathiapiprolin



Prosulfocarb



Pyriofenone



Dibromoacetic acid and **monobromoacetic acid** are two disinfection byproducts produced by the chlorination of water. Two biocidal products with monobromoacetic acid as active ingredient are permitted in the Netherlands (www.ctgb.nl).

In the Netherlands **S-metolachlor**[3] is authorized as a herbicide in several vegetable crops and fruit growing. It is the active ingredient in plant protection products with names like Camix (NL, BE), CODAL (BE), Dual Gold 960 EC (NL, BE), EFICA 960 EC (NL, BE), Gardo Gold (NL, BE), GARDOPRIM (BE), LECAR (BE) en PRIMAGRAM GOLD (BE) (source: Ctgb.nl, Fytoweb.be). S-metolachlor was placed Annex I of Directive 91/414/EEC and later approved under Implementing Regulation (EC) No 1107/2009. The term of approval was extended until 31 July 2020 by Implementing Regulation (EC) No 2019/707.

Mefentrifluconazole (BAS 750 F) is a fungicide used to control disease on cereals. The chemical has low aqueous solubility and might accumulate in soil. Its human toxicity is low. It is allowed in the Netherlands. The triazole fungicides, to which mefentrifluconazole belongs, are degraded into toxicologically relevant metabolites, called triazole derivative metabolites. (Anastassiadou et al., 2020) These are 1,2,4-triazole (1,2,4-T, part of list 2a), triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA). 1,2,4-triazole has the lowest (p)GLV, the (p)GLVs of TA and TLA are ten times higher, TAA even 100 times higher. (Brancato et al., 2018) These metabolites are persistent and mobile, it is recommended to evaluate screening data with respect to them.

The fungicide **oxathiapiprolin** is allowed and sold in the Netherlands under the trade name Zorvec. The metabolite 5-(trifluoromethyl)-1H-pyrazole-3-carboxylic acid (IN-E8S72) is highly persistent, mobile and likely to be found in groundwater above 0,1 µg/l, but is not toxicologically relevant (EFSA, https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2016.4504).

Prosulfocarb is the active ingredient in herbicides for the use in winter wheat and barley that used to be authorized in the Netherlands with names like Boxer. In Belgium herbicides with prosulfocarb as active ingredient are authorized under names like ADELFO, DEFI, FIDOX, FIDOX EC, JURA, ROXY 800 EC, ROXY EC and SPOW (source: Fytoweb.be). In 2019 and 2021 several spikes of prosulfocarb in the river Meuse were detected at the border monitoring station in Eijsden. There are indications that these spikes origin from the Wandre area.

The fungicide **pyriofenone** is since 2017 allowed in the Netherlands and is used in growth of cereals and grapes.

3 s-metolachlor is mixture of (aRS, 1 S)-2-chloro-N-(6-ethyl-o-tolyl)-N-(2-methoxy-1-methylethyl) acetamide (80-100 %) and (aRS, 1 R)-2-chloro-N-(6-ethyl-o-tolyl)-N-(2-methoxy-1-methylethyl) acetamide (20-0 %)

3.3.3 Industrial substances

The following substances have been selected in 2018 as candidate substance on List 2 because they belong to the REACH substances that were assessed to be persistent in aquatic environments, mobile and toxic (PMT): **1,2,4-triazole** is used as intermediate for the production of other chemicals, e.g., fungicides, but also as additive in fertilizer (Berger et al. 2018). It is one of the REACH substances that were assessed to be persistent in aquatic environments, mobile and toxic (PMT). 1,2,4-Triazole has registrants in Germany and France and has a registered production volume of 1000-10 000 tonnes per year (REACH registration file). **4-Aminophenol** is also used as intermediate, for example for the synthesis of paracetamol and in the manufacturing of sulphur- and azo-dyes. The substance acts as a corrosion inhibitor in paints and as an anticorrosion-lubricating agent in engine fuels. 4-Aminophenol has multiple registrants, also in the Netherlands and a registered production volume of 10-100 tonnes per year (REACH registration file). The registration file also identifies “wide dispersive use”, “industrial use” and “professional use” as intended uses. Therefore, emissions to the environment are expected also for this substance (Berger et al. 2018). 4-Mesyl-2-nitrotoluene has a registrant in Sweden and is registered with a low production volume of 0-10 tonnes per year and a confidential tonnage data (REACH registration file). The substance has an unknown application.

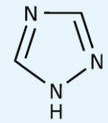
4-Amino-3-hydroxybenzoic acid is an industrial substance which is used as an intermediate, for example for the production of the pharmaceutical tafamidis[4] (REACH registration file). Tafamidis prevents the breakdown of the protein transthyretin and is used for people with the neurodegenerative disease transthyretin-related amyloidosis. The pharmaceutical is not often prescribed in the Netherlands with 10.192 DDD in 2020 (gipdatabank).

1,3-Di-o-tolylguanidine is used as process regulator and in vulcanization or polymerization processed and in rubber products. It is registered at 10-100 tonnes a year (REACH registration file). The chemical is pharmacologically active as an agonist of the sigma receptor (σ1/σ2 receptor). It has neuroprotective and antidepressant effects and potentiates the effects of the N-methyl-D-aspartate receptor (NMDA) antagonists.

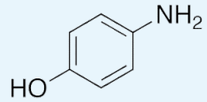
Adamantan-1-amine (or amantadine) is registered in REACH for its use as intermediate in industrial processes. The substance is also in use as antiparkinsonian pharmaceutical. It was first registered as antiviral medication (against influenza A virus), already in 1969. As a coincidence, since a Parkinson’s patient used adamantan-1-amine against influenza, it was discovered that the substance reduces tremor and rigidity in Parkinson’s disease. With its trade name Symmetrel it has approximately 1 million DDD (GIP databank). Amantadine is not biodegradable and poorly eliminated from water (ECHA). The pGLV, based on an ADI of 1,4 µg/kg/day, is low. It is however expected that concentrations in surface water are low, although Schultze et al. detected the substance in all measured SW samples.

4 https://www.chemicalbook.com/ChemicalProductProperty_EN_CB53159986.html

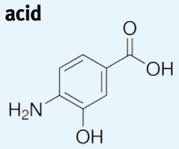
1,2,4-triazole



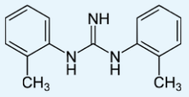
4-Aminophenol



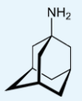
4-Amino-3-hydroxybenzoic acid



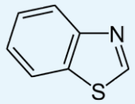
1,3-Di-o-tolylguanidine



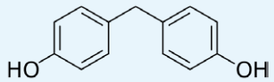
Adamantan-1-amine



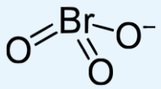
Benzothiazole



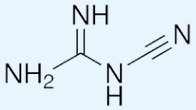
Bisphenol-F



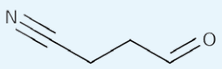
Bromate



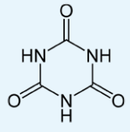
Cyanoguanidine



Cyanopropanal



Cyanuric acid



Benzothiazole is mainly used for the synthesis of other substances. Many benzothiazole derivatives are biologically active substances used in pharmaceuticals, biocides or pesticides. Many dyes also have a structure based on benzothiazole.

Bisphenol-F (BPF) is one of the mostly used substitutes for bisphenol-A (BPA). It is used in the manufacturing of plastics, to increase the thickness and durability of materials. The substance is utilized in pipe linings, industrial floors, liners, adhesives, coating of drinks and food cans, dental materials etc. Remarkably, BPF is a natural ingredient of mustard, which results in a low-level chronic exposure for humans. BPF, like a couple of other substitutes, cause the same endocrine disrupting effects as BPA. It is expected that BPF concentrations will increase, while BPA concentrations are expected to decrease due to application restrictions in the EU. It is not known yet if mixtures of bisphenols have enhanced toxicity effects. By monitoring already one BPA substitute, a start is made to investigate their presence in surface water. It is recommended to start monitoring more BPA substitutes.

Bromate is an inorganic compound that can be formed when water containing bromide is treated with ozone. This is a relevant point of interest since ozone techniques are more often implemented as additional step in the treatment of wastewater. Since bromate is a suspected human carcinogen, its presence in drinking water is undesirable.

Cyanoguanidine is used as a modifying agent for melamine resins; processing aid; used in fertilizers, textile treatment products and dyes; used for the manufacture of textile, leather and fur. The substance is registered at 10 000-100 000 tonnes a year (REACH registration file). Cyanoguanidine was detected in all surface water samples by Schultze et al. 2019, at concentrations exceeding 3 µg/l. The substance is persistent and mobile, not toxic.

The substance **cyanopropanal** is mentioned as drinking water relevant substance on the discharge permit of Sitech Services, who manages the integrated wastewater treatment of the Chemelot industrial area. No monitoring data is yet available for this substance, but Sitech calculated an estimated concentration of 254 µg/L in the effluent. Taking dilution into account, the estimated concentration in the Meuse will be › 10 µg/L. No information can be found on the use of cyanopropranal and the substance does not have a REACH registration file.

Cyanuric acid is an intermediate in the production of melamine. The substance can occur as impurity in melamine. The main use of cyanuric acid is as a raw material in the synthesis of di- and trichloroisocyanuric acids, which are used in swimming pools as a disinfectant, biocide and to chlorinate swimming pools. In swimming pool water, the substance is also detected as a dissociation product of di- and trichloroisocyanurates (Van den Berg, 2019). Various biocidal products with sodium dichloroisocyanurate and trichloroisocyanuric acid as active ingredients are permitted in the Netherlands, but instead of the expiry date is indicated “until member state measures” (www.ctgb.nl). Cyanuric acid is also an important intermediate for the synthesis of a variety of organic substances, including epoxy resins, chlorinated derivatives, detergents, antioxidants, dyes, pesticides and antitumor agents (Van den Berg, 2019).

There is no known production location of cyanuric acid in the Netherlands, but via the above mentioned applications, cyanuric acid can end up in surface water via sewage treatment plants. Cyanuric acid can also be present in wastewater at locations where melamine is produced (such as the Chemelot industrial area in Sittard-Geleen).

Dichloromethane sulfonic acid is a halogenated methane sulfonic acid that was detected with non-target screening in different water samples from Europe (Zahn et al. 2016). A target analysis was developed for this substance in the joint research of the Dutch drinking water companies (Vughs et al. 2018) and quantitative monitoring shows that the substance is present in the Meuse in concentrations above the ERM target value with a maximum concentration of 0.23 µg/L. No information can be found on the use of dichloromethane sulfonic acid and the substance does not have a REACH registration file.

Di-n-butyltin is used in adhesives and sealants and coating products. Releases of this substance to the environment are likely to occur from indoor use (e.g., laundry detergents/detergents, car care products, paints and coatings or adhesives, fragrances and air fresheners). When used outdoors, emissions may occur from long-life, low-release materials (e.g., metal, wood, and plastic construction and building materials) and indoors also from low-release, durable materials (e.g., floors, furniture, toys, construction).

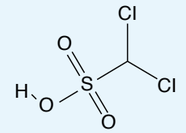
Ethyl dimethyl carbamate (EDMC or N’N-dimethyl urethane) is a by-product of the production process of a chemical company in Switzerland. The substance is classified as possibly carcinogenic, mutagenic and harmful to development. Furthermore, little is known about the toxicological properties, effects on the aquatic environment and the behavior of EDMC during the water treatment process (Scheurer and Fleig, 2020).

Kojic acid is produced by fermentation of carbohydrates by fungi of the genus Aspergillus. Kojic acid forms metal chelates with I.e., barium, calcium, copper, manganese, tin and zinc. It has an antibacterial effect. It is mainly used in cosmetic products for the whitening or depigmenting the skin because kojic acid inhibits the biosynthesis of melanine. Kojic acid is also used as a food additive to prevent enzymatic browning.

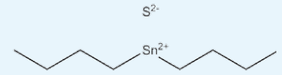
Methylglycindi acetic acid (MGDA) is a complexing agent that is detected in the surface water of the Rhine in concentrations above 1 µg/L (RIWA Rijn 2021). It is used i.e., as stabilizer for bleaching agents and enzymes by binding heavy metals from water (www.ikw.org). MGDA has a registered production volume of 10 000-100 000 tonnes per year (REACH registration file).

Sulfamic acid is an ingredient of many acidic cleaning agents for the removal of deposits: limescale in coffee makers and on chrome or stainless steel, for example in dairies and breweries, in steam boilers, cement veil on tiles and urine stone on sanitary facilities. Sulfamic acid is also used for the synthesis of artificial sweeteners (cyclamic acid and sodium cyclamate).

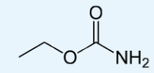
Dichloromethane sulfonic acid



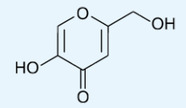
Di-n-butyltin



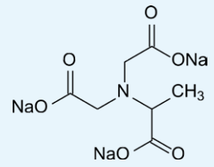
Ethyl dimethyl carbamate



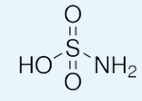
Kojic acid



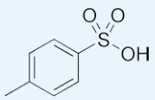
Methylglycindi acetic acid



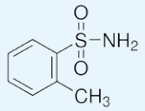
Sulfamic acid



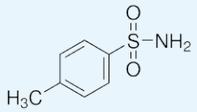
Para-Toluenesulfonic acid



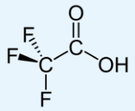
Ortho-toluenesulfonamide



Para-toluenesulfonamide



Trifluoroacetic acid



Para-Toluenesulfonic acid is a strong organic acid that is used as process regulator and pH-regulating agent. Used in vulcanization or polymerization processes and in water treatment products. The toxicity is very low, it is therefore unlikely that this substance will end up on List 1.

The industrial substance **toluenesulfonamide** is used as processing aid, laboratory chemical and manufacturing of polymers. Both the **ortho** and **para** isomer have been detected by Schulze et al. 2019 in surface water in Germany, Spain and the Netherlands. In Berlin, **para-toluenesulfonamide** was even found in drinking water up to 0,27 µg/l; and in wastewater to 50 µg/l (Richter et al., 2007). The substances are not biodegradable, but also not accumulating; the toxicity is expected to be low.

Trifluoroacetic acid (TFA) is the precursor to many other fluorinated substances such as trifluoroacetic anhydride, trifluoroperacetic acid, and 2,2,2-trifluoroethanol. TFA is also used in the synthesis of pharmaceutical products and agricultural chemicals and as a catalyst in polymerizations and condensation reactions. TFA can also be a metabolite of plant protection products and air conditioning fluids.

3.3.4 PFAS

Poly- and perfluoroalkyl substances (PFAS) are man-made chemicals that do not occur naturally in the environment. PFAS have useful properties: they are water, fat and dirt repellent. They are used in many different applications, for example in textiles, food packaging materials, extinguishing foam, and non-stick coatings of pans. They are also used in various industrial applications and processes (https://www.rivm.nl/pfas). PFAS are very persistent in the environment and are therefore called “forever chemicals” (https://chemtrust.org/pfas/). Because of new insights in the negative effects of PFAS on human health and the environment there has been a strong focus on PFAS in recent years. On 16 December 2020, the European Parliament formally adopted the revised Drinking Water Directive, which entered in force on 12 January 2021 (https://eur-lex.europa.eu/eli/dir/2020/2184/oj). Member States have two years to implement the revised directive into their national laws. The revised Drinking Water Directive includes for the first-time water quality standards for PFAS: a standard for the sum concentration of PFAS (0.5 µg/L) and a standard for the sum concentration of 20 defined PFAS (0.1 µg/L). Member States can choose which of these two PFAS standards they wish to include in their legislation and regulations.

The European Food Safety Authority (EFSA) recently issued a new scientific opinion on the health risks associated with the presence of PFAS in food (EFSA, 2020). The EFSA has calculated the amount of four PFAS[5] that people can safely ingest during their entire life (health-based limit value): the total intake should not exceed 4.4 ng/kg/week. The Dutch RIVM sees the EFSA opinion as a reason to reconsider the existing limit values for PFAS in food, soil, (drinking) water and air. For drinking water RIVM calculated a guideline value of 4.4 ng PFOA-equivalents/L for the sum of the four PFAS (Van der Aa et al., 2021). This drinking water guideline value is not yet formally implemented by the Dutch Ministry of Infrastructure and Water. Because

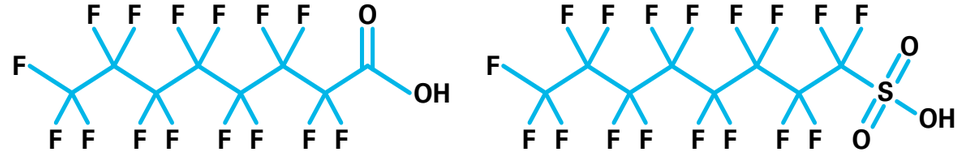
5 The four PFAS include perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorononanoic acid (PFNA) and perfluorohexanesulfonic acid (PFHxS)

there are still uncertainties, for example in the portion of intake via drinking water versus intake via food, the derivation of the drinking water guideline is the subject of discussion among experts. It is also not yet clear how the new Drinking Water Directive and the EFSA opinion will relate to each other.

At the moment several research projects are being conducted to gain more insight in the “PFAS issue”. Drinking water laboratories are working on sensitive methods that allow monitoring with lower detection limits. In the joint research of the drinking water companies a screening method has been developed with which a broader range of PFAS can be monitored (instead of focussing on the limited set of 20-30 PFAS that are monitored at the moment).

Although the drinking water guideline for PFAS compounds is not yet formal, it is clear that PFAS are a relevant group of substances for the drinking water production. The current research projects will on short term provide more insight in the most relevant PFAS and it may then be possible to identify individual PFAS as the most relevant. For PFAS as a group it is important to start focussing immediately on an approach that will ensure that these substances no longer end up in the environment and the sources of drinking water, preferably by banning these substances wherever this is feasible. For now it has been decided to include PFAS as a group parameter on List 1. For the present, this group includes the 20 PFAS compounds[6] that are mentioned as relevant compounds in European Drinking Water Directive (https://eur-lex.europa.eu/eli/dir/2020/2184/oj) that was adopted in December 2020 by the European Parliament.

Figure 3 - Chemical structure of perfluorooctanoic acid (PFOA) (left) and perfluorooctanesulfonic acid (PFOS) (right)



6 (1) Perfluorobutanoic acid (PFBA); (2) Perfluoropentanoic acid (PFPA); (3) Perfluorohexanoic acid (PFHxA); (4) Perfluoroheptanoic acid (PFHpA); (5) Perfluorooctanoic acid (PFOA); (6) Perfluorononanoic acid (PFNA); (7) Perfluorodecanoic acid (PFDA); (8) Perfluoroundecanoic acid (PFUnDA); (9) Perfluorododecanoic acid (PFDoDA); (10) Perfluorotridecanoic acid (PFTrDA); (11) Perfluorobutane sulfonic acid (PFBS); (12) Perfluoropentane sulfonic acid (PFPS); (13) Perfluorohexane sulfonic acid (PFHxS); (14) Perfluoroheptane sulfonic acid (PFHpS); (15) Perfluorooctane sulfonic acid (PFOS); (16) Perfluorononane sulfonic acid (PFNS); (17) Perfluorodecane sulfonic acid (PFDS); (18) Perfluoroundecane sulfonic acid; (19) Perfluorododecane sulfonic acid; (20) Perfluorotridecane sulfonic acid

4

Conclusions

Adaptations to the methodology

The methodology to define (candidate) relevant drinking water substances has been adapted slightly since the last update in 2018:

- List 2 with candidate relevant drinking water substances has been split in two lists:
- List 2A contains the candidate substances that are recommended to be monitored with a target analysis. This concerns the substances that are known to be present in the Meuse in a relevant concentration.
- List 2B contains the candidate substances that will first be monitored with a screening method. These substances are expected to be present in the Meuse based on the literature research, but no data is available yet.
- Public perception is no longer taken into account for the calculation of the substance score.
- Exceedance of the legal drinking water standard is added as criterium for the calculation of the substance score.
- The criterion for removal has changed: instead of a total of at least 4 points for volatility, biodegradability and polarity, a substance has to have at least 1 point for each of these parameters.
- For the candidate substances for which no measured data is available, a virtual concentration is added to make it possible to calculate a toxicity score. The virtual concentration is based on literature data.

List 1 Relevant drinking water substances

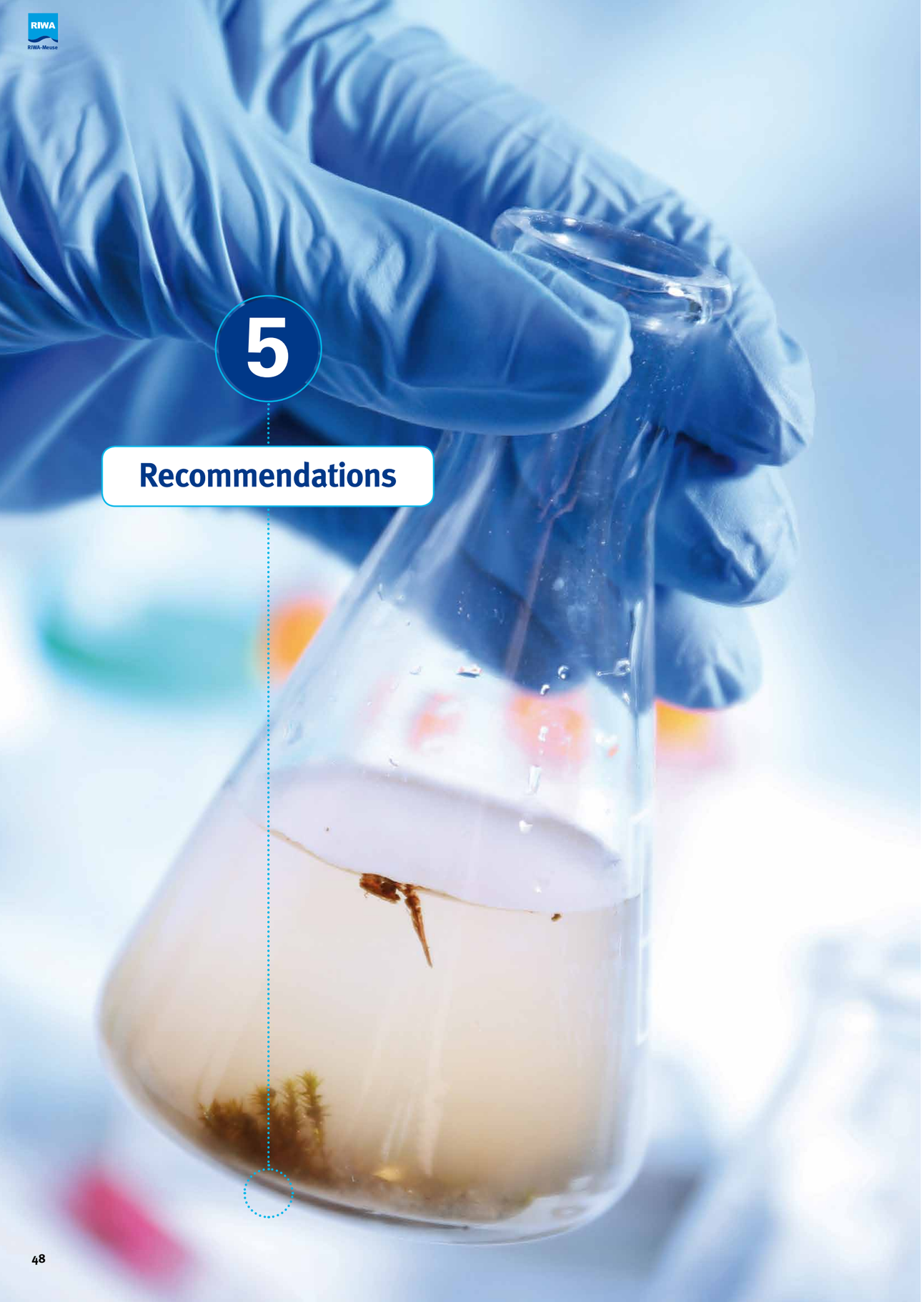
The RIWA lists of relevant drinking water substances (List 1) has been updated based on new monitoring data from the period 2016-2020. Based on the evaluation, 14 substances are newly included on List 1, and 12 substances are removed from the list.

New on List 1	Application	Score	Removed from List 1	Application
benzothiazole	Industrial	13	amidotrizoic acid	X-ray contrast agent
bromate	Industrial	12	benzo(a)pyrene	Industrial
cyanuric acid	Industrial	14	bisphenol A	Industrial
dibromoacetic acid	Industrial	19	gabapentin	Pharmaceutical
di-n-butyltin	Industrial	12	iohexol	x-ray contrast agent
ketoprofen	Pharmaceutical	12	iomeprol	x-ray contrast agent
metolachlor	Pesticide	14	iopamidol	x-ray contrast agent
monobromoacetic acid	Industrial/biocide	12	iopromide	x-ray contrast agent
naproxen	Pharmaceutical	12	ioxitalamic acid	x-ray contrast agent
N-formyl-4-aminoantipyrine	Pharmaceutical*	13	N,N-dimethylsulfamid (DMS)	Biocide (metabolite)
PFAS	Industrial	NA	pyrazole	Industrial
prosulfocarb	Pesticide	12	sotalol	Pharmaceutical
sulfamic acid	Industrial	10		
trifluoroacetic acid	Industrial	10		

List 2A and 2B Candidate relevant drinking water substances

The RIWA lists of candidate relevant drinking water substances (former List 2) has been updated based on new monitoring data from the period 2016-2020 and new candidate substances have been selected based on a literature study. It is recommended to monitor these candidates either with a target analysis (List 2A) or with a screening method (List 2B).

List 2A	Application	Score	List 2B	Application	Score
dichloromethane sulfonic acid	Industrial	26	cyanopropanal	Industrial	26
ritalinic acid	Pharmaceutical*	26	4-amino-3-hydroxybenzoic acid	Industrial	25
candesartan	Pharmaceutical	24	ethyldimethylcarbamate	Industrial	25
chlorate	Industrial	21	levothyroxine	Pharmaceutical	25
fluconazole	Pharmaceutical	20	toluenesulfonamide (ortho)	Industrial	25
oxipurinol	Pharmaceutical*	20	10-hydroxy-amitriptyline	Pharmaceutical*	24
1,2,4-triazole	Industrial	14	b-asarone	Pharmaceutical	24
fexofenadine	Pharmaceutical	14	enrofloxacin	Pharmaceutical	20
N-acetyl-4-aminoantipyrine	Pharmaceutical*	14	kojic acid	Food additive	20
4-aminophenol	Industrial	13	adamantan-1-amine	Pharmaceutical	19
4-mesyl-2-nitrotoluene	Industrial	13	gliclazide	Pharmaceutical (antidiabeticum)	19
bisphenol-F	Industrial	13	gamma-cyhalothrin	Pesticide	12
methylglycindi acedic acid (apha ADA, MGDA)	Industrial	13	benzovindiflupyr	Pesticide	10
1,3-di-o-tolylguanidine	Industrial	12	isofetamid	Pesticide	10
			mefentrifluconazole	Pesticide	10
			oxathiapiprolin	Pesticide	10
			pyriofenone	Pesticide	10
			cyanoguanidine	Industrial	8
			p-toluenesulfonic acid	Industrial	8
			toluenesulfonamide (para)	Industrial	7



5 Recommendations

It is recommended to use the new lists of 2021 as input for a joint monitoring program of the drinking water companies along the river Meuse. For 2022 the proposal is to monitor the following substances:

Targeted analysis List 1	Score	Targeted analysis List 2A	Score	Screening method List 2B	Score
valsartan	25	dichloromethane sulfonic acid	26	cyanopropanal	26
valsartanic acid	25	ritalinic acid	26	4-amino-3-hydroxybenzoic acid	25
metformin	14	candesartan	24	ethyldimethylcarbamate	25
guanylurea	20	chlorate	21	levothyroxine	25
lamotrigine	20	fluconazole	20	toluenesulfonamide (ortho)	25
dibromoacetic acid	19	oxipurinol	20	10-hydroxy-amitriptyline	24
1,4-dioxane	18	1,2,4-triazole	14	b-asarone	24
hydrochlorothiazide	15	fexofenadine	14	enrofloxacin	20
melamine	14	N-acetyl-4-aminoantipyrine	14	kojic acid	20
tramadol	14	4-aminophenol	13	adamantan-1-amine	19
cyanuric acid	14	4-mesyl-2-nitrotoluene	13	gliclazide	19
metolachlor	14	bisphenol-F	13	gamma-cyhalothrin	12
DTPA	13	methylglycindi acedic acid	13	benzovindiflupyr	10
EDTA	13	1,3-di-o-tolylguanidine	12	isofetamid	10
N-formyl-4-aminoantipyrine	13			mefentrifluconazole	10
NTA	13			oxathiapiprolin	10
terbuthylazine	13			pyriofenone	10
benzothiazole	13			cyanoguanidine	8
bromate	12			p-toluenesulfonic acid	8
di-n-butyltin	12			toluenesulfonamide (para)	7
ketoprofen	12				
monobromoacetic acid	12				
naproxen	12				
prosulfocarb	12				
glyphosate	11				
AMPA	11				
chloridazone-desphenyl	11				
diisopropyl ether	10				
trifluoroacetic acid	10				
sulfamic acid	10				
fluoride	N/A				
PFAS (20 compounds defined in the EU DWD)	N/A				

For the substances 1,2,4-triazole; 1,3-di-o-tolylguanidine; 4-aminophenol; 4-mesyl-2-nitrotoluene; and bisphenol F it is not known if an analytical method is available. It is recommended to develop an analytical method for these substances (or check the possibilities of adding these substances to an existing method).

6

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Appendices

1.1 Calculation of the substance score

The scoring system used was earlier described in Fischer et al. (2011).

The list of substances that are relevant to the drinking water function of the River Meuse are proposed to be scored, according to the following principles:

1. The main chemical properties that influence the removal by water treatment; polarity, volatility and removal by powdered activated carbon are ranked:
   a) For polarity the log K_{ow} of the substance is used.
   b) For volatility the vapor pressure of the substance is used.
   c) For biodegradability of the substance the primary biodegradation model (BioWIN3, in EPI Suite 4.1) is used.

2. The toxicological benchmark quotient (BQ) is derived for each substance. BQ is the maximum concentration found in the river (C_{max} water) divided by the (provisional) toxicological drinking water guideline value (pGLV). The derivation of the pGLV is described in van der Aa et al. (2017)):

$$pGLV = \frac{ADI\ or\ TDI^{*}m_{adult}^{*}20\%}{2L/day}$$

where ADI/TDI is the acceptanle or tolerable daily intake in µg (kg body mass)-1 day-1, and madult is the average adult body mass in kg. For the calculations a madult of 70 kg is assumed.

Table 5 - Point attribution for polarity, volatility, biodegradability, and toxicity

Polarity Log K_{ow}	Score	Volatility Vapor pressure (mm Hg)	Score	Biodegradability BioWIN3	Score	Toxicity BQ	Score
>6	0	>52,5	0	>4,75 – 5	0	<0,01	0
>3 - 6	1	>35 – 52,5	1	>3,25 – 4,75	1	0,01 – 0,1	6
0 – 3	2	17,5 – 35	2	2,25 – 3,25	2	>0,1 – 1	12
<0	3	<17,5	3	<2,25	3	>1	18

3. If the odour/taste threshold is breached by C_{max} water, 3 points are awarded.

4. If the drinking water standard from the Dutch Drinking Water Decree (Drinkwaterbesluit) is exceeded, 3 points are awarded

1.2 Background information on substances List 1

Table 6 - Information on the drinking water relevant substances (List 1). Information is given on the ERM value used for the substance, the Dutch drinking water standard if available, the number of monitoring stations where the substance was monitored, the total number of measurements in the period 2016-2020, the number and percentage of measurements above the ERM, and the list on which the substance was placed in 2018.

Substance name	CAS	ERM (µg/L)	Dutch legal DW standard (µg/L)	# monitoring stations	# measurements	# measurements > ERM	% > ERM	List in 2018	Remarks
1,4-dioxane	123-91-1	0.1		7	377	306	54%	List 1	SVHC substance; PMT
aminomethylphosphonic acid (AMPA)	1066-51-9	0.1	1	10	648	379	58%	List 1	Above standard Dutch DWB
benzothiazole	95-16-9	0.1		4	196	9	4.6%	New	Potential vPvM & PMT
bromate	15541-45-4	0.1	1	3	146	17	11%	New	SVHC
chloridazone-desphenyl	6339-19-1	0.1	1	8	490	316	64%	List 1	Above standard Dutch DWB
cyanuric acid	108-80-5	0.1		4	26	26	100%	New	vPvM
dibromoacetic acid	631-64-1	0.1		4	99	26	26%	New	
diethylenetriaminepentaacetic acid (DTPA)	67-43-6	1		8	192	34	18%	List 1	Potential SVHC substance; potential vPvM & PMT
diisopropyl ether	108-20-3	1		9	804	123	15%	List 1	Clear emitting source (Société de Prayon, Engis); vPvM & PMT
di-n-butyltin	1002-53-5	0.1		5	385	132	34%	New	
ethylenediaminetetraacetic acid (EDTA)	60-00-4	1		9	378	176	47%	List 1	potential vPvM & PMT
fluoride	16984-48-8	1		8	924	11	1.2%	List 1	Remains on the list based on expert judgements
glyphosate	1071-83-6	0.1	0.1	10	537	78	15%	List 1	Above standard Dutch DWB
guanylurea	141-83-3	0.1		7	372	361	97%	List 1	
hydrochlorothiazide	58-93-5	0.1		5	141	6	4.3%	List 1	
ketoprofen	22071-15-4	0.1		3	83	4	4.8%	New	
lamotrigine	84057-84-1	0.1		3	160	11	6.9%	List 1	
melamine	108-78-1	1		6	409	206	50%	List 1	
metformin	657-24-9	0.1		7	425	419	99%	List 1	
metolachlor	51218-45-2	0.1	0.1	10	729	9	1.2%	List 3	
monobromoacetic acid	79-08-3	0.1		4	99	20	20%	New	
naproxen	22204-53-1	0.1		7	262	8	3.1%	List 3	Potential vPvM & PMT
N-formyl-4-aminoantipyrine	1672-58-8	0.1		4	157	28	18%	List 2	
nitriloacetic acid (NTA)	139-13-9	1		7	202	19	14%	List 1	Not PMT
PFAS (sum of 20 compounds considered a concern)	N/A	0.1		N/A	N/A	N/A	N/A	N/A	PFAS are included on List 1 because of their toxicological relevante. A drinking water standard is not yet formally implemented in the Netherlands
prosulfocarb	52888-80-9	0.1	0.1	5	186	53	28%	New	
sulfamic acid	5329-14-6	0.1		4	26	26	100%	New	Concentrations > 10 µg/L
terbuthylazine	5915-41-3	0.1	0.1	10	668	8	1.2%	List 1	
tramadol	27203-92-5	0.1		8	376	51	14%	List 1	
trifluoroacetic acid	76-05-1	1		3	127	25	20%	List 3	
valsartan	137862-53-4	0.1		7	275	22	8.0%	List 1	vPvM & PMT
valsartanic acid	164265-78-5	0.1		1	36	22	61%	List 1	BQ higher than 1

vPvM = very persistent, very mobile (UBA classification); PMT = persistent, mobile, toxic (UBA classification);
SVHC = substance of very high concern (EU REACH regulation)

1.2 Background information on substances List 1

Table 7 - Information on the parameters that define the total score for the drinking water relevant substances (List 1)

Substance name	Total score	Max (µg/L)	(p)GLV (µg/L)	BQ	BQ score	Log K_{ow}		VP (mm Hg)		BIOWIN3		Exc. LS or T/O T	Reference (p)GLV
1,4-dioxane	18	1.50	3.0	0.50	12	**-0.42**	3	3.81E+01	1	2.99	2	0	https://rvszoeksysteem.rivm.nl
AMPA	11	21	1500	0.01	0	-2.47	3	5.76E-05	3	2.98	2	3	RIVM (exemption)
benzothiazole	13	0.56	36	0.02	6	2.01	2	7.42E-02	3	2.90	2	0	Ginsberg et al., 2011
bromate	>12	7.1	0.14a	50.7	12	N/A	-	N/A	-	N/A	-	0	Smit, 2021
chloridazone-desphenyl	11	2.36	700	0.003	0	-1.59	3	4.23E-06	3	2.73	2	3	ADI of 0.1 mg/kg bw/day (EFSA, 2007a)
cyanuric acid	14	2.40	9100	<0.001	6	-1.31	3	4.40E-11	3	2.91	2	0	ADI of 1.3 mg/kg bw/day (EFSA, 2010)
dibromoacetic acid	19	2.10	5.0	0.42	12	0.7	2	2.30E-02	3	3.14	2	0	OEHHA Canada, 2020
DTPA	13	18	700	0.03	6	**-4.91**	3	1.21E-16	3	3.39	1	0	https://rvszoeksysteem.rivm.nl
diisopropyl ether	10	28	1400	0.02	6	**2.40**	2	**1.49E+02**	0	2.96	2	3	https://rvszoeksysteem.rivm.nl
di-n-butyltin	12	1.37	14	0.10	6	1.49	2	1.68E+00	3	3.28	1	0	DNEL of 0.002 mg/kg bw day for dibutyltin dichloride and dibutyltin oxide (CAS 683-18-1/818-08-6) (REACH registration file)
EDTA	13	52	600	0.09	6	**-3.86**	3	**1.50E-12**	3	3.50	1	0	https://rvszoeksysteem.rivm.nl
fluoride	0	1.70	1500	0.001	0	N/A	-	N/A	-	N/A	-	0	WHO, 2017
glyphosate	11	1.60	1500	0.001	0	-3.40	3	1.58E-08	3	3.21	2	3	RIVM (exemption)
guanylurea	20	6.70	23	0.30	12	-1.22	3	8.68E-04	3	2.97	2	0	https://rvszoeksysteem.rivm.nl
hydrochlorothiazide	15	0.30	6.0	0.05	6	-0.07	3	1.78E-10	3	2.20	3	0	https://rvszoeksysteem.rivm.nl
ketoprofen	12	0.18	7.0	0.03	6	3.12	1	1.46E-06	3	2.93	2	0	Based on ADI of **1.0 µg/kg/day** in Khan and Nicell, 2015
lamotrigine	20	0.14	0.53	0.26	12	2.57	2	9.41E-09	3	1.95	3	0	Based on ADI of **0.15 µg/kg/day** in Khan and Nicell, 2015
melamine	14	20	350	0.06	6	**-1.22**	3	**8.93E-08**	3	2.27	2	0	https://rvszoeksysteem.rivm.nl
metformin	14	2.53	196	0.01	6	-2.64	3	7.58E-05	3	2.91	2	0	https://rvszoeksysteem.rivm.nl
metolachlor	14	0.21	10	0.02	6	2.9	2	3.14E-05	3	2.19	3	0	WHO, 2017
monobromoacetic acid	12	0.27	25	0.01	6	0.41	2	1.19E-01	3	3.29	1	0	OEHHA Canada, 2020; DNEL of 0.05 mg/kg lg/day (REACH registration file)
naproxen	12	0.28	10	0.03	6	3.18	1	1.27E-06	3	2.92	2	0	Based on ADI of **1.43 µg/kg/day** in Khan and Nicell 2015
N-formyl-4-aminoantipyrine	13	0.20	10	0.02	6	0.50	2	1.28E-08	3	2.66	2	0	TTC (as determined by RIVM for the structurally related substance AAA)
NTA	13	7.70	400	0.02	6	**-3.81**	3	7.16E-09	3	3.62	1	0	https://rvszoeksysteem.rivm.nl
PFAS (sum of 20 compounds considered a concern)b	N/A	N/A	0.004c	N/A	-	N/A	-	N/A	-	N/A	-	N/A	Van der Aa et al., 2021
prosulfocarb	12	2.76	35	0.08	6	4.65	1	5.18E-07	3	2.62	2	0	ADI of 0.005 mg/kg bw/day (EFSA, 2007b)
sulfamic acid	7	97	35000	0.003	0	0.10	2	6.00E-03	3	2.98	2	0	DNEL of 5 mg/kg bw/day day (REACH registration file)
terbuthylazine	13	0.15	7.0	0.02	6	3.40	1	6.75E-07	3	1.76	3	0	WHO, 2017
tramadol	14	0.23	4.9	0.05	6	2.53	2	4.57E-07	3	2.09	3	0	Based on ADI of **1.4 µg/kg/day** in Khan and Nicell 2015
trifluoroacetic acid	10	1.70	35	0.05	6	0.5	2	1.16E+02	0	2.80	2	0	RIVM (exemption)
valsartan	25	0.90	0.20	4.5	18	**1.20**	2	**8.18E-16**	3	2.85	2	0	Based on ADI of **0.057 µg/kg/day** in Khan and Nicell 2015
valsartanic acid	25	0.29	0.10	2.9	18	1.83	2	8.51E-11	3	2.70	2	0	TTC-waarde

Max = maximum concentration in the Meuse in 2016-2020; (p)GLV=provisional guideline value; BQ = benchmark quotiënt; VP= vapor pressure; Exc. LS of T/O T = Exceedance legal standard or taste/odour threshold; TTC = threshold of toxicological concern. Log Kow and VP values in bold are experimental values, otherwise they are estimated. Values in grey are from the EPI Suite database; values in blue from the REACH dossier. DIPE is the only substance with an exceedance of its odour threshold of <10 µg/L (Smit and Wuijts, 2012)

a This Is not an official drinking water guideline. It is based on the negligible risk limit of 0.005 µg/kg bw/day and a allocation of 80% to drinking water
b The 20 individual compounds are mentioned in the European Drinking Water Directive (https://eur-lex.europa.eu/eli/dir/2020/2184/oj). It is not possible to provide the information for a group parameter
c The pGLV of 4 ng/L is expressed as ng PFOA-equivalents per liter and is derived by RIVM based on the tolerable weekly intake calculated by EFSA.

1.3 Background information on substances List 2a

Table 8 - Information on the candidate drinking water relevant substances for monitoring (List 2a). Source refers to literature, monitoring or screening data from where the candidate substance was selected

Substance name	CAS	Source	Remarks
1,2,4-triazole	288-88-0	Berger et al., 2018	SVHC substance, PMT
1,3-di-o-tolylguanidine	97-39-2	Schultze et al., 2019	vPvM & PMT
4-aminophenol	123-30-8	Berger et al., 2018	Potential SVHC substance
4-mesyl-2-nitrotoluene	1671-49-4	Berger et al., 2018	vPvM & PMT
bisphenol-F	620-92-8	Steenbeek et al., 2020	Potential SVHC substance, BPF is the most important substitute for Bisphenol A
candesartan	139481-59-7	Monitoring data	vPvM & PMT
chlorate	14866-68-3	Monitoring data	
dichloromethane sulfonic acid	53638-45-2	Monitoring data	
fexofenadine	83799-24-0	Screening	
fluconazole	86386-73-4	Screening	
methylglycindi acedic acid (MGDA)	164462-16-2	IAWR ,2019	
N-acetyl-4-aminoantipyrine	83-15-8	Monitoring data	
oxipurinol	2465-59-0	Monitoring data	
ritalinic acid	19395-41-6	Screening	

vPvM = very persistent, very mobile (UBA classification); PMT = persistent, mobile, toxic (UBA classification); SVHC = substance of very high concern (EU REACH regulation)

1.3 Background information on substances List 2a

Table 9 - Information on the parameters that define the total score for the candidate drinking water relevant substances for monitoring (List 2a)

Substance name	Total score	Max (µg/L)	(p)GLV (µg/L)	BQ	BQ score	Log K_{ow}		VP (mm Hg)		BIOWIN3		Exc. LS or T/O T	Reference (p)GLV
1,2,4-triazole	14	10	560	0.02	6	-0.58	3	6.27E-02	3	3.05	2	0	Based on DNEL of 0.08 mg/kg bw/day in REACH registration file
1,3-di-o-tolylguanidine	12	10	350	0.03	6	3.88	1	3.61E-06	3	2.39	2	0	Based on DNEL of 0.05 mg/kg bw/day in REACH registration file
4-aminophenol	13	10	700	0.01	6	0.04	2	4.00E-05	3	2.88	2	0	Based on NOAEL of 10 mg/kg bw/day in REACH registration file
4-mesyl-2-nitrotoluene	13	10	525	0.02	6	**0.93**	2	1.64E-05	3	2.48	2	0	Based on DNEL of 0.075 mg/kg bw/day in REACH registration file
bisphenol-F	13	1	28	0.04	6	2.91	2	3.72E-07	3	2.79	2	0	EFSA, 2015a (based on temporary TDI of bisphenol A)
candesartan	24	0.12	0.01	24.8	18	4.79	1	1.79E-18	3	2.26	2	0	Based on ADI of 0.0014 µg/kg/day in Khan and Nicell 2015
chlorate	21	18	70	0.26	12	N/A	3	negligible	3	N/A	3	0	RIVM, 2018
dichloromethane sulfonic acid	26	0.23	0.10	2.3	18	-0.47	3	1.87E-04	3	2.68	2	0	TTC
fexofenadine	14	1	12	0.08	6	2.81	2	9.51E-19	3	1.98	3	0	DDD of 120 mg/dag and UF = 1000
fluconazole	20	1	2.0	0.49	12	0.50	2	6.78E-09	3	1.50	3	0	Based on ADI of.**29 µg/kg/day** in Khan and Nicell 2015
MGDA	13	10	287	0.03	6	-7.2	3	4.85E-15	3	3.58	1	0	NICNAS, 2004
N-acetyl-4-aminoantipyrine	14	0.14	10	0.01	6	-0.13	3	6.14E-09	3	2.62	2	0	https://rvszoeksysteem.rivm.nl
oxipurinol	20	0.91	8.0	0.11	12	-0.28	3	9.91E-08	3	2.98	2	0	https://rvszoeksysteem.rivm.nl
ritalinic acid	26	1	0.25	4.0	18	-1.07	3	6.23E-10	3	3.05	2	0	Based on ADI of **0.036 µg/kg/day** for the parent substance methylphenidate in Khan en Nicell (2015)

Max = maximum concentration in the Meuse in 2016-2020; (p)GLV=provisional guideline value; BQ = benchmark quotiënt; VP= vapor pressure; Exc. LS of T/O T = Exceedance legal standard or taste/odour threshold; TTC = threshold of toxicological concern. Log Kow and VP values in bold are experimental values, otherwise they are estimated. Values in grey are from the EPI Suite database; values in blue from the REACH dossier. DIPE is the only substance with an exceedance of its odour threshold of <10 µg/L (Smit and Wuijts, 2012)

a This Is not an official drinking water guideline. It is based on the negligible risk limit of 0.005 µg/kg bw/day and a allocation of 80% to drinking water

b The 20 individual compounds are mentioned in the European Drinking Water Directive (https://eur-lex.europa.eu/eli/dir/2020/2184/oj). It is not possible to provide the information for a group parameter

c The pGLV of 4 ng/L is expressed as ng PFOA-equivalents per liter and is derived by RIVM based on the tolerable weekly intake calculated by EFSA.

1.4 Background information on substances List 2b

Table 10 - Information on the candidate drinking water relevant substances for screening (List 2b). Source refers to literature, monitoring or screening data from where the candidate substance was selected

Substance name	CAS	Source	Remarks
10-hydroxy-amitriptyline	1246833-15-7	Deere et al., 2020	High concentrations in effluent
4-amino-3-hydroxybenzoic acid	2374-03-0	Angeles et al., 2021	High concentrations in surface water Europe
adamantan-1-amine	768-94-5	Schultze et al., 2019	Scarcely investigated and high frequency of detection; PMT
β-asarone	5273-86-9	Picardo et al., 2020	High concentrations in surface water Europe
benzovindiflupyr	1072957-71-1	Kraamer-Ouwehand, 2020	
cyanoguanidine	461-58-5	Schultze et al., 2019	Scarcely investigated and high frequency of detection; PMT
cyanopropanal	3515-93-3	Discharge permit Sitech	
ethyldimethylcarbamate	687-48-9	Scheurer and Fleig, 2020	
gamma-cyhalothrin	76703-62-3	Kraamer-Ouwehand, 2020	
gliclazide	21187-98-4	GIPDatabank	
isofetamid	875915-78-9	Kraamer-Ouwehand, 2020	
kojic acid	501-30-4	Picardo et al., 2020	High concentrations in surface water Europe
levothyroxine	51-48-9	GIPDatabank	
mefentrifluconazole	1417782-03-6	Kraamer-Ouwehand, 2020	
oxathiapiprolin	1003318-67-9	Kraamer-Ouwehand, 2020	
p-toluenesulfonic acid	104-15-4	Schultze et al., 2019/ Kiefer et al., 2021	Scarcely investigated and high frequency of detection
pyriofenone	688046-61-9	Kraamer-Ouwehand, 2020	
toluenesulfonamide (ortho)	88-19-7	Schultze et al., 2019	Scarcely investigated and high frequency of detection; PMT
toluenesulfonamide (para)	70-55-3	Schultze et al., 2019	Scarcely investigated and high frequency of detection; not PMT

PMT = persistent, mobile, toxic (UBA classification)

1.4 Background information on substances List 2b

Table 11 - Information on the parameters that define the total score for the candidate drinking water relevant substances for screening (List 2b)

Substance name	Total score	Max (µg/L)	(p)GLV (µg/L)	BQ	BQ score	Log K_{ow}		VP (mm Hg)		BIOWIN3		Exc. LS or T/O T	Reference (p)GLV
10-hydroxy-amitriptyline	**24**	1	**0.10**	**10**	**18**	**3.41**	**1**	**2.37E-09**	**3**	**2.38**	**2**	0	**TTC**
4-amino-3-hydroxybenzoic acid	**25**	10	**0.1**	**100**	**18**	**0.5**	**2**	**4.62E-07**	**3**	**2.87**	**2**	0	**TTC**
adamantan-1-amine	**19**	1	**4.9**	**0.20**	**12**	**2,44**	**2**	**3,98E-03**	**3**	**2.68**	**2**	0	Based on ADI of **1.4 µg/kg/day** in Khan and Nicell 2015
β-asarone	**24**	10	**0.1**	**100**	**18**	**3.03**	**1**	**1.09E-03**	**3**	**2.56**	**2**	0	**TTC**
benzovindiflupyr	**10**	1	**350**	**0.003**	**0**	**4.30**	**1**	**3.03E-10**	**3**	**1.77**	**3**	**3**	**EFSA, 2015b**
cyanoguanidine	**8**	10	**22750**	**0.000**	**0**	**-1,15**	**3**	**1,64E-03**	**3**	**3.01**	**2**	0	Based on DNEL of 6.5 mg/kg bw/day in REACH registration file
cyanopropanal	**26**	10	**0.1**	**100**	**18**	**-0.65**	**3**	**1.16E+00**	**3**	**2.96**	**2**	0	TTC
ethyldimethylcarbamate	**25**	1	**0.01**	**100**	**18**	**0.89**	**2**	**1.24E+01**	**3**	**2.89**	**2**	0	TTC
gamma-cyhalothrin	**12**	1	**17.5**	**0.057**	**6**	**6.80**	**0**	**1.50E-09**	**3**	**1.33**	**3**	**3**	EFSA, 2014
gliclazide	**19**	1	**7.7**	**0.13**	**12**	**2.12**	**2**	**1.23E-09**	**3**	**2.41**	**2**	0	Based on ADI of **1.1 µg/kg/day** in Khan and Nicell 2015
isofetamid	**10**	1	**140**	**0.007**	**0**	**5.58**	**1**	**1.98E-10**	**3**	**1.91**	**3**	**3**	**EFSA, 2015c**
kojic acid	**20**	10	**42**	**0.24**	**12**	**-0.64**	**3**	**7.68E-07**	**3**	**3.17**	**2**	0	**SCCP, 2008**
levothyroxine	**25**	1	**0.013**	**77**	**18**	**4.12**	**1**	**2.05E-16**	**3**	**1.61**	**3**	0	**Based on LOTD of 12.5 µg/day (Farmacotherapeutischkompas)**
mefentrifluconazole	**10**	1	**245**	**0.004**	**0**	**4.56**	**1**	**1.36E-10**	**3**	**1.33**	**3**	**3**	**EFSA, 2018**
oxathiapiprolin	**10**	1	**980**	**0.001**	**0**	**5.74**	**1**	**5.64E-13**	**3**	**0.48**	**3**	**3**	**EFSA, 2016**
p-toluenesulfonic acid	**8**	10	**17500**	**0.001**	**0**	**-0.62**	**3**	**2.90E-06**	**3**	**2.89**	**2**	0	Based on DNEL of 2.5 mg/kg bw/day in REACH registration file
pyriofenone	**10**	1	**490**	**0.002**	**0**	**3.74**	**1**	**1.16E-08**	**3**	**1.57**	**3**	**3**	**EFSA, 2013**
toluenesulfonamide (ortho)	**25**	10	**1.5**	**7**	**18**	**0.84**	**2**	**6.06E-05**	**3**	**2.75**	**2**	0	**TTC**
toluenesulfonamide (para)	7	10	**11200**	**0.001**	**0**	**0.82**	**2**	**9.56E-05**	**3**	**2.75**	**2**	0	Based on DNEL of 1.6 mg/kg bw/day in REACH registration file

Max in red = virtual estimated value based on literature; (p)GLV=provisional guideline value; BQ = benchmark quotiënt; VP= vapor pressure; Exc. LS of T/O T = Exceedance legal standard or taste/odour threshold; TTC = threshold of toxicological concern. Log Kow and VP values in bold are experimental values, otherwise they are estimated. Values in black are from the EPI Suite database, values in blue from the REACH dossier. Values in red under legal standard exceedance indicate a potential exceedance.

1.5 Considered candidate substances with a score below 10

Table 12 - Information on the parameters that define the total score for the candidate drinking water relevant substances

Substance name	Total score	Max (µg/L)	(p)GLV (µg/L)	BQ	BQ score	Log K_{ow}		VP (mm Hg)		BIOWIN3		Exc. T/O T	Reference (p)GLV
2,4-dimethylbenzenesulfonic acid	**8**	<		<	**0**	-0.07	3	3.96E-06	3	2.78	2	**0**	-
2-buthoxyethanol (EGBE)	**6**	1	**44100**	**0.00002**	**0**	**0.81**	2	**8.80E-01**	3	3.39	1	**0**	Based on DNEL of 6.3 mg/kg bw/day in REACH registration file
4-dodecylbenzenesulfonic acid	**6**	1	**700**	**0.001**	**0**	4.78	1	7.93E-11	3	2.84	2	**0**	Based on NOAEL of 100 mg/kg bw/day in REACH registration file
4-methyl-7-ethylaminocoumarin	**7**	1	**525**	**0.002**	**0**	2.18	2	1.67E-05	3	2.76	2	**0**	**ECC Canada, 2020 (Read across 91-44-1)**
5-amino-2-chlorotoluene-4-sulfonic acid (CLT-acid)	**8**	10	**7000**	**0.001**	**0**	**-0.83**	3	1.55E-08	3	2.44	2	**0**	**EC Canada, 2016 (Red Lake C Amine)**
ATMP salt = [nitrilotris(methylene)] trisphosphonic acid, sodium salt	**8**	15	**19250**	**0.001**	**0**	-8.34	3	2.06E-11	3	2.28	2	**0**	Based on NOAEL of 275 mg/kg bw/day in REACH registration file
benzoguanamine	**7**	1	**665**	**0.002**	**0**	1.36	2	1.24E-07	3	2.29	2	**0**	Based on DNEL of 0.095 mg/kg bw/day in REACH registration file
benzyldimethylamine	**7**	<		<	**0**	1.98	2	9.20E-01	3	2.67	2	**0**	-
benzylparaben	**6**	<		<	**0**	3.56	1	3.76E-06	3	2.91	2	**0**	-
benzyltrimethylammonium	**8**	<		<	**0**	-2,17	3	2.31E-08	3	2.81	2	**0**	-
bis(2-methoxyethoxy)methane	**8**	1	**5810**	**0.00017**	**0**	-0.69	3	8.78E-01	3	2.80	2	**0**	Based on DNEL of 0.83 mg/kg bw/day in REACH registration file
di-(2-ethylhexyl)phosphoric acid (DEHPA)	**6**	1	**1750**	**0.001**	**0**	**2,88**/6,07	1	1.80E-07	3	3.08	2	**0**	Based on DNEL of 0.25 mg/kg bw/day in REACH registration file
diethylene glycol dibenzoate	**6**	1	**5600**	**0.00018**	**0**	**3.20**	1	1.30E-07	3	2.82	2	**0**	Based on DNEL of 0.8 mg/kg bw/day in REACH registration file
dimethylbenzenesulfonic acid	**8**	<		<	**0**	-1.86	3	1.14E-11	3	2.78	2	**0**	
ethylparaben	**7**	1	**52500**		**0**	2,47	2	9,29E-05	3	3.10	2	**0**	Based on DNEL of 12.5 mg/kg bw/day in REACH registration file
gadobutrol	**9**	1	**423**	**0.002**	**0**	-7.05	3	3.47E-23	3	2.05	3	**0**	**Based on dosing administration of 0,1 mmol/kg**
gadoterate	**9**	1	**391**	**0.003**	**0**	-6.84	3	2.79E-16	3	2.03	3	**0**	**Based on dosing administration of 0,1 mmol/kg**
linezolide	**8**	1	**900**	**0.001**	**0**	1.26	2	2.03E-10	3	1.68	3	**0**	**Based on LOTD of 30 mg/kg/day for children (assuming 30 kg lg) (Rxlist.com)**
methacrylamido propyl trimethyl ammonium	**8**	<		<	**0**	-2.58	3	6.66E-10	3	2.66	2	**0**	
methyl sulfate	**8**	<		<	**0**	-3.71	3	4.38E-09	3	2.95	2	**0**	
methylparaben	**7**	1	**14560**		**0**	1,96	2	8,55E-04	3	3.06	2	**0**	Based on DNEL of 2.08 mg/kg bw/day in REACH registration file
nitrobenzenesulfonate	**8**	10	**3500**	**0.003**	**0**	**-2.61**	3	7.75E-02	3	2.72	2	**0**	Based on DNEL of 0.5 mg/kg bw/day in REACH registration file
phthalic acid	**7**	1	**35000**	**0.00003**	**0**	**0.73**	2	6.36E-07	3	3.01	2	**0**	Based on DNEL of 5 mg/kg bw/day in REACH registration file
sparfloxacin	**9**	1	**200**	**0.005**	**0**	-0.02	3	7.59E-15	3	1.24	3	**0**	**Based on LOTD of 200 mg/day (https://www.rxlist.com)**
steviol	**7**	1	**28000**	**0.00004**	**0**	4.97	1	1.60E-09	3	2.01	3	**0**	**EFSA, 2011**
tetracycline	**9**	1	**210**	**0.005**	**0**	-1.30	3	2.08E-21	3	1.82	3	**0**	**WHO, 1999**
tetraethylene glycol	**8**	1	**23660**	**0.00004**	**0**	**-2.02**	3	**4.65E-05**	3	3.06	2	**0**	**Lowest NOAEL of 3380 mg/kg lg/day with UF of 1000 (REACH registration file)**
triacetin	7	1	5600	0.00018	0	**0.25**	2	**2.48E-03**	3	3.14	2	**0**	**US EPA, 201**2

Max in red =virtual indicative value based on literature; (p)GLV=provisional guideline value; BQ = benchmark quotiënt; VP= vapor pressure; Exc. T/O T = Exceedance taste/odour threshold; TTC = threshold of toxicological concern. Log Kow and VP values in bold are experimental values, otherwise they are estimated. Values in black are from the EPI Suite database, values in blue from the REACH dossier.

1.6 No longer relevant substances - List 3

Table 13 - Complete list of no longer drinking water relevant substances (including the substances from the previous evaluations in 2015 and 2018))

Substance name	CAS	List 2018
1,2-Benzisothiazol-3(2H)-one	2634-33-5	List 3
1,3-Diethyldiphenylurea	85-98-3	List 3
1,3-Diphenylguanidine	102-06-7	List 3
10,11-Dihydro-10,11-dihydroxycarbamazepine	58955-93-4	New
1H-Benzotriazole	95-14-7	List 3
2-(Methylthio)benzothiazole	615-22-5	New
2,2,6,6-Tetramethyl-4-oxopiperidinonoxy	2896-70-0	List 2
2,3,3,3-Tetrafluoro-2-(heptafluorpropoxy) propanoate (GenX substance)	62037-80-3	List 2
2,4-D (2,4-dichlorophenoxyacetic Acid)	94-75-7	List 3
2'-Aminoacetophenone	551-93-9	New
3,5,6-Trichloro-2-pyridinol (TCP)	6515-38-4	List 2
4-Methylbenzotriazole	29878-31-7	New
4-n-Nonyl phenol	104-40-5	List 3
Acesulfame-K	55589-62-3	List 3
Acetaminophen (paracetamol)	103-90-2	New
Acetone	67-64-1	List 3
AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline)	1506-02-01	List 3
Amidotrizoic acid	117-96-4	List 1
Amoxicillin	26787-78-0	List 3
Anti-androgenic activity (expressed in flutamide-equivalents)	N/A	List 2
Aspirin (acetylsalicylic acid)	50-78-2	List 3
Azelaic acid	123-99-9	List 3
BAM (2,6-dichlorobenzamide)	2008-58-4	List 3
Barbital	57-44-3	List 3
BBP (butylbenzylphtalate)	85-68-7	List 3
Benzo(a)pyrene	50-32-8	List 1
Bis(2-chloroisopropyl) ether	39638-32-9	New
Bisphenol A	80-05-7	List 1
BPS (4,4'-sulfonyldiphenol)	80-09-1	List 3
Caffeine	58-08-2	List 3
Carbamazepine	298-46-4	List 3
Carbendazim	10605-21-7	List 3
Cetirizine	83881-51-0	List 2
Chloridazon	1698-60-8	List 3
Chlorotoluron	15545-48-9	List 3
Ciprofloxacin	85721-33-1	List 3
Citalopram	59729-33-8	List 2
Clarithromycin	81103-11-9	List 3
Clindamycin	18323-44-9	List 3
DBP (dibutyl phthalate)	84-74-2	List 3
DEP (diethyl phthalate)	84-66-2	List 3
DIBP (di-(2-methyl-propyl)phthalate)	84-69-5	List 3
Diclofenac	15307-86-5	List 3
Diglyme (bis(2-methoxyethyl)ether)	111-96-6	List 3
Dimethenamid	87674-68-8	List 3
Dimethyldisulfide	624-92-0	New
Diuron (DMCU)	330-54-1	List 3
DMSA (N,N-dimethylaminosulfanilide)	4710-17-2	List 3
Erythromycin	114-07-8	List 3
Estrogenic activity (expressed in 17β-estradiol-equivalents)	not applicable	List 3
Estrone	53-16-7	List 3
ETBE (ethyl-tertiairy-butyl-ether)	637-92-3	List 3
Ethyl sulphate	540-82-9	List 2
Gabapentin	60142-96-3	List 1
Galaxolide (HHCB)	1222-05-5	List 3
Glucocorticoid activity (expressed in dexamethasone-equivalents)	-	List 3
Hexa(methoxymethyl)melamine	68002-20-0/ 3089-11-0	List 2
Ibuprofen	15687-27-1	List 3
Iohexol	66108-95-0	List 1
Iomeprol	78649-41-9	List 1
Iopamidol	60166-93-0	List 1
Iopromide	73334-07-3	List 1
Ioxaglic acid	59017-64-0	List 3
Ioxitalamic acid	28179-44-4	List 1
Irbesartan	138402-11-6	List 2
Isoproturon	34123-59-6	List 3
Lincomycin	154-21-2	List 3
MCPA (4-chloro-2-methylphenoxyacetic acid)	94-74-6	List 3
Mecoprop (MCPP)	93-65-2	List 3
Metazachlor	67129-08-2	List 3
Metazachlor-ethane sulfonic acid	172960-62-2	List 2
Metazachlor-oxanilic acid	1231244-60-2	List 2
Methenamine/urotropine/hexamine	100-97-0	List 3
Methoxymethyltriphenylphosphonium	4009-98-7	List 2
Methyl-desfenylchloridazon	17254-80-7	List 3
Metolachlor-ethane sulfonic acid	171118-09-5	List 2
MTBE (methyl-tert-butylether)	1634-04-04	List 3
Musk (ketone)	81-14-1	List 3
Musk (xylene)	81-15-2	List 3
N,N-dimethylsulfamid (DMS)	3984-14-3	List 1
N-butylbenzenesulphonamide	3622-84-2	List 3
NDMA (nitrosodimethylamine)	62-75-9	List 3

1.6 No longer relevant substances - List 3

Substance name	CAS	List 2018
Nicosulfuron	111991-09-4	List 3
O-desmethylvenlafaxine	93413-62-8	List 2
Oxadiazon	19666-30-9	List 3
Pentobarbital	76-74-4	List 3
Phenanthrene	85-01-8	List 3
Phenazone	60-80-0	List 3
Phenobarbital	50-06-6	List 3
Pyrazole	288-13-1	List 1
Salicylic Acid	69-72-7	List 3
Sebuthylazine	7286-69-3	List 2
Sotalol	3930-20-9	List 1
Sucralose	56038-13-2	List 3
Sulfamethoxazole	723-46-6	List 3
Surfynol 104	126-86-3	List 3
TBP (tributylphosphate)	126-73-8	List 3
TCEP (tris(2-chloroethyl) phosphate)	115-96-8	List 3
TCPP (tri-(2-chloroisopropyl) phosphate)	13674-84-5	List 3
Telmisartan	144701-48-4	List 2
Tetrachloroethene	127-18-4	New
Tetrahydrofuran	109-99-9	New
Thiabendazole	148-79-8	New
Tolyltriazole	29385-43-1	List 3
Triamcinolonehexacetonide	5611-51-8	List 3
Tribromomethane	75-25-2	New
Trichloroacetic acid (TCA)	76-03-9	List 3
Trichloroethene	79-01-6	New
Trichloromethane	67-66-3	New
Trifluoromethanesulfonic acid (F3-MSA)	1493-13-6	List 3
Triflusulfuron-methyl	126535-15-7	New
Triisobutyl phosphate	126-71-6	List 3
Triphenylphosphine oxide (TPPO)	791-28-6	List 3
Venlafaxine	93413-69-5	List 2
Vigabatrin	60643-86-9	List 2
Vinylchloride	75-01-4	List 3

1.7 No longer relevant substances - List 3

Table 14 - Companies that have an analytical substance available for the substances on List 2a

Substance name	CAS	Company
1,2,4-triazole	288-88-0	
1,3-di-o-tolylguanidine	97-39-2	
4-aminophenol	123-30-8	
4-mesyl-2-nitrotoluene	1671-49-4	
bisphenol-F	620-92-8	
candesartan	139481-59-7	Het Waterlaboratorium
chlorate	14866-68-3	Het Waterlaboratorium
dichloromethane sulfonic acid	53638-45-2	KWR Watercycle Research Institute
fexofenadine	83799-24-0	Aqualab Zuid
fluconazole	86386-73-4	Aqualab Zuid
methylglycindi acedic acid (apha ADA, MGDA)	164462-16-2	Het Waterlaboratorium (from 2022)
N-acetyl-4-aminoantipyrine	83-15-8	Het Waterlaboratorium
oxipurinol	2465-59-0	Het Waterlaboratorium
ritalinic acid	19395-41-6	Aqualab Zuid

1.8 Literature list

List of consulted literature.

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Nontarget Screening Reveals Time Trends of Polar Micropollutants in a Riverbank Filtration System
https://doi.org/10.1021/acs.est.9b01750

Angeles et al. 2021
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https://doi.org/10.1016/j.jhazmat.2021.125369

Backe et al. 2021
Suspect and non-target screening of reuse water by large-volume injection liquid chromatography and quadrupole time-of-flight mass spectrometry
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HWL report 202007

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Chen et al. 2016
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Gani et al. 2021
Emerging contaminants in South African water environment- A critical review of their occurrence, sources and ecotoxicological risks
https://doi.org/10.1016/j.chemosphere.2020.128737

Golovko et al. 2021
Occurrence and removal of chemicals of emerging concern in wastewater treatment plants and their impact on receiving water systems
https://doi.org/10.1016/j.scitotenv.2020.142122

Hartmann et al. 2020
The effective design of sampling campaigns for emerging chemical and microbial contaminants in drinking water and its resources based on literature mining
https://doi.org/10.1016/j.scitotenv.2020.140546

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https://doi.org/10.1186/s13750-019-0177-z

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Konradt et al. 2020
Removal of Trace Organic Contaminants by Parallel Operation of Reverse Osmosis and Granular Activated Carbon for Drinking Water Treatment
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Analyse van de bijdrage van verschillende emissieroutes van gewasbeschermingsmiddelen aan de waterkwaliteit
KIWK 2020-12

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