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Analytical methods for possible WFD 1st watch list substances

Directive 2008/105/EC, as amended by
Directive 2013/39/EU in the field of water policy

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Abstract

Directive 2013/39/EU amending the Environmental Quality Standards Directive 2008/105/EC under the European Water Framework Directive (WFD) has introduced the new "Watch List" monitoring mechanism in order to collect high-quality Union-wide monitoring data for the purpose of supporting future prioritisation exercises. Diclofenac, 17-beta-estradiol, and 17-alpha-ethinylestradiol were identified in Directive 2013/39/EU for inclusion in the 1st Watch List. The Joint Research Centre (JRC) has been tasked with proposing seven substances as candidates for the completion of the 1st Watch List and identifying analytical methods for their monitoring. The procedure and criteria used to identify a short-list of substances for possible inclusion in the Watch List is described in the JRC Science and Policy Report "Development of the 1st Watch List under the Environmental Quality Standards Directive" (Carvalho et al., 2015). EU Member States and stakeholder groups had the opportunity to comment on the proposed substances and on the analytical methods, whose availability was a criterion for the selection of the compounds. The finally proposed 10 (groups of) substances for inclusion in the 1st Watch List are diclofenac, 17-beta-estradiol (E2) and estrone (E1), 17-alpha-ethinylestradiol (EE2), oxadiazon, methiocarb, 2,6-ditert-butyl-4-methylphenol, tri-allate, neonicotinoid insecticides as a group (imidacloprid, thiacloprid, thiamethoxam, clothianidin, acetamiprid), macrolide antibiotics (erythromycin, clarithromycin, azithromycin), and 2-ethylhexyl-4-methoxycinnamate. Analytical methods for additional substances were searched and investigated because they were among those considered for inclusion in the list, but either did not fulfil all selection criteria, in some cases because enough monitoring data were found to exist already, or were not ranked highly enough. These substances were trichlorfon, cyclododecane, aminotriazole (amitrole), dimethenamid-P, diflufenican, dichlofluanid, formaldehyde, triphenyl phosphate, tolylfluanid, ciprofloxacin, and free cyanide. Little or no information on analytical methods was found for trichlorfon, aminotriazole, cyclododecane, and tolylfluanid. For the other compounds analytical methods are available and published. Some of them have already been analysed in the aquatic environment. The analysis of free cyanide in water is difficult. The available analytical methods do not reach the proposed PNEC value of 0.26 µg/l.

List of Abbreviations

ASE	Accelerated solvent extraction (= PLE)
BHT	Butylated hydroxytoluene
DW	Drinking water
EHMC	Ethylhexyl methoxycinnamate
EQS	Environmental quality standard
FMOC-Cl	9-Fluorenylmethoxycarbonyl chloride
FW	Fresh water
GC	Gas chromatography
GC-MS	Gas chromatography mass spectrometry
GC-MS-MS	Gas chromatography (tandem) triple quadrupole mass spectrometry
GPC	Gel permeation chromatography
HH	Human health
HR	High resolution
HPLC	High pressure liquid chromatography
IC	Ion chromatography
LC	Liquid chromatography
LC-MS-MS	Liquid chromatography (tandem) triple quadrupole mass spectrometry
LOD	Limit of detection
LOQ	Limit of quantification
LLE	Liquid liquid extraction
MDL	Method detection limit
MS	Mass spectrometry
PAD	Pulsed amperometric detector
PLE	Pressurized liquid extraction (=ASE)
PNEC	Predicted no-effect concentration
QuEChERS	Quick, easy, cheap, effective, rugged, and safe
SBSE	Stir bar sorptive extraction
SLE	Solid liquid extraction
SPE	Solid-phase extraction
SPMDs	Semipermeable membrane devices
SW	Surface water
UV	Ultraviolet
WW	Waste water

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2. Summary

Directive 2013/39/EU amending the Environmental Quality Standards Directive 2008/105/EC under the European Water Framework Directive (WFD) has introduced the new “*Watch List*” monitoring mechanism in order to collect high-quality Union-wide monitoring data for the purpose of supporting future prioritisation exercises. Diclofenac, 17-beta-estradiol, and 17-alpha-ethinylestradiol were identified in Directive 2013/39/EU for inclusion in the 1st *Watch List*. The Joint Research Centre (JRC) has been tasked with proposing seven substances as candidates for the completion of the 1st *Watch List* and identifying analytical methods for their monitoring. The procedure and criteria used to identify a short-list of substances for possible inclusion in the *Watch List* is described in the JRC Science and Policy Report “Development of the 1st *Watch List* under the Environmental Quality Standards Directive” (Carvalho et al., 2015). EU Member States and stakeholder groups had the opportunity to comment on the proposed substances and on the analytical methods, whose availability was a criterion for the selection of the compounds. The finally proposed 10 (groups of) substances for inclusion in the 1st *Watch List* are diclofenac, 17-beta-estradiol (E2) and estrone (E1), 17-alpha-ethinylestradiol (EE2), oxadiazon, methiocarb, 2,6-ditert-butyl-4-methylphenol, tri-allate, neonicotinoid insecticides as a group (imidacloprid, thiacloprid, thiamethoxam, clothianidin, acetamiprid), macrolide antibiotics (erythromycin, clarithromycin, azithromycin), and 2-ethylhexyl-4-methoxycinnamate. Analytical methods for additional substances were searched and investigated because they were among those considered for inclusion in the list, but either did not fulfil all selection criteria, in some cases because enough monitoring data were found to exist already, or were not ranked highly enough. These substances were trichlorfon, cyclododecane, aminotriazole (amitrole), dimethenamid-P, diflufenican, dichlofluanid, formaldehyde, triphenyl phosphate, tolylfluanid, ciprofloxacin, and free cyanide. Little or no information on analytical methods was found for trichlorfon, aminotriazole, cyclododecane, and tolylfluanid. For the other compounds analytical methods are available and published. Some of them have already been analysed in the aquatic environment. The analysis of free cyanide in water is difficult. The available analytical methods do not reach the proposed PNEC value of 0.26 µg/l.

Analytical methods for the substances were searched for on the internet using *Science Direct*, *Scopus* and *Environmental Science & Technology*.

3. Introduction

According to the Environmental Quality Standards Directive 2008/105/EC (EU, 2008) as regards priority substances in the field of water policy, amended by Directive 2013/39/EU (EU, 2013), a new mechanism is needed to provide high-quality monitoring information on the concentrations of potentially polluting substances in the aquatic environment to support future prioritisation exercises in accordance with Article 16(2) of the Water Framework Directive (WFD) (EU, 2000), and thereby to improve the protection of the aquatic environment and of human health *via* the environment. The mechanism is aimed at emerging pollutants and other substances for which the available monitoring data are either insufficient or of insufficient quality for the purpose of identifying the risk posed across the EU. It involves including a limited number of such substances in a “*Watch List*”, and monitoring them EU-wide at selected representative monitoring stations over at least a 12-month period, and for up to four years. Frequent reviews of the list will ensure that substances are not monitored for longer than necessary, and that substances posing a significant risk at EU level are identified as candidate priority substances with as little delay as possible. Article 8b of the Environmental Quality Standards Directive sets out the information to be taken into account when identifying substances to include in the *Watch List*. The 1st list may contain a maximum of 10 substances or groups of substances and should indicate the monitoring matrices and the possible methods of analysis not entailing excessive costs for each substance. A suspected significant risk at Union level to, or *via*, the aquatic environment, and a lack of sufficient monitoring data are both regarded as conditions for a substance selection. However, three compounds, *i.e.* diclofenac, 17-beta-estradiol (E2), and 17-alpha-ethinylestradiol (EE2), have already been selected for inclusion in this first list for the purpose of facilitating the determination of appropriate measures to address the risk posed by those substances.

The Joint Research Centre (JRC) has been tasked with proposing seven substances as candidates for the completion of the first *Watch List* and identifying analytical methods for their monitoring. The procedure and criteria used to identify a short-list of substances for possible inclusion in the *Watch List* is described in the JRC Science and Policy Report “Development of the 1st Watch List under the Environmental Quality Standards Directive. Following these criteria, the initial list of substances selected as candidates for the *Watch List* comprises substances identified during the last review of the Priority Substances (PS) list, and substances directly proposed by Member States and other stakeholders (Carvalho et al., 2015).

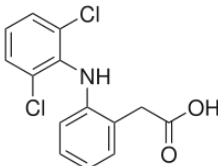
For the *Watch List* exercise it is sufficient that the method detection limit (MDL) of the analytical methods reaches the Environmental Quality Standards (EQSs) or Predicted No-Effect Concentrations (PNECs) of the substances; it is not necessary that the LOQ is 30 % (or less) than the EQS, as described in the QA/QC Directive 2009/90/EC.

4. Selected substances

Analytical methods for diclofenac, 17- α -ethinylestradiol and 17- β -estradiol were already given in the report “Analytical methods relevant to the European Commission's 2012 proposal on Priority Substances under the Water Framework Directive” (Loos, R. 2012). Some of this information is reproduced here, with updates marked in brown-green font.

The EQS for those substances were in the Commission's 2011 proposal (EU, 2011) for amending the priority substances list. The PNECs for the other substances have been copied from Carvalho et al. (2015).

4.1. Diclofenac

CAS Number 15307-86-5	Log K_{ow} 4.0-4.5	Water Solubility [g/l] 50
Chemical structure (MW 296.2) Non-steroidal anti-inflammatory drug (NSAID)	AA-EQS Inland (fresh) and other (salt) surface waters [$\mu\text{g/l}$]	MAC-EQS Inland (fresh) and other (salt) surface waters [$\mu\text{g/l}$]
	Fresh 0.1 $\mu\text{g/l}$ Salt 0.01 $\mu\text{g/l}$ = 10 ng/l	not applicable

Standard Methods

No analytical standard method is available for Diclofenac, but the EPA method 1694 can be applied (EPA 1694).

Description: EPA Method 1694 determines pharmaceuticals and personal care products (PPCPs) in environmental samples by high performance liquid chromatography combined with tandem mass spectrometry (HPLC-MS-MS) using isotope dilution and internal standard quantitation techniques. This method has been developed for use with aqueous, solid, and biosolids matrices.

Methods applied by EU Member States

Italy: LOQ: 10 ng/l; Internal Method, validated.

France: LOQ: 7 ng/l; Aqua-Ref Method; SPE-MS-MS; 1000 ml water; extraction with 500 mg Oasis HLB.

Analytical methods

Extraction (volume)	Analysis	LOD (Q) ($\mu\text{g/l}$)	Reference
SPE (0.4 l)	LC-MS-MS	LOQ: 0.010	Hao et al., 2006
SPE (surface water)	LC-MS-MS	LOD: 0.002 LOQ: 0.005	Gros et al., 2006
SPE (0.2 l); waste water	LC-ion-trap-MS-MS	LOD: 0.0004 LOQ: 0.001	Martínez Bueno et al., 2007
SPE (0.5 l)	LC-MS-MS	LOD: 0.001 LOQ: 0.007	Gros et al., 2009
SPE (0.1 l)	LC-ion-trap-MS-MS	LOD: 0.00015 LOQ: 0.00049	Grujic et al., 2009
SPE (0.1 l); surface water	LC-MS-MS	LOD: 0.0007 LOQ: 0.0024	Gros et al., 2012
SPE (0.5 l); river water	LC-MS-MS	LOD: 0.0041	Petrović et al., 2014

		LOQ: 0.0135	
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Conclusion

Diclofenac is often analysed together with other pharmaceuticals within multi-compound analytical methods based on SPE – LC-MS-MS. Methods already used in EU Member States and available literature shows that LOQ in the low ng/l range is achievable, which is sufficient to reach the proposed EQS for inland surface and other surface (coastal) waters. In addition, the JRC has fully validated a method for the analysis of diclofenac according to ISO 17025.

References

EPA Method 1694. December **2007**. Pharmaceuticals and personal care products in water, soil, sediment, and biosolids by HPLC/MS/MS. EPA-821-R-08-002. U.S. Environmental Protection Agency, Office of Water, Washington, DC, USA.

Gros, M., Petrovic, M., Barceló, D. **2006**. Development of a multi-residue analytical methodology based on liquid chromatography–tandem mass spectrometry (LC–MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. *Talanta* 70, 678–690.

Gros, M., Petrovic, M., Barceló, D. **2009**. Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/quadrupole-linear ion trap mass spectrometry and automated library searching. *Analytical Chemistry* 81, 898–912.

Gros, M., Rodríguez-Mozaz, S. Barceló, D. **2012**. Fast and comprehensive multi-residue analysis of a broad range of human and veterinary pharmaceuticals and some of their metabolites in surface and treated waters by ultra-high-performance liquid chromatography coupled to quadrupole-linear ion trap tandem mass spectrometry. *Journal of Chromatography A*, 1248, 104– 121.

Grujic, S., Vasiljevic, T., Lausevic, M. **2009**. Determination of multiple pharmaceutical classes in surface and ground waters by liquid chromatography–ion trap–tandem mass spectrometry. *Journal of Chromatography A*, 1216, 4989–5000.

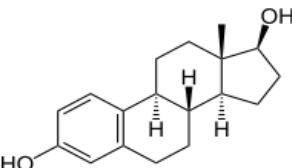
Hao, C., Lissemore, L., Nguyen, B., Kleywegt, S., Yang, P., Solomon, K. **2006**. Determination of pharmaceuticals in environmental waters by liquid chromatography/electrospray ionization/tandem mass spectrometry. *Analytical and Bioanalytical Chemistry* 384, 505–513.

Martínez Bueno, M.J., Agüera, A., Gómez, M.J., Hernando, M.D., García-Reyes, J.F., Fernández-Alba, A.R. **2007**. Application of liquid chromatography/quadrupole-linear ion trap mass spectrometry and time-of-flight mass spectrometry to the determination of pharmaceuticals and related contaminants in wastewater. *Analytical Chemistry* 79, 9372-9384.

Petrović, M., Škrbić, B., Živančev, J., Ferrando-Climent, L., Barcelo, D. **2014**. Determination of 81 pharmaceutical drugs by high performance liquid chromatography coupled to mass spectrometry with hybrid triple quadrupole–linear ion trap in different types of water in Serbia. *Science of the Total Environment* 468–469, 415–428.

4.2. 17-beta-Estradiol (E2) and Estrone (E1)

17-beta-estradiol (E2) is the predominant natural female sex hormone and is the most active of the naturally occurring estrogenic hormones and is also a key intermediate in industrial synthesis of other estrogens and of various hormonal 19-norsteroids.

CAS Number 50-28-2	Log K _{ow} 4.0	Water Solubility [mg/l] 1.7-3.6
Chemical structure (MW 272.4)	AA-EQS Inland (fresh) and other (salt) surface waters [µg/l]	MAC-EQS Inland (fresh) and other (salt) surface waters [µg/l]
	Fresh $4 \cdot 10^{-4} = 0.4 \text{ ng/l}$ Salt $8 \cdot 10^{-5} = 80 \text{ pg/l}$	not applicable

Standard Methods

MDL: $1 \cdot 10^{-4} \mu\text{g/l} = 0.1 \text{ ng/l}$ (sample volume: 1 l) ([EPA 1698](#));

LOD: 0.39 ng/l (sample volume: 1 l) ([EPA 539](#)).

Description: EPA Method 1698 determines steroids and hormones in environmental samples by isotope dilution and internal standard high resolution gas chromatography combined with high resolution mass spectrometry (HRGC/HRMS). EPA Method 1698 was developed for use with aqueous, solid, and biosolids matrices. This method involves solvent extraction of the sample (LLE for water samples), followed by cleanup with a layered alumina/florisil column, and an option to remove sulfur using copper. Following cleanup, the target analytes are derivatized to their trimethylsilyl-ethers using *N,O*-Bis(trimethylsilyl) trifluoroacetamide with trimethylchlorosilane (BSTFA: TMCS) to make them sufficiently volatile for analysis by GC/HRMS. Quantitation is performed by isotope dilution and internal standard techniques, depending on the analyte and the availability of labeled analogs ([EPA 1698](#)).

Description of EPA Method 539: Samples are dechlorinated with sodium thiosulfate and protected from microbial degradation using 2-mercaptopyridine-1-oxide sodium salt during sample collection. Samples are fortified with surrogates and passed through solid phase extraction (SPE) disks containing octadecyl (C18) functional groups in order to extract the method analytes and surrogates. The compounds are eluted from the solid phase with a small amount of methanol. The extract is concentrated to dryness with nitrogen in a heated water bath, and then adjusted to a 1-mL volume with 50:50 methanol:water after adding the internal standards. An aliquot of the sample is injected into an LC equipped with a C18 column that is interfaced to a MS/MS. The analytes are separated and identified by comparing the acquired mass spectra and retention times to reference spectra and retention times for calibration standards acquired under identical LC-MS/MS conditions. The concentration of each analyte is determined using the internal standard technique ([EPA 539](#)).

Methods applied by EU Member States

Italy: 0.9 ng/l; LC-MS/MS (IT: ISS); performance data on drinking waters (LOD) in the context of drinking water directive. The methods in some cases are from other MS. The methods are validated with ring-test.

France: LOQ: 0.5 ng/l; Aqua-Ref Method (SPE-MS-MS); see above.

LOQ: 2-4 ng/g for sewage sludge; Aqua-Ref Method (PFE/SPE/LC/MS-MS).

Literature methods

Steroid hormones are endocrine-disrupting compounds, which affect the endocrine system at very low concentrations; so interest in the sensitive determination of steroids in the environment has increased in recent years.

Recently a very comprehensive review on the analysis of steroid hormones in environmental samples has been published ([Tomsikova et al., 2012](#)); this review cites many other articles including LODs. It is discussed in detail how to enhance the sensitivity of analytical procedures for the determination of female steroid hormones (estrogens and progestogens) in environmental matrices. A number of steps in the analytical procedure, starting with the sample pre-treatment and ending with detection, could significantly contribute to enhancing sensitivity, so they need to be thoroughly optimized. The best results in analysis of estrogens and progestogens have been achieved with liquid chromatography (LC), as separation method, and tandem mass spectrometry (MS-MS), as detection method. Analysis using gas chromatography coupled to MS is discussed as well. Sample preparation depends on the kind of sample. Its optimization is important in reducing matrix interferences and plays a significant role in enhancing sensitivity. Liquid samples were most frequently prepared with off-line solid-phase extraction, while solid samples were also extracted by liquid-liquid, pressurized-

liquid, microwave and ultrasound extraction techniques. In several studies, derivatisation improved the sensitivity of LC-MS detection ([Tomsikova et al., 2012](#)).

Steroid estrogens and phenolic xenoestrogens are weak acids and their ionization on ESI and APCI are not very efficient compared with other more polar chemicals. Chemical derivatization can add on moieties improving ionization and enhance signals. Selective extraction, additional clean-up, efficient LC separation is important for the analysis of estrogens, because matrix effects can cause a loss in sensitivity. Dansyl chloride or pentafluorobenzyl bromide (PFBBBr) can react with phenolic groups, significantly improving sensitivity ([Lien et al., 2009](#)).

Lien and co-workers ([Lien et al., 2012](#)) compared the signal sensitivities and matrix effects of four ionization modes and four reversed phase liquid chromatographic (LC) systems on analyzing Estrone (E1), 17-beta-Estradiol (E2), Estriol (E3), 17-alpha-Ethinylestradiol (EE2), 4-Nonylphenol (NP), 4-tert-Octylphenol (OP), Bisphenol A (BPA) and their derivatives of dansyl chloride or pentafluorobenzyl bromide (PFBBBr) in water matrixes using a triple-quadrupole mass spectrometer with selected reaction monitoring (SRM). Dansylated compounds with ESI at UHPLC condition had the most intense signals and less matrix effects of the various combinations of ionization and LC systems ([Lien et al., 2009](#)).

Grover and co-workers compared GC-MS, GC-MS-MS, and LC-MS-MS for the analysis of steroidal estrogens in environmental water samples ([Grover et al., 2009](#)).

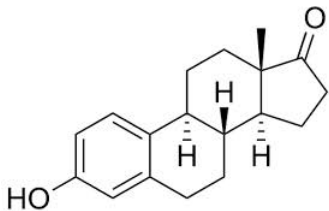
Analytical methods

Extraction (volume)	Analysis	LOD(Q) (ng/l)	Reference
On-line SPE; derivatisation	LC-MS-MS	0.4	Salvador et al., 2007
SPE (0.25 l); clean-up with florisil	LC-MS-MS (derivatisation)	LOQ: 0.26	Matejcek and Kuban, 2008
SPE (1 l)	LC-MS-MS	MDL: 0.01	Vulliet et al., 2008
SPE (2 l)	GC-MS-MS (derivatisation) LC-MS-MS	0.3 0.4	Grover et al., 2009
C18 speedisks	UHPLC-MS-MS	0.81	Lien et al., 2009
SPE (0.25 l); clean-up with florisil	LC-MS-MS	LOQ: 0.6	Miège et al., 2009
SPE (2 l)	UHPLC-MS-MS	0.10	Chang et al., 2011
SPE disks (C18 + SDB); silica clean-up (4 L)	GC-MS (derivatisation)	0.54	Wang et al., 2012
SPE (SDB); clean-up with GPC (1-2 L)	LC-MS-MS	0.05	Williams et al., 2012
SPE disks (C18); clean-up with florisil (0.5 L)	GC-MS-MS (derivatisation)	0.8	Alvarez et al., 2013
SPE (Oasis HLB 200mg); silica gel column clean-up; pH3 (2 L)	LC-MS-MS	0.11	Li et al., 2013
On-line SPE (EQuan Hypersil GOLD column, 20 × 2.1 mm) (5 mL)	UHPLC-MS-MS	0.12	Esteban et al., 2014

Conclusion

See under “17-alpha-ethinylestradiol”.

Estrone

CAS: 53-16-7 Estrogenic hormone and oxidation product of estradiol $PNEC_{fw} = 0.0036 \mu\text{g/l} = 3.6 \text{ ng/l}$	
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Analytical methods

Extraction (volume)	Analysis	LOD(Q) (ng/l)	Reference
On-line SPE derivatisation	LC-MS-MS	0.4	Salvador et al., 2007
SPE (0.25 l); clean-up with florisil	LC-MS-MS (derivatisation)	0.23	Matejcek and Kuban, 2008
SPE (1 l)	LC-MS-MS	0.02	Vulliet et al., 2008
SPE (2 l)	GC-MS-MS (derivatisation) LC-MS-MS	0.3 0.6	Grover et al., 2009
C18 speedisks	UHPLC-MS-MS (derivatisation)	0.64	Lien et al., 2009
SPE (0.25 l); clean-up with florisil	LC-MS-MS	0.4	Miège et al., 2009
SPE (2 l); clean-up with florisil	UHPLC-MS-MS	0.20	Chang et al., 2011
SPE disks (C18 + SDB); silica clean-up (4 L)	GC-MS (derivatisation)	0.41	Wang et al., 2012
SPE (SDB); clean-up with GPC (1-2 L)	LC-MS-MS	0.05	Williams et al., 2012
SPE disks (C18); clean-up with florisil (0.5 L)	GC-MS-MS (derivatisation)	0.8	Alvarez et al., 2013
SPE (Oasis HLB 200mg); silica gel column clean-up; pH3 (2 L)	LC-MS-MS	0.10	Li et al., 2013
On-line SPE (EQuan Hypersil GOLD column, 20 × 2.1 mm) (5 mL)	UHPLC-MS-MS	0.17	Esteban et al., 2014

Conclusion

Estrone is usually analysed together with 17-beta-estradiol and 17-alpha-ethinylestradiol. Environmental concentrations of estrone are often 10 times higher than for estradiol (E2), which is the reason why it is detected more often. The PNEC of 3.6 ng/l is achievable by SPE – GC-MS or LC-MS-MS techniques. It is recommended to monitor estrone (E1) in association with the two estradiols E2 and EE2.

References

- Alvarez, D.A., Shappell, N.W., Billey, L.O., Bermudez, D.S., Wilson, V.S., Kolpin, D.W., Perkins, S.D., Evans, N., Foreman, W.T., Gray, J.L., Shipitalo, M.J., Meyer, M.T. **2013**. Bioassay of estrogenicity and chemical analyses of estrogens in streams across the United States associated with livestock operations. *Water Research* 47, 3347-3363.
- Chang, H., Wan, Y., Wu, S., Fan, Z., Hu, J. **2011**. Occurrence of androgens and progestogens in wastewater treatment plants and receiving river waters: Comparison to estrogens. *Water Research* 45, 732-740.
- EPA Method 1698. December **2007**. Steroids and hormones in water, soil, sediment, and biosolids by HRGC/HRMS. EPA-821-R-08-003. U.S. Environmental Protection Agency, Office of Water, Washington, DC, USA.

EPA Method 539. November **2010**. Determination of hormones in drinking water by solid-phase extraction (SPE) and liquid chromatography electrospray ionization tandem mass spectrometry (LC-ESI-MS-MS). EPA-815-B-10-001. U.S. Environmental Protection Agency, Office of Water, Washington, DC, USA.

Esteban, S., Gorga, M., Petrovic, M., González-Alonso, S., Barceló, D., Valcárcel, Y. **2014**. Analysis and occurrence of endocrine-disrupting compounds and estrogenic activity in the surface waters of Central Spain. *Science of the Total Environment* 466–467, 939–951.

Gabet-Giraud, V., Miège, C., Herbreteau, B., Hernandez-Raquet, G., Coquery, M. **2010**. Development and validation of an analytical method by LC-MS/MS for the quantification of estrogens in sewage sludge. *Analytical and Bioanalytical Chemistry* 396, 1841–1851.

Grover, D.P., Zhang, Z.L., Readman, J.W., Zhou, J.L. **2009**. A comparison of three analytical techniques for the measurement of steroidal estrogens in environmental water samples. *Talanta* 78, 1204–1210.

Li, J., Fu, J., Zhang, H., Li, Z., Ma, Y., Wu, M., Liu, X. **2013**. Spatial and seasonal variations of occurrences and concentrations of endocrine disrupting chemicals in unconfined and confined aquifers recharged by reclaimed water: A field study along the Chaobai River, Beijing. *Science of the Total Environment* 450–451, 162–168.

Lien, G.-W., Chen, C.-Y., Wang, G.-S., **2009**. Comparison of electrospray ionization, atmospheric pressure chemical ionization and atmospheric pressure photoionization for determining estrogenic chemicals in water by liquid chromatography tandem mass spectrometry with chemical derivatizations. *Journal of Chromatography A*, 1216, 956–966.

Loos, R. **2012**. Analytical methods relevant to the European Commission's 2012 proposal on Priority Substances under the Water Framework Directive. *JRC scientific and policy report*, JRC 73257, EUR 25532 EN, ISBN 978-92-79-26642-3, doi:10.2788/51497.

Matejcek, D., Kuban, V. **2008**. Enhancing sensitivity of liquid chromatographic/ion-trap tandem mass spectrometric determination of estrogens by on-line pre-column derivatization. *Journal of Chromatography A*, 1192, 248–253.

Miège, C., Bados, P., Brosse, C., Coquery, M. **2009**. Method validation for the analysis of estrogens (including conjugated compounds) in aqueous matrices. *Trends in Analytical Chemistry* 28, 237–244.

Salvador, A., Moretton, C., Piram, A., Faure, R. **2007**. On-line solid-phase extraction with on-support derivatization for high-sensitivity liquid chromatography tandem mass spectrometry of estrogens in influent/effluent of wastewater treatment plants. *Journal of Chromatography A*, 1145, 102–109.

Tomsikova, H., Aufartova, J., Solich, P., Sosa-Ferrera, Z., Santana-Rodriguez, J.J., Novakova, L. **2012**. High-sensitivity analysis of female-steroid hormones in environmental samples. *Trends in Analytical Chemistry* 34, 35–58.

Vulliet, E., Wiest, L., Baudot, R., Grenier-Loustalot, M.-F. **2008**. Multi-residue analysis of steroids at sub-ng/L levels in surface and ground-waters using liquid chromatography coupled to tandem mass spectrometry. *Journal of Chromatography A* 1210, 84–91.

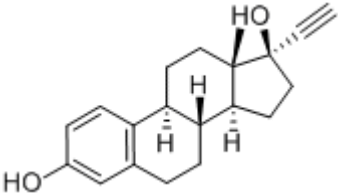
Williams, R.J., Churchley, J.H., Kanda, R., Johnson, A.C. **2012**. Comparing predicted against measured steroid estrogen concentrations and the associated risk in two United Kingdom river catchments. *Environ. Toxicol. Chem.* 31 (4), 892–898.

Wang, G., Ma, P., Zhang, Q., Lewis, J., Lacey, M., Furukawa, Y., O'Reilly, S.E., Meaux, S., McLachlan, J., Zhang, S. **2012**. Endocrine disrupting chemicals in New Orleans surface waters and Mississippi Sound sediments. *Journal of Environmental Monitoring* 14(5), 1353–64.

4.3. 17-alpha-Ethinylestradiol

17-alpha-ethinylestradiol (EE2) is a synthetic estradiol used in contraceptive pills and for the treatment of menopausal and post-menopausal symptoms.

CAS Number 57-63-6	Log K_{ow} 3.67-4.2	Water Solubility [mg/l] 4.7-19
Chemical structure (MW 296.4)	AA-EQS Inland (fresh) and other (salt) surface waters [µg/l]	MAC-EQS Inland (fresh) and other (salt) surface waters [µg/l]

	<p>Fresh $3.5 \cdot 10^{-5}$ = 0.035 ng/l = 35 pg/l</p> <p>Salt $7 \cdot 10^{-6}$ = 7 pg/l</p>	<p>not applicable</p>
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Standard Methods

MDL: $1 \cdot 10^{-4}$ µg/l = 0.1 ng/l (sample volume: 1 l) ([EPA 1698](#));

LOD: 0.33 ng/l (sample volume: 1 l) ([EPA 539](#)).

Methods applied by EU Member States

Italy: LOQ: 1.8 ng/l; LC-MS/MS (IT: ISS); Performance data on drinking waters (LOD) in the context of drinking water directive. The methods in some cases are from other MS. The methods are validated with ring-test.

France: LOQ: 1.2 ng/l; Aqua-Ref Method (SPE-MS-MS); 250 ml water; extraction with 200 mg Oasis HLB followed by florisil clean-up ([Miège et al., 2009](#)).

LOQ: 5 ng/g for sewage sludge; Aqua-Ref Method (PFE/SPE/LC/MS-MS) ([Gabet-Giraud et al., 2010](#)).

Analytical methods

Extraction (volume)	Analysis	LOD(Q) (ng/l)	Reference
On-line SPE derivatisation	LC-MS-MS	0.7	Salvador et al., 2007
SPE (0.25 l); clean-up with florisil	LC-MS-MS (derivatisation)	LOQ: 0.22	Matejcek and Kuban, 2008
SPE (1 l)	LC-MS-MS	MDL: 0.2	Vulliet et al., 2008
SPE (2 l)	GC-MS-MS (derivatisation) LC-MS-MS	0.3 0.4	Grover et al., 2009
C18 speedisks	UHPLC-MS-MS (derivatisation)	0.91	Lien et al., 2009
SPE (0.25 l); clean-up with florisil	LC-MS-MS	LOQ: 1.2	Miège et al., 2009
SPE (2 l); clean-up with florisil	UHPLC-MS-MS	0.10	Chang et al., 2011
SPE disks (C18 + SDB); silica clean-up (4 l)	GC-MS (derivatisation)	1.64	Wang et al., 2012
SPE (SDB); clean-up with GPC (1-2 l)	LC-MS-MS	0.05	Williams et al., 2012
SPE disks (C18); clean-up with florisil (0.5 l)	GC-MS-MS (derivatisation)	0.8	Alvarez et al., 2013
SPE (Oasis HLB 200mg); silica gel column clean-up; pH3 (2 l)	LC-MS-MS	0.18	Li et al., 2013
On-line SPE (EQuan Hypersil GOLD column, 20 × 2.1 mm) (5 ml)	UHPLC-MS-MS	0.47	Esteban et al., 2014

Conclusion

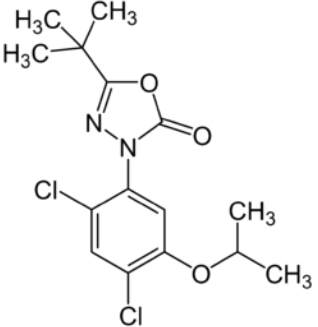
The lowest LOQ reported in the literature both for 17-beta-estradiol and 17-alpha-ethinylestradiol is 0.05 ng/l ([Williams et al., 2012](#)), which is enough to reach the AA-EQS of 17-beta-estradiol (0.4 ng/l) in inland surface waters, but not sufficient for 17-alpha-ethinylestradiol (AA-EQS 0.035 ng/l). The EQS values for other surface (coastal) waters are not achievable in both cases. To reach LOQs in the low pg/l concentration range is extremely difficult, if not impossible with current analytical methods. Therefore, the JRC is currently developing and validating a **large volume** analytical method based on

the extraction of 10 litre water using SPE disks. In addition, it must be considered that due to the instability of the estradiol hormones in water, SPE has to be performed at least 48 h after sampling, preferentially after 24 h (Ternes, T. personal communication). Moreover, the analysis of estradiol hormones involves often a column clean-up with silica or florisil for increasing selectivity.

References

See under “17-beta-estradiol”.

4.4. Oxadiazon

CAS: 19666-30-9 Herbicide $PNEC_{fw} = 0.088 \mu\text{g/l}$ $PNEC_{sed} = 50 \mu\text{g/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
LLE (surface water)	GC-MS	0.002	Sudo et al., 2002
SPE (river delta lagoon transitional water)	GC-MS	0.005	Comoretto et al., 2007
SPE (run-off water)	GC-MS	0.020	Comoretto et al., 2008
Chemcatcher® passive sampling with Empore disk® (SW)	GC-MS	0.0035	Schäfer et al., 2008

Conclusion

Oxadiazon can be analysed by GC-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

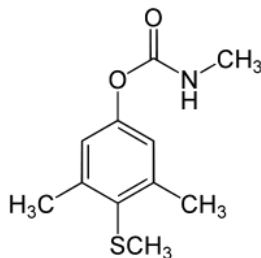
Comoretto, L., Arfib, B., Chiron, S. **2007**. Pesticides in the Rhône river delta (France): Basic data for a field-based exposure assessment. *Science of the Total Environment* 380, 124–132.

Comoretto, L., Arfib, B., Talva, R., Chauvelon, P., Pichaud, M., Chiron, S., Höhener, P. **2008**. Runoff of pesticides from rice fields in the Ile de Camargue (Rhône river delta, France): Field study and modeling. *Environmental Pollution* 151, 486-493.

Schäfer, R.B., Paschke, A., Vrana, B., Mueller, R., Liess, M. **2008**. Performance of the Chemcatchers passive sampler when used to monitor 10 polar and semi-polar pesticides in 16 Central European streams, and comparison with two other sampling methods. *Water Research* 42, 2707-2717.

Sudo, M., Kunitatsu, T., Okubo, T. **2002**. Concentration and loading of pesticide residues in Lake Biwa basin (Japan). *Water Research* 36, 315–329.

4.5. Methiocarb

CAS: 2032-65-7 Insecticide $PNEC_{fw} = 0.01 \mu\text{g/l}$ $PNEC_{sed} = 0.5 \mu\text{g/kg}$ $PNEC_{dw,hh} = 45.5 \mu\text{g/l}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (water)	LC-MS	0.04-0.05	Moore et al., 1995
In-tube SPME (water)	Capillary LC	0.16	Gou and Pawliszyn, 2000
SLE (fruits)	LC-MS	20 $\mu\text{g/kg}$	Blasco et al., 2002
SPE (water) QuEChERS (sediments and biota)	LC-MS-MS	0.001 (water) 0.75 $\mu\text{g/kg}$ 1.69 $\mu\text{g/kg}$	Masiá et al., 2013a;b
LLE (waste water)	GC-MS		Qiang et al., 2014

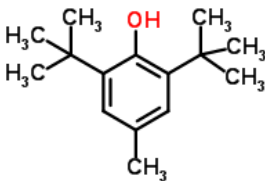
Conclusion

Analysis of methiocarb is performed by GC- or LC-MS techniques. The two publications by [Masiá et al. \(2013a;b\)](#) indicate that LOQ in the low ng/l range can be achieved by SPE-LC-MS-MS analysis.

References

- Blasco, C., Fernández, M., Picó, Y., Font, G., Mañes, J. **2002**. Simultaneous determination of imidacloprid, carbendazim, methiocarb and hexythiazox in peaches and nectarines by liquid chromatography–mass spectrometry. *Analytica Chimica Acta* 461, 109–116.
- Gou, Y., Pawliszyn, J. **2000**. In-tube solid-phase microextraction coupled to capillary LC for carbamate analysis in water samples. *Anal. Chem.* 72, 2774-2779.
- Qiang, Z., Tian, F., Liu, W., Liu, C. **2014**. Degradation of methiocarb by monochloramine in water treatment: Kinetics and pathways. *Water Research* 50, 237-244.
- Masiá, A., Campo, J., Vázquez-Roig, P., Blasco, C., Picó, Y. **2013a**. Screening of currently used pesticides in water, sediments and biota of the Guadalquivir River Basin (Spain). *Journal of Hazardous Materials* 263P, 95–104.
- Masiá, A., Ibanez, M., Blasco, C., Sancho, J.V., Pico, Y., F. Hernandez, F. **2013b**. Combined use of liquid chromatography triple quadrupole mass spectrometry and liquid chromatography quadrupole time-of-flight mass spectrometry in systematic screening of pesticides and other contaminants in water samples. *Analytica Chimica Acta* 761, 117– 127.
- Moore, K.M., Jones, S.R., James, C. **1995**. Multi-residue analytical method for uron and carbamate pesticides in water using solid-phase extraction and liquid chromatography-mass spectrometry. *Water Research* 29, 1225-1230.

4.6. 2,6-Ditert-butyl-4-methylphenol

<p>CAS: 128-37-0</p> <p>Butylated hydroxytoluene (BHT)</p> <p>Antioxidant used in many materials such as packaging materials, adhesives that come in contact with food and also in cosmetics, personal care products and pharmaceuticals; food additive; it is also used as a thermostabilizer for PE, PP, polyesters and PVC plastics;</p> <p>It is primarily used to preserve the freshness of foods. While the parent compound does not pose adverse human health effects, the metabolites of BHT (hydroxybenzaldehyde) are possible cancer initiators and damage cellular DNA.</p> <p>$PNEC_{fw} = 3.16 \mu\text{g/l}$</p> <p>$PNEC_{sed} = 1.290 \text{ mg/kg}$</p> <p>$PNEC_{biota,hh} = 15.217 \text{ mg/kg food}$</p> <p>$PNEC_{dw,hh} = 875 \mu\text{g/l}$</p>	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPME (bottled DW)	GC-MS	13.9	Tombesi and Freije, 2002
SPE (river, ground, rain and drinking water)	GC-MS	0.005	Fries and Püttmann, 2002
SPE (water) followed by clean-up with a carbonate buffer; SLE (sludge, sediment) followed by clean-up with a carbonate buffer; Extraction, clean-up (fish)	Derivatisation GC-MS		Remberger et al., 2003
LLE (bottled DW; 100 ml)	GC-MS		Higuchi et al., 2004
SPME (drinking water)	GC-MS	1-20	Stiles et al., 2008
SPE (waste water)	GC-MS-MS	0.025	Trenholm et al., 2008
Miniaturised SPE (sewage and river water)	Derivatisation (silylation) GC-MS	0.019 (SW)	Rodil et al., 2010
SPE (brine water)	GC-TOF-MS		Serrano et al., 2012

Monitoring data

Concentrations of BHT and its metabolite 3,5-di-tert-butyl-4-hydroxybenzaldehyde (BHT-CHO) were determined in Germany in samples of river water, ground water and rain water in the year 2000. The German rivers Rhine, Main, Elbe, Nidda and Schwarzbach, and groundwater samples from 45 wells in the so-called “Oderbruch” area close to the Oder River in the east of Germany were investigated. In addition, drinking water and rain water samples were collected in November 2000 in Frankfurt/Main. The concentrations of BHT in samples of river water varied from non-detectable (below 5 ng/l) to 791 ng/l (Rhine River in November 2000) with a median of 176 ng/l. The

concentrations of the degradation product BHT-CHO ranged from non-detectable levels (below 16 ng/l) to 223 ng/l, with a median of 79 ng/l. The highest concentration for this compound (i.e. 223 ng/l) was found in a sample from the Oder River in March 2000. BHT was detected in these groundwater samples, with concentrations ranging from 5 to 2156 ng/l. The median for the samples collected in March 2000 was 137 ng/l and 704 ng/l for those samples collected in November 2000. BHT-CHO ranged from 16 up to 674 ng/l, with a median of 68 ng/l in March 2000 and a median of 135 ng/l in November 2000 (Fries and Püttmann, 2002). In the Oder River BHT and BHT-CHO were detected in all samples (from the years 2000-2001) with mean concentrations of 178 and 102 ng/l, respectively. The median values of BHT and BHT-CHO in ground water samples of the Oderbruch area were 132 and 84 ng/l, respectively (Fries and Püttmann, 2004).

Tombesi and Freije (2002) found BHT amounts ranging from 21 to 38 µg/L in polyethylene terephthalate (PET)-bottled water. Later on, the same research group (Tombesi et al., 2004), again detected BHT, but amounts were 10 times lower than in the first studies. It should be mentioned that their first results were not reproducible. Further, Higuchi et al. (2004) found only BHT in glass-bottled water (2.5 µg/L) concluding that the origin of this compound is the PE bottle caps. This conclusion seems to be logical because this additive may be used in the production of PE (Bach et al., 2012).

BHT was analysed together with other tertiary butylphenols, methylphenols, and alkylphenols in the Swedish environment (in air, water, sediment, sludge, fish) in 130 samples. BHT was found in 40 % of the water samples in a concentration range of ca. 0.1 – 3 µg/L. In sediment the detection frequency was 39 % with concentrations between 0.1 – 5 µg/kg (Remberger et al., 2003).

Rodil et al. (2010) analysed BHT and other synthetic phenolic antioxidants and their metabolites in the River Sar in Galicia and WWTP in- and effluents (near Santiago di Compostela). BHT concentrations in the river ranged from 32-112 ng/L, and in the treated effluent up to 251 ng/L.

Conclusion

Analysis of BHT is performed by GC-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved after SPE.

References

- Bach, C., Dauchy, X., Chagnon, M.-C., Etienne, S. **2012**. Chemical compounds and toxicological assessments of drinking water stored in polyethylene terephthalate (PET) bottles: A source of controversy reviewed. *Water Research* 46, 571-583.
- Fries, E., Püttmann, W. **2002**. Analysis of the antioxidant butylated hydroxytoluene (BHT) in water by means of solid phase extraction combined with GC/MS. *Water Research* 36, 2319– 2327.
- Fries, E., Püttmann, W. **2004**. Monitoring of the antioxidant BHT and its metabolite BHT-CHO in German river water and ground water. *Science of the Total Environment* 319, 269–282.
- Higuchi, A., Yoon, B.O., Kaneko, T., Hara, M., Maekawa, M., Nohmi, T. **2004**. Separation of endocrine disruptors from aqueous solutions by pervaporation: dioctylphthalate and butylated hydroxytoluene in mineral water. *Journal of Applied Polymer Science* 94 (4), 1737-1742.
- Remberger, M., Kaj, L., Palm, A., Sternbeck, J., Kvernes, E., Brorström-Lundén, E. **2003**. Screening tertiary butylphenols, methylphenols and long-chain alkylphenylphenols in the Swedish environment, IVL Swedish Environmental Research Institute, Stockholm, <http://www3.ivl.se/rapporter/pdf/-B1594.pdf>.
- Rodil, R., Quintana, J., Basaglia, G., Pietrogrande, M., Cela, R. **2010**. Determination of synthetic phenolic antioxidants and their metabolites in water samples by downscaled solid-phase extraction, silylation and gas chromatography–mass spectrometry, *J. Chromatogr. A* 1217, 6428–6435.
- Rodil, R., Benito Quintana, J., Cela, R. **2012**. Oxidation of synthetic phenolic antioxidants during water chlorination. *Journal of Hazardous Materials* 199– 200, 73– 81.
- Salam, D.A., Suidan, M.T., Venosa, A.D. **2012**. Effect of butylated hydroxytoluene (BHT) on the aerobic biodegradation of a model vegetable oil in aquatic media. *Environ. Sci. Technol.* 46, 6798–6805.

Serrano, R., Portolés, T., Blanes, M.A., Hernández, F., Navarro, J.C., Varó, I., Amat, F. **2012**. Characterization of the organic contamination pattern of a hyper-saline ecosystem by rapid screening using gas chromatography coupled to high-resolution time-of-flight mass spectrometry. *Science of the Total Environment* 433, 161–168.

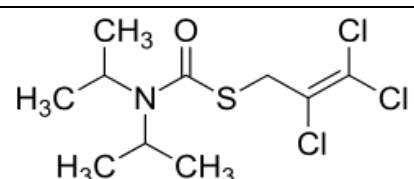
Stiles, R., Yang, I., Lippincott, R.L., Murphy, E., Buckley, B. **2008**. Measurement of drinking water contaminants by solid phase microextraction initially quantified in source water samples by the USGS. *Environ. Sci. Technol.* 42, 2976–2981.

Trenholm, R.A., Vanderford, B.J., Drewes, J.E., Snyder, S.A. **2008**. Determination of household chemicals using gas chromatography and liquid chromatography with tandem mass spectrometry, *J. Chromatogr. A* 1190, 253–262.

Tombesi, N.B., Freije, H. **2002**. Application of solid-phase microextraction combined with gas chromatography-mass spectrometry to the determination of butylated hydroxytoluene in bottled drinking water. *Journal of Chromatography A* 963, 179-183.

Tombesi, N.B., Freije, R.H., Augusto, F. **2004**. Factorial experimental design optimization of solid phase microextraction (SPME) conditions for analysis of butylated hydroxytoluene (BHT) in bottled water. *Journal of the Brazilian Chemical Society* 15 (5), 658-663.

4.7. Tri-allate

CAS: 2303-17-5 Herbicide $PNEC_{fw} = 0.67 \mu\text{g/l}$ $PNEC_{sed} = 0.145 \text{ mg/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (water)	GC-ECD or MS	0.050 (water)	Wang et al., 1998
SLE (soil)		5 $\mu\text{g/kg}$ (soil)	
LLE (rainwater)	GC-MS(-MS)	0.010	Waite et al., 2005
(surface and groundwater)	Direct injection (100 μl) LC-MS-MS	0.010	Reemtsma et al., 2013

Conclusion

Little information on tri-allate is available. Analysis is performed by GC- or LC-MS-MS techniques. The available literature indicates that LOQ of around 10 ng/l can be achieved.

References

Reemtsma, T., Alder, L., Banasiak, U. **2013**. A multimethod for the determination of 150 pesticide metabolites in surface water and groundwater using direct injection liquid chromatography–mass spectrometry. *Journal of Chromatography A* 1271, 95–104.

Waite, D., Cessna, A., Grover, R., Kerr, L., Snihura, A., **2002**. Environmental concentrations of agricultural herbicides: 2, 4-D and triallate. *Journal of Environmental Quality* 31, 129-144.

Waite, D., Bailey, P., Sproull, J., Quiring, D., Chau, D., Bailey, J., Cessna, A. **2005**. Atmospheric concentrations and dry and wet deposits of some herbicides currently used on the Canadian Prairies. *Chemosphere* 58, 693-703.

Wang, W., Kreuzig, R., Bahadir, M. **1998**. Determination of triallate and its metabolite 2,3,3-trichloro-prop-2-en sulfonic acid in soil and water samples. *Fresenius J. Anal. Chem.* 360, 564-567.

4.8. Neonicotinoids

4.8.1. Imidacloprid

CAS: 105827-78-9/138261-41-3 Neonicotinoid insecticide PNEC_{fw} = 0.009 µg/l	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
SPE (honey and pollen)	LC-MS-MS		Garcia-Chao et al., 2010
SPE (water)	Derivatisation GC-MS		Mohr et al., 2012
SPE (SW)	LC-MS-MS	0.0049	Hladik et al., 2012; 2014
SPE (SW)	LC-MS-MS	0.0011	Main et al., 2014
QuEChERS (soil)	LC-MS-MS	1 µg/kg	Stewart et al., 2014
QuEChERS (soil)	LC-MS-MS	4.0 µg/kg	Dankyi et al., 2014

Monitoring data

Imidacloprid was analysed in surface water in the Netherlands. Data available in the Dutch pesticides atlas at www.bestrijdingsmiddelenatlas.nl ([van Dijk et al., 2013](#)).

An area of intense corn and soybean production in the Midwestern United States with high agricultural use of neonicotinoids via both seed treatments and other forms of application was studied for the occurrence of these insecticides in nine streams during the 2013 growing season. The analytical summary results for the 79 water samples are shown in the following table ([Hladik et al., 2014](#)):

	Clothianidin	Thiamethoxam	Imidacloprid
Frequency of detection (%)	75	47	23
Max. concentration (ng/l)	257	185	43
Median concentration (ng/l)	8.2	< 2	< 2

Conclusion

See under “thiacloprid”.

References

- Baskaran, S., Kookana, R.S., Naidu, R. **1997**. Determination of the insecticide imidacloprid in water and soil using high-performance liquid chromatography. *J. Chromatogr. A* 787, 271–275.
- Dankyi, E., Gordon, C., Carboo, D., Fomsgaard, I.S. **2014**. Quantification of neonicotinoid insecticide residues in soils from cocoa plantations using a QuEChERS extraction procedure and LC-MS/MS. *Science of the Total Environment* 499, 276–283.
- Garcia-Chao, M., Agruna, M.J., Flores Calvete, G., Sakkas, V., Llompart, M., Dagnac, T., **2010**. Validation of an off line solid phase extraction liquid chromatography tandem mass spectrometry method for the determination of systemic insecticide residues in honey and pollen samples collected in apiaries from NW Spain. *Anal. Chim. Acta* 672, 107–113.
- Hladik, M.L., Calhoun, D.L. **2012**. Analysis of the herbicide diuron, three diuron degradates, and six neonicotinoid insecticides in water - Method details and application to two Georgia Streams. U.S. Geological Survey Scientific Investigations Report 2012 - 5206, 10 pp. Available at: <http://pubs.usgs.gov/sir/2012/5206>.
- Hladik, M.L., Kolpin, D.W., Kuivila, K.M. **2014**. Widespread occurrence of neonicotinoid insecticides in streams in a high corn and soybean producing region, USA. *Environmental Pollution* 193, 189-196.

Main, A.R., Headley, J.V., Peru, K.M., Michel, N.L., Cessna, A.J., Morrissey, C.A. **2014**. Widespread use and frequent detection of neonicotinoid insecticides in wetlands of Canada's Prairie Pothole region. *PLOS ONE* 9, e92821.

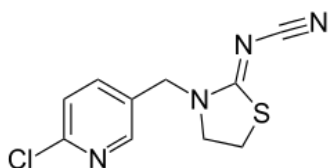
Mohr, S., Berghahn, R., Schmiediche, R., Hübner, V., Loth, S., Feibicke, M., Mailahn, W., Wogram, J. **2012**. Macroinvertebrate community response to repeated short-term pulses of the insecticide imidacloprid. *Aquat. Toxicol.* 110–111, 25–36.

Starner, K., Goh, K. **2012**. Detections of the neonicotinoid insecticide imidacloprid in surface waters of three agricultural regions of California, USA, 2010–2011. *Bull. Environ. Contam. Toxicol.* 88, 316–321.

van Dijk, T.C., van Staalduinen, M.A., van der Sluijs, J.P. **2013**. Macroinvertebrate decline in surface water polluted with imidacloprid. *PLOS One* 8 (5), e62374.

Stewart, S.D., Lorenz, G.M., Catchot, A.L., Gore, J., Cook, D., Skinner, J., Mueller, T.C., Johnson, D.R., Zawislak, J., Barber, J. **2014**. Potential exposure of pollinators to neonicotinoid insecticides from the use of insecticide seed treatments in the mid-southern United States. *Environ. Sci. Technol.* 48, 9762–9769.

4.8.2. Thiacloprid

CAS: 111988-49-9 Neonicotinoid insecticide $PNEC_{fw} = 0.050 \mu\text{g/l}$ $PNEC_{dw,hh} = 35 \mu\text{g/L}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (drinking water)	LC-MS	0.03	Seccia et al., 2005
SPE (water)	LC-MS	0.03	Beketov et al., 2008
SPE (honey and pollen)	LC-MS-MS		Garcia-Chao et al., 2010
SLE (honeybees)	LC-MS-MS	0.5 $\mu\text{g/kg}$	Martel et al., 2011
Subcritical water extraction (fish)	LC-MS-MS	0.42-1.12 $\mu\text{g/kg}$	Xiao et al., 2013
SPE (SW)	LC-MS-MS	0.0038	Hladik et al., 2012; 2014
Passive sampling with Empore™ extraction disks (SW)	HPLC-UV	0.6-1.0	Sánchez-Bayo and Hyne, 2014
QuEChERS (soil)	LC-MS-MS	2.0 $\mu\text{g/kg}$	Dankyi et al., 2014

Conclusion

Analysis of the neonicotinoid insecticides thiacloprid, clothianidin, thiamethoxam, imidacloprid, and acetamiprid is performed by LC-MS-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

Beketov, M.A., Schäfer, R.B., Marwitz, A., Paschke, A., Liess, M. **2008**. Long-term stream invertebrate community alterations induced by the insecticide thiacloprid: Effect concentrations and recovery dynamics. *Science of the Total Environment* 405, 96-108.

Dankyi, E., Gordon, C., Carboo, D., Fomsgaard, I.S. **2014**. Quantification of neonicotinoid insecticide residues in soils from cocoa plantations using a QuEChERS extraction procedure and LC-MS/MS. *Science of the Total Environment* 499, 276–283.

Hladik, M.L., Calhoun, D.L. **2012**. Analysis of the herbicide diuron, three diuron degradates, and six neonicotinoid insecticides in water - Method details and application to two Georgia Streams. U.S. Geological Survey Scientific Investigations Report 2012 - 5206, 10 pp. Available at: <http://pubs.usgs.gov/sir/2012/5206>.

Hladik, M.L., Kolpin, D.W., Kuivila, K.M. **2014**. Widespread occurrence of neonicotinoid insecticides in streams in a high corn and soybean producing region, USA. *Environmental Pollution* 193, 189-196.

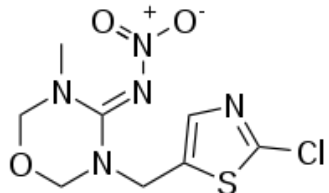
Martel, A.C., Lair, C. **2011**. Validation of a highly sensitive method for the determination of neonicotinoid insecticides residues in honeybees by liquid chromatography with electrospray tandem mass spectrometry. *Int. J. Environ. Anal. Chem.* 91, 978–988.

Sánchez-Bayo, F., Hyne, R.V. **2014**. Detection and analysis of neonicotinoids in river waters – Development of a passive sampler for three commonly used insecticides. *Chemosphere* 99, 143–151.

Seccia, S., Fidente, P., Barbini, D.A., Morrica, P. **2005**. Multiresidue determination of nicotinoid insecticide residues in drinking water by liquid chromatography with electrospray ionization mass spectrometry. *Analytica Chimica Acta* 553, 21–26.

Xiao, Z., Yang, Y., Li, Y., Fan, X., Ding, S. **2013**. Determination of neonicotinoid insecticides residues in eels using subcritical water extraction and ultra-performance liquid chromatography–tandem mass spectrometry. *Analytica Chimica Acta* 777, 32– 40.

4.8.3. Thiamethoxam

CAS: 153719-23-4 Neonicotinoid insecticide PNEC _{fw} = 0.14 µg/l	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
SPE (SW)	LC-MS-MS	0.0018	Main et al., 2014
QuEChERS (soil)	LC-MS-MS	5.0 µg/kg	Dankyi et al., 2014
SPE (SW)	LC-MS-MS	0.0039	Hladik et al., 2012; 2014

Conclusion

See under “thiacloprid”.

References

Dankyi, E., Gordon, C., Carboo, D., Fomsgaard, I.S. **2014**. Quantification of neonicotinoid insecticide residues in soils from cocoa plantations using a QuEChERS extraction procedure and LC-MS/MS. *Science of the Total Environment* 499, 276–283.

Hladik, M.L., Calhoun, D.L. **2012**. Analysis of the herbicide diuron, three diuron degradates, and six neonicotinoid insecticides in water - Method details and application to two Georgia Streams. U.S. Geological Survey Scientific Investigations Report 2012 - 5206, 10 pp. Available at: <http://pubs.usgs.gov/sir/2012/5206>.

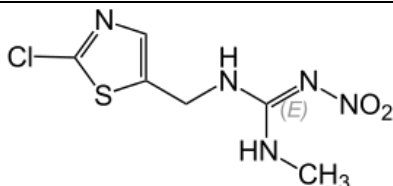
Hladik, M.L., Kolpin, D.W., Kuivila, K.M. **2014**. Widespread occurrence of neonicotinoid insecticides in streams in a high corn and soybean producing region, USA. *Environmental Pollution* 193, 189-196.

Main, A.R., Headley, J.V., Peru, K.M., Michel, N.L., Cessna, A.J., Morrissey, C.A. **2014**. Widespread use and frequent detection of neonicotinoid insecticides in wetlands of Canada’s Prairie Pothole region. *PLOS ONE* 9, e92821.

Stewart, S.D., Lorenz, G.M., Catchot, A.L., Gore, J., Cook, D., Skinner, J., Mueller, T.C., Johnson, D.R., Zawislak, J., Barber, J. **2014**. Potential exposure of pollinators to neonicotinoid insecticides from the use of insecticide seed treatments in the mid-southern United States. *Environ. Sci. Technol.* 48, 9762–9769.

Henry, M., Béguin, M., Requier, F., Rollin, O., Odoux, J.-F., Aupinel, P., Aptel, J., Tchamitchian, S., Decourtye, A. **2012**. A common pesticide decreases foraging success and survival in honey bees. *Science* 336, 348-350.

4.8.4. Clothianidin

CAS: 210880-92-5 Neonicotinoid insecticide $PNEC_{fw} = 0.13 \mu\text{g/l}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (SW)	LC-MS-MS	0.0012	Main et al., 2014
QuEChERS (soil)	LC-MS-MS	9.0 $\mu\text{g/kg}$	Dankyi et al., 2014
SPE (SW)	LC-MS-MS	0.0049	Hladik et al., 2012; 2014

Conclusion

See under “thiacloprid”.

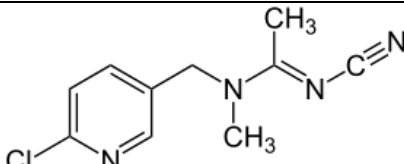
Monitoring data

In Canada, water was sampled in 2012-2013 four times from 136 wetlands across four rural municipalities in Saskatchewan; the analysis revealed clothianidin and thiamethoxam in the majority of samples. Peak concentrations were recorded during summer 2012 for both thiamethoxam (range: < LOQ-1490 ng/l) and clothianidin (range: < LOQ – 3110 ng/l) ([Main et al., 2014](#)).

References

- Dankyi, E., Gordon, C., Carboo, D., Fomsgaard, I.S. **2014**. Quantification of neonicotinoid insecticide residues in soils from cocoa plantations using a QuEChERS extraction procedure and LC-MS/MS. Science of the Total Environment 499, 276–283.
- Hladik, M.L., Calhoun, D.L. **2012**. Analysis of the herbicide diuron, three diuron degradates, and six neonicotinoid insecticides in water - Method details and application to two Georgia Streams. U.S. Geological Survey Scientific Investigations Report 2012 - 5206, 10 pp. Available at: <http://pubs.usgs.gov/sir/2012/5206>.
- Hladik, M.L., Kolpin, D.W., Kuivila, K.M. **2014**. Widespread occurrence of neonicotinoid insecticides in streams in a high corn and soybean producing region, USA. Environmental Pollution 193, 189-196.
- Main, A.R., Headley, J.V., Peru, K.M., Michel, N.L., Cessna, A.J., Morrissey, C.A. **2014**. Widespread use and frequent detection of neonicotinoid insecticides in wetlands of Canada's Prairie Pothole region. PLOS ONE 9, e92821.
- Stewart, S.D., Lorenz, G.M., Catchot, A.L., Gore, J., Cook, D., Skinner, J., Mueller, T.C., Johnson, D.R., Zawislak, J., Barber, J. **2014**. Potential exposure of pollinators to neonicotinoid insecticides from the use of insecticide seed treatments in the mid-southern United States. Environ. Sci. Technol. 48, 9762–9769.

4.8.5. Acetamiprid

CAS: 135410-20-7 Neonicotinoid insecticide $PNEC_{fw} = 0.5 \mu\text{g/l}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (SW)	LC-MS-MS	0.0036	Hladik et al., 2012

Conclusion

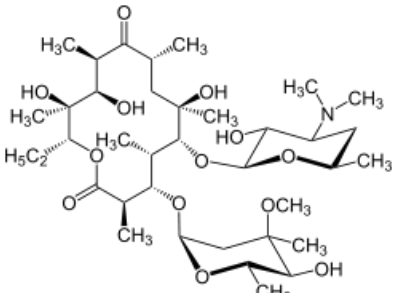
See under “thiacloprid”.

References

Hladik, M.L., Calhoun, D.L. **2012**. Analysis of the herbicide diuron, three diuron degradates, and six neonicotinoid insecticides in water - Method details and application to two Georgia Streams. U.S. Geological Survey Scientific Investigations Report 2012 - 5206, 10 pp. Available at: <http://pubs.usgs.gov/sir/2012/5206>.

4.9. Macrolide antibiotics

4.9.1. Erythromycin

CAS: 114-07-8 Macrolide antibiotic $PNEC_{fw} = 0.20 \mu\text{g/l}$ $PNEC_{sed} = 1.2 \mu\text{g/kg}$ $PNEC_{dw,hh} = 2 \mu\text{g/l}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (surface water and WWTPs)	LC-MS	0.008 0.020 (WWTPs)	McArdell et al., 2003
SPE (surface water)	LC-MS-MS	< 0.0003	Calamari et al., 2003
SPE (surface water)	LC-MS-MS	0.014	Gros et al., 2006
SPE (surface water; 250 ml)	LC-MS-MS	0.0006	Managaki et al., 2007
SPE (surface water)	LC-MS-MS	0.0006	Gros et al., 2009
On-line SPE (surface water; 250 ml)	LC-MS-MS	0.022	Heeb et al., 2012
SPE (WW effluent)	LC-MS-MS	0.099	Martínez Bueno et al., 2012
SPE (groundwater)	LC-TOF-MS	0.020	Estévez et al., 2012
SPE (0.1 l); surface water	LC-MS-MS	LOD: 0.0002 LOQ: 0.0005	Gros et al., 2012
On-line SPE (surface water)	LC-MS-MS	0.008	Gibs et al., 2013
SPE (water) SLE and SPE clean-up (sediment)	LC-MS-MS	0.010 (water) 0.29 $\mu\text{g/kg}$ (sediment)	Liang et al., 2013
SPE (water) SLE and SPE clean-up (sediment)	LC-MS-MS	0.0005 (water) 1.4 $\mu\text{g/kg}$ (sediment)	Jiang et al., 2014
SPE (0.5 l); river water	LC-MS-MS	LOD: 0.0015 LOQ: 0.0051	Petrović et al., 2014

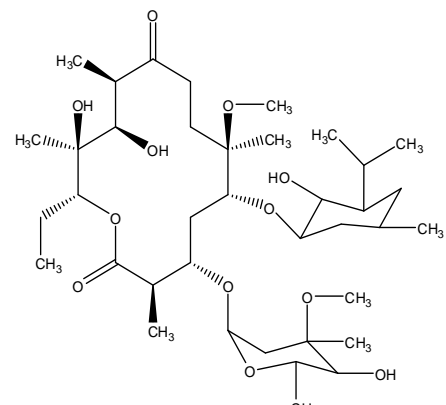
Conclusion

Erythromycin is analysed by SPE – LC-MS techniques. Many publications on the occurrence, fate and analysis of erythromycin in waste and surface water and sediment are available (most of them are from China). Ethylenediaminetetraacetic acid (EDTA) should be added before extraction for masking of metals. The available literature shows that LOQ around 10 ng/l is achievable ($PNEC_{fw} = 40 \text{ ng/l}$).

References

- Calamari, D., Zuccato, E., Castiglioni, S., Bagnati, R., Fanelli, R. **2003**. Strategic survey of therapeutic drugs in the rivers Po and Lambro in Northern Italy. *Environ. Sci. Technol.* 37, 1241-1248.
- Gibs, J., Heckathorn, H.A., Meyer, M.T., Klapinski, F.R., Alebus, M., Lippincott, R.L. **2013**. Occurrence and partitioning of antibiotic compounds found in the water column and bottom sediments from a stream receiving two wastewater treatment plant effluents in Northern New Jersey, 2008. *Science of the Total Environment* 458-460, 107-116.
- Gros, M., Petrovic, M., Barceló, D. **2006**. Development of a multi-residue analytical methodology based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. *Talanta* 70, 678-690.
- Gros, M., Petrovic, M., Barceló, D. **2009**. Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/quadrupole-linear ion trap mass spectrometry and automated library searching. *Anal. Chem.* 81, 898-912.
- Gros, M., Rodríguez-Mozaz, S. Barceló, D. **2012**. Fast and comprehensive multi-residue analysis of a broad range of human and veterinary pharmaceuticals and some of their metabolites in surface and treated waters by ultra-high-performance liquid chromatography coupled to quadrupole-linear ion trap tandem mass spectrometry. *Journal of Chromatography A* 1248, 104- 121.
- Estévez, E., del Carmen Cabrera, M., Molina-Díaz, A., Robles-Molina, J., del Pino Palacios-Díaz, M. **2012**. Screening of emerging contaminants and priority substances (2008/105/EC) in reclaimed water for irrigation and groundwater in a volcanic aquifer (Gran Canaria, Canary Islands, Spain). *Science of the Total Environment* 433, 538-546.
- Heeb, F., Singer, H., Pernet-Coudrier, B., Qi, W., Liu, H., Longrée, P., Müller, B., Berg, M. **2012**. Organic micropollutants in rivers downstream of the megacity Beijing: Sources and mass fluxes in a large-scale wastewater irrigation system. *Environ. Sci. Technol.* 46, 8680-8688.
- Jiang, Y., Li, M., Guo, C., An, D., Xu, J., Zhang, Y., Xi, B. **2014**. Distribution and ecological risk of antibiotics in a typical effluent-receiving river (Wangyang River) in north China. *Chemosphere* 112, 267-274.
- Liang, X., Chen, B., Nie, X., Shi, Z., Huang, X., Li, X. **2013**. The distribution and partitioning of common antibiotics in water and sediment of the Pearl River Estuary, South China. *Chemosphere* 92, 1410-1416.
- Managaki, S., Murata, A., Takada, H., Tuyen, B.C., Chiem, N.H. **2007**. Distribution of macrolides, sulfonamides, and trimethoprim in tropical waters: Ubiquitous occurrence of veterinary antibiotics in the Mekong Delta. *Environ. Sci. Technol.* 41, 8004-8010.
- McArdell, C.S., Molnar, E., Suter, M.J.-F., Giger, W. **2003**. Occurrence and fate of macrolide antibiotics in wastewater treatment plants and in the Glatt Valley watershed, Switzerland. *Environ. Sci. Technol.* 37, 5479-5486.
- Martínez Bueno, M.J., Gomez, M.J., Herrera, S., Hernando, M.D., Agüera, A., Fernández-Alba, A.R. **2012**. Occurrence and persistence of organic emerging contaminants and priority pollutants in five sewage treatment plants of Spain: Two years pilot survey monitoring. *Environmental Pollution* 164, 267-273.
- Petrović, M., Škrbić, B., Živančev, J., Ferrando-Climent, L., Barcelo, D. **2014**. Determination of 81 pharmaceutical drugs by high performance liquid chromatography coupled to mass spectrometry with hybrid triple quadrupole-linear ion trap in different types of water in Serbia. *Science of the Total Environment* 468-469, 415-428.

4.9.2. Clarithromycin

CAS: 81103-11-9 Macrolide antibiotic $PNEC_{fw} = 0.13 \mu\text{g/l}$ $PNEC_{sed} = 1.2 \mu\text{g/kg}$	
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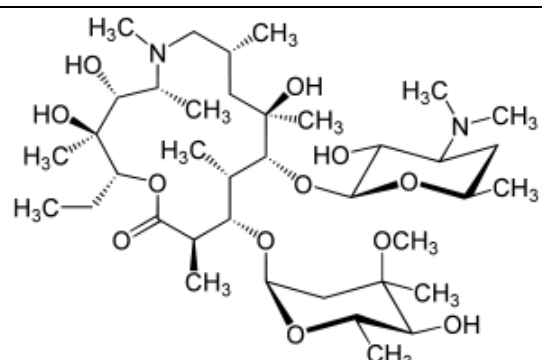
Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (surface water and WWTPs)	LC-MS	0.004 0.010 (WWTPs)	McArdell et al., 2003
SPE (surface water)	LC-MS-MS	< 0.0003	Calamari et al., 2003
SPE (surface water; 250 ml)	LC-MS-MS	0.0001	Managaki et al., 2007
SPE (surface water)	LC-MS-MS	0.002	Gros et al., 2009
On-line SPE (surface water; 250 ml)	LC-MS-MS	0.014	Heeb et al., 2012
SPE (WW effluent)	LC-MS-MS	0.010	Martínez Bueno et al., 2012
SPE (groundwater)	LC-TOF-MS	0.001	Estévez et al., 2012
SPE (0.1 l); surface water	LC-MS-MS	LOD: 0.0004 LOQ: 0.0014	Gros et al., 2012
SPE (0.5 l); river water	LC-MS-MS	LOD: 0.0006 LOQ: 0.0019	Petrović et al., 2014

Conclusion and References

See under “erythromycin”; the same applies.

4.9.3. Azithromycin

CAS: 83905-01-5 Macrolide antibiotic $PNEC_{fw} = 0.090 \mu\text{g/l}$ $PNEC_{sed} = 14 \mu\text{g/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (surface water)	LC-MS-MS	0.003	Gros et al., 2006
SPE (surface water)	LC-MS-MS	0.0005	Managaki et al., 2007

SPE (surface water)	LC-MS-MS	0.001	Gros et al., 2009
SPE (waste water effluent)	LC-MS-MS	0.010	Nelson et al., 2011
SPE (0.1 l); surface water	LC-MS-MS	LOD: 0.0002 LOQ: 0.0006	Gros et al., 2012
SPE (0.5 l); river water	LC-MS-MS	LOD: 0.00014 LOQ: 0.0005	Petrović et al., 2014

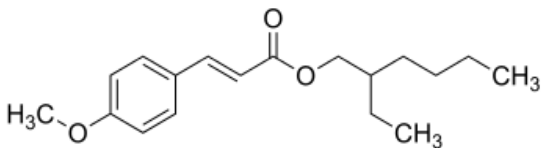
Conclusion

Azithromycin is analysed by LC-MS-MS techniques. LOQ in the low ng/l range can be achieved.

References

- Gros, M., Petrovic, M., Barceló, D. **2006**. Development of a multi-residue analytical methodology based on liquid chromatography–tandem mass spectrometry (LC–MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. *Talanta* 70, 678–690.
- Gros, M., Petrovic, M., Barceló, D. **2009**. Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/quadrupole-linear ion trap mass spectrometry and automated library searching. *Anal. Chem.* 81, 898–912.
- Gros, M., Rodríguez-Mozaz, S. Barceló, D. **2012**. Fast and comprehensive multi-residue analysis of a broad range of human and veterinary pharmaceuticals and some of their metabolites in surface and treated waters by ultra-high-performance liquid chromatography coupled to quadrupole-linear ion trap tandem mass spectrometry. *Journal of Chromatography A* 1248, 104– 121.
- Managaki, S., Murata, A., Takada, H., Tuyen, B.C., Chiem, N.H. **2007**. Distribution of macrolides, sulfonamides, and trimethoprim in tropical waters: Ubiquitous occurrence of veterinary antibiotics in the Mekong Delta. *Environ. Sci. Technol.* 41, 8004–8010.
- Nelson, E.D., Do, H., Lewis, R.S., Carr, S.A. **2011**. Diurnal variability of pharmaceutical, personal care product, estrogen and alkylphenol concentrations in effluent from a tertiary wastewater treatment facility. *Environ. Sci. Technol.* 45, 1228–1234.
- Petrović, M., Škrbić, B., Živančev, J., Ferrando-Climent, L., Barcelo, D. **2014**. Determination of 81 pharmaceutical drugs by high performance liquid chromatography coupled to mass spectrometry with hybrid triple quadrupole–linear ion trap in different types of water in Serbia. *Science of the Total Environment* 468–469, 415–428.

4.10. 2-Ethylhexyl 4-methoxycinnamate (EHMC)

CAS: 5466-77-3 Octyl methoxycinnamate Sunscreen agent PNEC _{fw} = 6.0 µg/l PNEC _{sed} = 0.2 mg/kg	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
SPE (surface water)	GC-MS	0.002	Straub, 2002
SPE and SPMDs for integrative sampling (surface water; waste water) ASE or SLE-GPC (fish)	GC-MS	0.002 for SW 0.010 for WW	Balmer et al., 2005
SPE (sea water, lake water, river water, WW)	Derivatisation GC-MS	0.054-0.25	Cuderman and Heath, 2007
SBSE (grey water)	GC-MS		Hernandez Leal et al., 2010
(Water)	GC-MS; LC-MS		MacManus-Spencer et al., 2011

SPE (Water)	GC-MS-MS (derivatisation)		Remberger et al., 2011
Microwave-assisted SLE (sediment)	GC-MS-MS	5 µg/kg d.w.	Amine et al., 2012
SPE (WW effluent)	LC-MS-MS	0.00085	Tsui et al., 2014a
SPE (marine water)	LC-MS-MS	0.00041	Tsui et al., 2014b

Monitoring data

EHMC has been detected in untreated and treated wastewater (0.5-19 µg/l and up to 100 ng/l, respectively), surface waters (<2-92 ng/l), and fish (50- 1800 ng/g) in Switzerland ([MacManus-Spencer, 2010](#)). EHMC was analysed in the River Rhine in Basel (CH) during the summer season 1997. The average concentration of 47 data points was 5.5 ng/l. In addition, Lake Zürich was analysed in 1998 ([Straub, 2002](#)). Concentrations of EHMC in treated wastewater effluent samples from Swiss WWTPs were between < 0.01-0.1 µg/l. Maximum concentrations in Swiss lakes were 7 ng/l ([Balmer et al., 2005](#)).

Several sunscreen UV-filters were analysed in Sweden in the years 2009-2010 in 52 samples, distributed on 24 surface waters, 8 WWTP-effluents, 8 sludge, 7 sediments and 5 fish. A suitable analytical method for the different samples was developed. EHMC concentrations were in effluents up to 49 ng/l, in surface water up to 15 ng/l, and in sediment up to 45 ng/g ([Remberger et al., 2011](#)).

Conclusion

Analysis of EHMC is performed by GC- or LC-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

- Amine, H., Gomez, E., Halwani, J., Casellas, C., Fenet, H. **2012**. UV filters, ethylhexyl methoxycinnamate, octocrylene and ethylhexyl dimethyl PABA from untreated wastewater in sediment from eastern Mediterranean river transition and coastal zones. *Marine Pollution Bulletin* 64, 2435–2442.
- Balmer, M.E., Buser, H.-R., Müller, M.D.; Poiger, T. **2005**. Occurrence of some organic UV filters in wastewater, in surface waters, and in fish from Swiss lakes. *Environ. Sci. Technol.* 39, 953–962.
- Cuderman, P., Heath, E. **2007**. Determination of UV filters and antimicrobial agents in environmental water samples. *Anal. Bioanal. Chem.* 387, 1343–1350.
- Hernandez Leal, L., Vieno, N., Temmink, H., Zeeman, G., Buisman, C.J.N. **2010**. Occurrence of xenobiotics in gray water and removal in three biological treatment systems. *Environ. Sci. Technol.* 44, 6835–6842.
- MacManus-Spencer, L.A., Tse, M.L., Klein, J.L., Kracunas, A.E. **2011**. Aqueous photolysis of the organic ultraviolet filter chemical octyl methoxycinnamate. *Environ. Sci. Technol.* 45, 3931–3937.
- Straub, J.O. **2002**. Concentrations of the UV filter ethylhexyl methoxycinnamate in the aquatic compartment: a comparison of modelled concentrations for Swiss surface waters with empirical monitoring data. *Toxicol. Lett.* 131, 29–37.
- Remberger, M., Lilja, K., Kaj, L., Viktor, T., Brorström-Lundén, E. **2011**. Results from the Swedish National Screening Programme 2009 - Subreport 3: UV-filters, URL: <http://www.ivl.se/webdav/files/B-rapporter/B1971.pdf>
- Tsui, M.M.P., Leung, H.W., Lam, P.K., Murphy, M.B., **2014a**. Seasonal occurrence, removal efficiencies and preliminary risk assessment of multiple classes of organic UV filters in wastewater treatment plants. *Water Research* 53, 58-67.
- Tsui, M.M.P., Leung, H.W., Wai, T.-C., Yamashita, N., Taniyasu, S., Liu, W., Lam, P.K.S., Murphy, M.B. **2014b**. Occurrence, distribution and ecological risk assessment of multiple classes of UV filters in surface waters from different countries. *Water Research* 67, 55-65.

5. Additional substances investigated

The following substances were also under discussion before inclusion in the 1st *Watch List*, but were not among those finally recommended.

5.1. Trichlorfon

CAS: 52-68-6 An organophosphate insecticide used in agriculture, household, and veterinary medicine. It is degraded to dichlorvos which is already a priority substance PNEC_{fw} = 0.00096 µg/l	 <chem>COP(=O)(OC)C(O)C(Cl)(Cl)Cl</chem>
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
(drinking water and surface water)	GC/ECD GC/MS/MS	0.050 0.50	Draft risk assessment report, July 2004
Cloud point extraction (vegetable, water)	HPLC-UV	2.0	Zhua et al., 2008
SLE with acetonitrile (fish, vegetable, tea)	GC-MS		Hoaia et al., 2011

Conclusion

Little information is available for trichlorfon. Extraction and analysis is difficult due to its polar non-aromatic structure. The draft risk assessment report from 2004 states that “trichlorfon could be analysed by GC/ECD and GC/MS/MS in drinking water and surface water at a LOQ of 0.050 and 0.50 µg/L, respectively” ([draft risk assessment report, 2004](#)). The low PNEC of trichlorfon (0.96 ng/l) is difficult to achieve. Moreover, it is degraded to dichlorvos which is already a priority substance.

References

Draft risk assessment report, July **2004**. Monograph prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC, Trichlorfon, Volume 1. Rapporteur Member State: Spain.

Hoaia, P.M., Sebesvari, Z., Minh, T.B., Viet, P.H., Renaud, F.G. **2011**. Pesticide pollution in agricultural areas of Northern Vietnam: Case study in Hoang Liet and Minh Dai communes. *Environmental Pollution* 159, 3344-3350.

Zhua, H.-Z. Liu, W., Mao, J.-W., Yang, M.-M. **2008**. Cloud point extraction and determination of trace trichlorfon by high performance liquid chromatography with ultraviolet-detection based on its catalytic effect on benzidine oxidizing. *Analytica Chimica Acta* 614, 58-62.

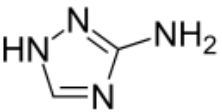
5.2. Cyclododecane

CAS: 294-62-2 Cyclododecane is mainly used as an intermediate in production of flame retardants, detergents, and other chemicals PNEC_{dw,hh} = 2.188 mg/l PNEC_{fw} = 0.468 mg/l PNEC_{biota, sec.pois} = 5 mg/kg (food)	 <chem>C1CCCCCCCCCCC1</chem>
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Conclusion

No information was found for cyclododecane. Analysis in sediment or biota should be possible by GC-MS techniques.

5.3. Aminotriazole (Amitrole)

CAS: 61-82-5 Herbicide $PNEC_{fw} = 32 \mu\text{g/l}$ $PNEC_{dw, hh} = 4 \mu\text{g/l}$	
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Analytical methods

Amitrole is a highly polar water soluble substance, which does not partition into organic solvents. Therefore, traditional LLE or SPE do not work for extracting it from water; extraction is impossible using organic solvents (Mol and van Dam, 2014; Sánchez-Bayoa et al., 2010). Pre-concentration of amitrole residues requires special ion-exchange matrices (Girod et al., 2006; Pichon and Hennion, 1993). Amitrole can be derivatised with FMOC-Cl, and LC-MS-MS is the most reliable and sensitive method to analyse these derivatives of amitrole (Bobeldijk et al., 2001). The direct detection of amitrole has been sought, and it has been achieved by using ion-pair HPLC (Pichon and Hennion, 1993), but unfortunately this method is not suitable for analysis of environmental samples because the inorganic cations present in natural waters compete with the analyte (Pichon et al., 1998). According to the European Commission risk assessment report, an analytical method using LC-LC-MS-MS is considered as validated for the determination of amitrole in drinking and surface water with LOQ 0.05 $\mu\text{g/l}$ (European Commission, January 2013). Also the risk assessment report by EFSA (2014) states that amitrole is analysed in soil and water by LC-LC-MS/MS.

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
Ion-pair extraction (water)	Cation-exchange LC		Pichon and Hennion, 1993
Derivatisation on-line SPE (drinking water, ground and surface water)	LC-MS-MS	0.025	Bobeldijk et al., 2001
SPE (apple)	Derivatisation ion-pairing LC		Sun et al., 2009
LLE with urea in formic acid (milk)	LC-MS-MS		Abernethy and Higgs, 2013
SLE (foods of plant origin)	LC-MS-MS	10 $\mu\text{g/kg}$	EURL-SRM, Anastassiades et al., 2013
SLE (fruits, vegetables and cereal flour)	Flow injection-MS/MS	500 $\mu\text{g/kg}$	Mol and van Dam, 2014

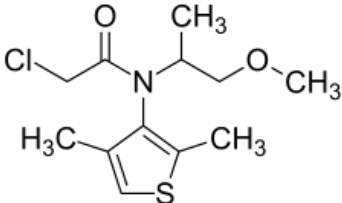
Conclusion

Extraction and analysis of amitrole in water is difficult due to its highly polar water soluble character. The European Commission risk assessment report states that an analytical method using LC-LC-MS-MS is considered as validated for the determination of amitrole in drinking and surface water with LOQ 0.05 $\mu\text{g/l}$ (European Commission, January 2013), but the reference to this method (Amic, S., 2012) is not given in the report, and could not be found on the internet. Therefore, EU Member States and Stakeholders are asked to provide information, if available. The achievable LOQ for amitrole by direct injection (LC-)LC-MS-MS analysis should be tested.

References

- Abernethy, G., Higgs, K. **2013**. Rapid detection of economic adulterants in fresh milk by liquid chromatography–tandem mass spectrometry. *Journal of Chromatography A* 1288, 10– 20.
- Bobeldijk, I., Broess, K., Speksnijder, P., van Leerdam, T. **2001**. Determination of the herbicide amitrole in water with pre-column derivatization, liquid chromatography and tandem mass spectrometry. *J. Chromatogr. A* 938, 15-22.
- EFSA, European Food Safety Authority, **2014**. Conclusion on the peer review of the pesticide risk assessment of the active substance amitrole. *EFSA Journal* 12(7), 3742.
- European Commission, January **2013**. Second Programme for the Renewal of the Inclusion of Active Substances in Annex I of Council Directive 91/414/EEC; Draft Renewal Assessment Report prepared according to the Commission Regulation (EU) N° 1141/2010; Amitrole; Rapporteur Member State: France; Co-Rapporteur Member State: Hungary.
- EURL-SRM, EU Reference Laboratories for Residues of Pesticides, Anastassiades, M., Kolberg, D.I., Mack, D., Wildgrube, C., Sigalov, I., Dörk, D. **2013**. Quick method for the analysis of residues of numerous highly polar pesticides in foods of plant origin involving simultaneous extraction with methanol and LC-MS/MS determination (QuPPE-method).
- Girod, M., Delaurent, C., Charles, L. **2006**. Analysis of amitrole by normal-phase liquid chromatography and tandem mass spectrometry using a sheath liquid electrospray interface. *Rapid Commun. Mass Spectrom.* 20, 892-896.
- Mol, H.G.J., van Dam, R.C.J. **2014**. Rapid detection of pesticides not amenable to multi-residue methods by flow injection–tandem mass spectrometry. *Anal. Bioanal. Chem.* 406, 6817–6825.
- Pichon, V., Hennion, M.-C. **1993**. Comparison of on-line enrichment based on ion-pair and cation-exchange liquid chromatography for the trace-level determination of 3-amino-1,2,4-triazole (aminotriazole) in water. *Analytica Chimica Acta* 284, 317-326.
- Pichon, V., Charpak, M., Hennion, M.-C. **1998**. Multiresidue analysis of pesticides using new laminar extraction disks and liquid chromatography and application to the French priority list. *J. Chromatogr. A* 795, 83-92.
- Sánchez-Bayoa, F., Hyne, R.V., Desseille, K.L. **2010**. An amperometric method for the detection of amitrole, glyphosate and its aminomethyl-phosphonic acid metabolite in environmental waters using passive samplers. *Analytica Chimica Acta* 675, 125–131.
- Sun, Y., Luo, L., Wang, F., Li, J., Cao, Y. **2009**. Ion-pairing high-performance liquid chromatography determination of amitrole in apple after solid-phase extraction and precolumn derivatization. *Anal. Bioanal. Chem.* 395, 465–471.

5.4. Dimethenamid-P

<p>CAS: 87674-68-8</p> <p>Chloroacetamide herbicide</p> <p>Dimethenamid exists, similar to the related chloroacetamides alachlor and metolachlor, as four stereoisomers. Today, in Europe dimethenamid-P is in use, which is a mixture of two particularly efficient isomers. (S)-dimethenamid or dimethenamid-P is a more effective herbicide which can be dosed at lower concentrations than the mixture of the four stereoisomers</p> <p>$PNEC_{fw} = 2.7 \mu\text{g/l}$</p> <p>$PNEC_{sed} = 5 \mu\text{g/kg}$</p>	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
SPE (rainwater)	GC-MS	0.0003	Bucheli et al., 1997
SPE (water; 50 ml)	LC-MS-MS	0.1	Yokley et al., 2002
SPME (SW)	GC-MS	0.001-0.01	Leu et al., 2004
SPE (drinking water)	GC-MS	0.0003	Hladik et al., 2005; 2008
On-line SPE (sea water; 1 l)	LC-MS-MS	0.005	De la Broise and Stachowski-Haberkorn, 2012

Conclusion

Analysis of dimethenamid is performed by GC- or LC-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved. No information was found on the isomer specific analysis of dimethenamid-P, which could be performed with chiral chromatographic separation columns.

References

Bucheli, T.D., Gruebler, F.C., Müller, S.R., Schwarzenbach, R.P. **1997**. Simultaneous determination of neutral and acidic pesticides in natural waters at the low nanogram per liter level. *Anal. Chem.* 69, 1569-1576.

De la Broise, D., Stachowski-Haberkorn, S. **2012**. Evaluation of the partial renewal of in situ phytoplankton microcosms and application to the impact assessment of bentazon and dimethenamid. *Marine Pollution Bulletin* 64, 2480-2488.

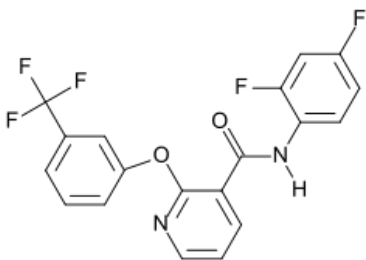
Hladik, M.L., Roberts, A.L., Bouwer, E.J. **2005**. Removal of neutral chloroacetamide herbicide degradates during simulated unit processes for drinking water treatment. *Water Research* 39, 5033-5044.

Hladik, M.L., Bouwer, E.J., Roberts, A.L. **2008**. Neutral chloroacetamide herbicide degradates and related compounds in Midwestern United States drinking water sources. *Science of the Total Environment* 390, 155-165.

Leu, C., Singer, H., Stamm, C., Müller, S.R., Schwarzenbach, R.P. **2004**. Simultaneous assessment of sources, processes, and factors influencing herbicide losses to surface waters in a small agricultural catchment. *Environ. Sci. Technol.* 38, 3827-3834.

Yokley, R.A., Mayer, L.C., Huang, S.-B., Vargo, J.D. **2002**. Analytical method for the determination of metolachlor, acetochlor, alachlor, dimethenamid, and their corresponding ethanesulfonic and oxanillic acid degradates in water using SPE and LC/ESI-MS/MS. *Anal. Chem.* 74, 3754-3759.

5.5. Diflufenican

CAS: 83164-33-4 Herbicide PNEC _{fw} = 0.01 µg/l PNEC _{sed} = 20 µg/kg	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
(soil)	GC-MS		Conte et al., 1998
(soil)	GC- or LC-MS		Bending et al., 2006
SPE (water) SLE (sediment and fish)	LC-MS-MS	0.0034 (water) 48 µg/kg	Lazartigues et al., 2011a

QuEChERS	LC-MS-MS	0.27-0.54 µg/kg	Lazartigues et al., 2011b
SPE (SW)	GC-MS (EN ISO 10695)	0.005	Botta et al., 2012
LLE (SW and GW; 500 ml)	GC-MS-MS	< 0.01	Hermosin et al., 2013

Monitoring data

Diflufenican was analysed in the years 2009-2010 in surface and groundwater in the Guadalquivir river basin (southern Spain). The maximum concentration found in 2009 in SW was 1.16 µg/l (mean 0.05 µg/l, and median 0.01 µg/l). In the year 2010 the maximum concentration was 0.09 µg/l. The maximum concentration in GW was 0.03 µg/l ([Hermosin et al., 2013](#)).

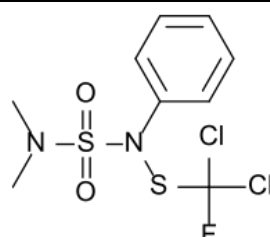
Conclusion

Analysis of diflufenican is performed by GC- or LC-MS-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

- Bending, G.D., Lincoln, S.D., Edmondson, R.N. **2006**. Spatial variation in the degradation rate of the pesticides isoproturon, azoxystrobin and diflufenican in soil and its relationship with chemical and microbial properties. *Environmental Pollution* 139, 279-287.
- Botta, F., Fauchon, N., Blanchoud, H., Chevreuil, M., Guery, B. **2012**. Phyt'Eaux Cités: Application and validation of a programme to reduce surface water contamination with urban pesticides. *Chemosphere* 86, 166–176.
- Conte, E., Morali, G., Galli, M., Imbroglini, G., Leake, C.R. **1998**. Long-term degradation and potential plant uptake of diflufenican under field conditions. *Journal of Agriculture and Food Chemistry* 46, 4766-4770.
- Hermosin, M.C., Calderon, M.J., Real, M., Cornejo, J. **2013**. Impact of herbicides used in olive groves on waters of the Guadalquivir river basin (southern Spain). *Agriculture, Ecosystems and Environment* 164, 229– 243.
- Lazartigues, A., Fratta, C., Baudot, R., Wiest, L., Feidt, C., Thomas, M., Cren-Olivé, C. **2011a**. Multiresidue method for the determination of 13 pesticides in three environmental matrices: water, sediments and fish muscle. *Talanta* 85, 1500-1507.
- Lazartigues, A., Wiest, L., Baudot, R., Thomas, M., Feidt, C., Cren-Olivé, C. **2011b**. Multiresidue method to quantify pesticides in fish muscle by QuEChERS-based extraction and LC-MS/MS. *Anal. Bioanal. Chem.* 400, 2185–2193.
- Lazartigues, A., Thomas, M., Cren-Olivé, C., Brun-Bellut, J., Le Roux, Y., Banas, D., Feidt, C. **2013**. Pesticide pressure and fish farming in barrage pond in Northeastern France. Part II: Residues of 13 pesticides in water, sediments, edible fish and their relationships. *Environ. Sci. Poll. Res.* 20, 117–125.

5.6. Dichlofluanid

CAS: 1085-98-9 Fungicide; wood preservative; used as booster biocide in antifouling paints PNEC _{fw} = 0.265 µg/l PNEC _{sed} = 18 µg/kg	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) (µg/l)	Reference
SPE with Speedisk® extraction disk (sea water) SLE (marine sediment)	GC-MS	0.010 (water) 10 µg/kg (sediment)	Hamwijk et al., 2005
SPE (sea water)	LC-MS-MS	0.0003 – 0.0005	Sánchez-Rodríguez et al., 2011a;b
LLE (sea water)	GC-MS	0.00177	Lee et al., 2011
Microwave-assisted	LC-MS-MS	0.1-0.3 µg/kg	Sánchez-Rodríguez et al., 2011c

extraction (sediment)			
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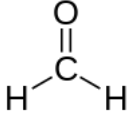
Conclusion

Dichlofluanid can be analysed by GC-MS and LC-MS-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

- Hamwijk, C., Schouten, A., Foekema, E.M., Ravensberg, J.C., Collombon, M.T., Schmidt, K., Kugler, M. **2005**. Monitoring of the booster biocide dichlofluanid in water and marine sediment of Greek marinas. Chemosphere 60, 1316–1324.
- Lee, S., Chung, J., Won, H., Lee, D., Lee, Y.-W. **2011**. Analysis of antifouling agents after regulation of tributyltin compounds in Korea. Journal of Hazardous Materials 185, 1318–1325.
- Sánchez Rodríguez, Á., Sosa Ferrera, Z., Santana Rodríguez, J., **2011a**. An evaluation of antifouling booster biocides in Gran Canaria coastal waters using SPE–LC MS/MS. International Journal of Environmental Analytical Chemistry 91, 1166–1177.
- Sánchez-Rodríguez, A., Sosa-Ferrera, Z., Santana-del Pino, A., Santana-Rodríguez, J.J. **2011b**. Probabilistic risk assessment of common booster biocides in surface waters of the harbours of Gran Canaria (Spain). Marine Pollution Bulletin 62, 985–991.
- Sánchez-Rodríguez, A., Sosa-Ferrera, Z., Santana-Rodríguez, J.J. **2011c**. Applicability of microwave-assisted extraction combined with LC–MS/MS in the evaluation of booster biocide levels in harbour sediments. Journal of Hazardous Materials 185, 1318–1325.

5.7. Formaldehyde

CAS: 50-00-0 Commercial solutions of formaldehyde in water, commonly called formol, were formerly used as disinfectants and for preservation of biological specimens. It is commonly used in nail hardeners and/or nail varnish PNEC _{fw} = 470 µg/l PNEC _{sed} = 2.44 mg/kg PNEC _{dw, hh} = 525 µg/l	
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Formaldehyde in (drinking) water is generally determined by a high-performance liquid chromatographic (HPLC) method following derivatisation with 2,4-dinitrophenylhydrazine and UV detection including extraction from water by SPE. The detection limit is 6.2 µg/l (WHO, 2005; US EPA, 1992; 1996).

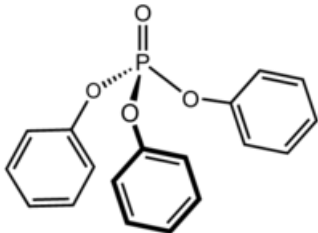
Conclusion

Formaldehyde can be analysed in water with LOQ 6.2 µg/l (US EPA method).

References

- WHO, **2005**. Formaldehyde in drinking-water. Background document for development of WHO guidelines for drinking-water quality. WHO/SDE/WSH/05.08/48.
- US EPA Method 554, **1992**. Determination of carbonyl compounds in drinking water by dinitrophenylhydrazine derivatization and high performance liquid chromatography.
- US EPA Method 8315A, **1996**. Determination of carbonyl compounds by high performance liquid chromatography (HPLC).

5.8. Triphenyl phosphate

CAS: 115-86-6 Flame retardant / plasticizer $PNEC_{fw} = 3.7 \mu\text{g/l}$ $PNEC_{sed} = 240 \mu\text{g/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
LLE (surface water and WWTP effluents)	GC-MS	0.010	Andresen et al., 2004
LLE (surface water, WW)	LC-MS-MS	0.0044 (SW) 0.007 (WW)	Martínez-Carballo et al., 2007
SLE (sediment)		0.79 $\mu\text{g/kg}$ (sediment)	

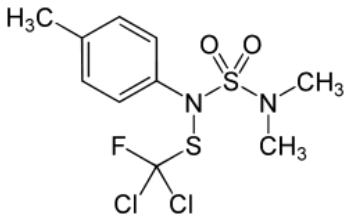
Conclusion

Triphenyl phosphate can be analysed by GC-MS and LC-MS-MS techniques. The available literature indicates that LOQ in the low ng/l range can be achieved.

References

- Andresen, J.A., Grundmann, A., Bester, K. **2004**. Organophosphorus flame retardants and plasticisers in surface waters. *Science of the Total Environment* 332, 155-166.
- Benito Quintana, J., Rodil, R., Reemtsma, T., Garcia-Lopez, M., Rodriguez, I. **2008**. Organophosphorus flame retardants and plasticizers in water and air II. Analytical methodology. *Trends in Analytical Chemistry* 27, 904-915.
- Martínez-Carballo, E., González-Barreiro, C., Sitka, A., Scharf, S., Gans, O. **2007**. Determination of selected organophosphate esters in the aquatic environment of Austria. *Science of the Total Environment* 388, 290-299.

5.9. Tolyfluanid

CAS: 731-27-1 Tolyfluanid degrades into N,N-dimethyl-sulfamide (N,N-DMS) which may be transformed into N-nitrosodimethylamine (NDMA) when exposed to ozone during the process of producing drinking water $PNEC_{fw} = 0.265 \mu\text{g/l}$ $PNEC_{sed} = 58 \mu\text{g/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
QuEChERS (strawberries)	GC-MS-MS	0.3 $\mu\text{g/kg}$	Fernandes et al., 2012
(surface and groundwater)	Direct injection (100 μl) LC-MS-MS	0.010	Reemtsma et al., 2013

Conclusion

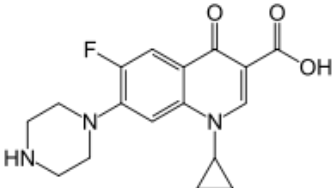
Little information on tolylfluanid is available; it is not commonly analysed in water. Analysis can be performed by GC- or LC-MS techniques.

References

Fernandes, V.C., Domingues, V.F., Mateus, N., Delerue-Matos, C. **2012**. Pesticide residues in Portuguese strawberries grown in 2009-2010 using integrated pest management and organic farming. *Environ. Sci. Pollut. Res.* 19, 4184–4192.

Reemtsma, T., Alder, L., Banasiak, U. **2013**. A multimethod for the determination of 150 pesticide metabolites in surface water and groundwater using direct injection liquid chromatography–mass spectrometry. *Journal of Chromatography A* 1271, 95–104.

5.10. Ciprofloxacin

CAS: 85721-33-1 Fluoroquinolone antibiotic $PNEC_{fw} = 0.089 \mu\text{g/l}$ $PNEC_{sed} = 272 \mu\text{g/kg}$	
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Analytical methods

Extraction (matrix)	Analysis	LOD(Q) ($\mu\text{g/l}$)	Reference
SPE (surface and drinking water)	LC-MS-MS	0.0084 (DW) 0.024 (SW)	Vieno et al., 2006; 2007
SPE (surface water)	LC-MS-MS	0.002	Gros et al., 2009
SPE (surface water) Strong cation exchange (biota fish)	LC-MS-MS	0.0034 10 $\mu\text{g/kg}$	Wagil et al., 2014
SPE (0.5 l); river water	LC-MS-MS	LOD: 0.0055 LOQ: 0.0183	Petrović et al., 2014

Conclusion

Many publications are available. Ciprofloxacin is analysed by LC-MS-MS techniques. LOQ in the low ng/l range can be achieved.

References

Gros, M., Petrovic, M., Barceló, D. **2009**. Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/quadrupole-linear ion trap mass spectrometry and automated library searching. *Anal. Chem.* 81, 898–912.

Petrović, M., Škrbić, B., Živančev, J., Ferrando-Climent, L., Barcelo, D. **2014**. Determination of 81 pharmaceutical drugs by high performance liquid chromatography coupled to mass spectrometry with hybrid triple quadrupole–linear ion trap in different types of water in Serbia. *Science of the Total Environment* 468–469, 415–428.

Vieno, N., Tuhkanen, T., Kronberg, L. **2006**. Analysis of neutral and basic pharmaceuticals in sewage treatment plants and in recipient rivers using solid phase extraction and LC-MS/MS detection. *J. Chromatogr. A* 1134, 101–111.

Vieno, N.M., Härkki, H., Tuhkanen, T., Kronberg, L. **2007**. Occurrence of pharmaceuticals in riverwater and their elimination in a pilot-scale drinking water treatment plant. *Environ. Sci. Technol.* 41, 5077–5084.

Wagil, M., Kumirska, J., Stolte, S., Puckowski, A., Maszkowska, J., Stepnowski, P., Białk-Bielińska, A. **2014**. Development of sensitive and reliable LC-MS/MS methods for the determination of three fluoroquinolones in water and fish tissue samples and preliminary environmental risk assessment of their presence in two rivers in northern Poland. *Science of the Total Environment* 493, 1006–1013.

5.11. Free cyanide

CAS: 57-12-5 PNEC _{fw} = 0.26 µg/l	HCN and CN ⁻
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The toxicity of cyanide is well known. Cyanide occurs naturally in many foods (cassava, sorghum, African lima beans, bamboo shoots, bitter almonds, and apricot, cherry, and peach pits) and is naturally generated by microorganisms. In addition, cyanide is used in many industries (e.g., plating and mining) and it can be released into the air from burning coal and plastics ([Dionex Application note 173](#)).

Numerous cyanide species can occur in water, but identification and quantification of these species is not commonly practiced. Cyanide is determined as total cyanide, disassociated cyanide, and free cyanide. Cyanide forms strong metal complexes with Fe, Co, Pt, and Au, and weak to moderately strong metal complexes with Ag, Co, Hg, and Ni. Some metal-cyanide complexes such as Zn, Ni, Co and Cd cyanide are easily dissociable under acidic conditions and are classified as weak acid dissociable (WAD) species. In the literature it is not always clearly described if a method determines total or free cyanide or other species. Free cyanide is defined as the sum of the cyanide present as hydrogen cyanide (HCN) and as the cyanide ion (CN⁻) and is dependent on pH and temperature. The bulk measurement “total cyanide by distillation”, which does not differentiate different forms of cyanide (and excludes thiocyanate, cyanate, organocyanides, and some other forms), is usually employed to assess cyanide content of water. Since different forms of cyanide have different toxicity characteristics and physical-chemical properties, total cyanide analytical data have limitations for use in risk assessment and in evaluation of cyanide fate and transport in the aquatic environment and treatment processes. Free cyanide is a more reliable measure of toxicity to aquatic life than total cyanide because total cyanide can include nitriles and other stable metalocyanide complexes that are not very toxic to aquatic life. US EPA recently approved methods for free cyanide and preliminary research indicates that these analytical costs are more expensive than the analysis for total cyanide ([Dionex Application note 173](#); [State of Oregon, 2012](#); [Zheng et al., 2003](#)).

A variety of different methods are available for the analysis of cyanide. Total cyanide methods rely on analysis after distillation (the water sample is pretreated with acid and an oxidizing agent under heat which breaks down most cyanide-bearing compounds to generate hydrogen cyanide gas that is captured in a pH 13 sodium hydroxide solution). The cyanide concentration is determined with titration, ion chromatography, colorimetric procedure (spectrophotometric), selective ion electrode, or flow injection analysis with gas diffusion separation and amperometric detection. US EPA recommends EPA methods 335.2, 335.3, 335.4 and methods SM 4500-CN C, D, E, and F published in the *Standard Methods for the Examination of Water and Wastewater* ([NEMI](#)). Method ASTM D6888 is an additional approved method for analysis of total cyanide. Other methods are available for cyanides that are amenable to chlorination after distillation ([Dionex Application note 173](#); [State of Oregon, 2012](#)).

US EPA has approved three methods for free cyanide: OIA 1677, ASTM method D4282 and ASTM method D7237. The analyses for free cyanide by these new methods are available at a limited number of laboratories because they utilize relatively new technology. It should be noted that the costs for analysis of free cyanide is more expensive relative to the analysis of other forms of cyanide ([State of Oregon, 2012](#)).

However, EPA method OIA 1677 is not a real free cyanide method since it also captures the cyano-complexes of zinc, copper, cadmium, mercury, nickel, and silver (the weak acid dissociable (WAD) species). Cyanide detection is accomplished using a flow-injection analysis (FIA) system. A 200 µl aliquot of the pre-treated sample is injected into the flow injection manifold of the system. The addition of hydrochloric acid converts cyanide ion to hydrogen cyanide (HCN) that passes under a gas diffusion membrane. The HCN diffuses through the membrane into an alkaline receiving solution where it is converted back to cyanide ion. The cyanide ion is monitored amperometrically with a

silver working electrode, silver/silver chloride reference electrode, and platinum/stainless steel counter electrode, at an applied potential of zero volt. The current generated is proportional to the cyanide concentration present in the original sample. Total analysis time is approximately two minutes ([US EPA, 1999](#); [Zheng et al., 2003](#)).

ISO 14403-2:2012 specifies methods for the determination of total cyanide (free cyanide can be also analysed with some system changes) in various types of water (such as ground, drinking, surface, leachate, and waste water) with cyanide concentrations usually from 2 µg/l to 500 µg/l expressed as cyanide ions in the undiluted sample. In this method, a suitable mass concentration range from 10 µg/l to 100 µg/l is described (LOQ of 10 µg/l). The range of application, however, can be changed by varying the operation conditions, e.g. by diluting the original sample or changing the pathlength of the flow cell (to increase sensitivity). This approach is applied in Portugal by using a new robotic sample preparation system, and LOQ of 1 µg/l for free cyanide has been achieved ([Viana, P., personal communication](#)). Seawater can be analysed with possible changes in sensitivity and adaptation of the reagent and calibration solutions to the salinity of the samples. Analysis can be performed by flow injection analysis (FIA) or continuous flow analysis (CFA). Both methods share the feature of an automatic introduction of the sample into a flow system (manifold) in which the analytes in the sample react with reagent solutions on their way through the manifold. Sample preparation may be integrated in the manifold. The reaction product is measured spectrophotometrically in a flow detector (e.g. flow photometer). Methods using flow analysis automate wet chemical procedures and are particularly suitable for the processing of many analytes in water in large series of samples at a high frequency of analysis ([ISO 14403-2:2012](#)).

Total cyanide methods:

Sample preparation (application)	Analysis	LOQ (µg/L)	Reference
The cyanide as hydro-cyanic acid (HCN) is released from cyanide complexes by means of UV digestion and distillation. (drinking and surface waters)	Cyanides are converted to cyanogen chloride by reactions with chloramine-T which subsequently reacts with pyridine and barbituric acid to give a red-colored complex (Colorimetry)	5	US EPA method 335.3 (1978)
	Continuous flow system with spectrophotometric determination	0.6	Meeussen et al. 1989
Manual reflux-distillation operation and sodium hydroxide absorption (drinking, ground, surface, and saline waters)	Cyanides are converted to cyanogen chloride by reactions with chloramine-T which subsequently reacts with pyridine and barbituric acid to give a red-colored complex (Colorimetry)	5	US EPA method 335.4, 1993
Sodium hydroxide absorption (water)	Ion-selective electrode detection	50	American Public Health Association, 1998
Ligand exchange. Cyanide ion (CN ⁻), hydrogen cyanide in water (HCN), and the cyano-complexes of zinc, copper, cadmium, mercury, nickel, and silver may be determined by this method	Flow injection and amperometry: Method OIA-1677 is an additional test procedure for measuring the same cyanide species as are measured by currently approved methods for cyanide amenable to chlorination (CATC); it captures the WAD) species. In some matrices, CATC methods are subject to significant test interferences. Method OIA-1677 has been added to the list of approved	0.5	US EPA method OIA-1677, 1999

	methods because it is more specific for available cyanide, is more rapid, measures cyanide at lower concentrations, offers improved safety, reduces laboratory waste, and is more precise and accurate than currently approved CATC methods		
Non-distillation method; automated in-line UV digestion to dissociate cyanide complexes (water)	Amperometric detection	3	ASTM, 2010
	Ligand displacement and flow injection analysis (FIA) utilizing gas diffusion separation and amperometric detection	2	ASTM D6888
Stabilization with 50% sodium hydroxide (tap and river water)	IC - Pulsed amperometric detector (PAD)	1	Dionex Application note 173
(ground, drinking, surface, leachate, and waste water)	Flow injection analysis (FIA) or continuous flow analysis (CFA) followed by spectrophotometric detection	10	ISO 14403-2:2012

Free cyanide methods:

Sample preparation (application)	Analysis	LOQ (µg/L)	Reference
Microdiffusion with sodium hydroxide absorption	An aliquot of the sodium hydroxide absorber solution is removed and treated with acidified phosphate buffer and chloramine-T to convert the CN ⁻ to cyanogen chloride. The cyanogen chloride is reacted with pyridine-barbituric acid to form a color complex that absorbs at 578 to 587 nm. The free cyanide is determined spectrophotometrically by measuring the absorbance of the sample and determining the concentration through comparison with a standard calibration curve	5	US EPA method 9016, 2010
Stabilization with 50% sodium hydroxide (tap and river water)	IC - Pulsed amperometric detector (PAD)	1	Dionex Application note 173
This free cyanide method is based on the same instrumentation and technology that is described in standard test method ASTM D6888, but employs milder conditions (pH 6-8 buffer versus HCl or H ₂ SO ₄ in the reagent stream), and does not utilize ligand	Flow injection analysis (FIA) utilizing gas diffusion separation and amperometric detection	2	ASTM D7237

displacement reagents. (natural water, saline waters, and wastewater effluent)			
Microdiffusion: Here free cyanide refers to those simple cyanides (HCN, CN-) and/or readily dissociable metalcyanide complexes that yield, at pH6 and room temperature, HCN which diffuses from the sample, through the enclosed vapor phase, to an NaOH trap. (waters, and wastewater)	Colorimetry: Cyanide concentration in the NaOH solution is determined by a colorimetric procedure in which cyanides are converted, by reaction with chloramine-T, to cyanogen chloride which subsequently is reacted with pyridine and barbituric acid to give a red-colored complex.	10	ASTM D4282
(ground, drinking, surface, leachate, and waste water)	Flow injection analysis (FIA) or continuous flow analysis (CFA) followed by spectrophotometric detection	10 (1 µg/l can be reached by changing the path length of the flow cell)	ISO 14403-2:2012

Cyanide is reactive and unstable, therefore (drinking) water samples should be stabilized as soon as possible and free cyanide determined as soon as possible. Oxidizing agents decompose cyanide. Also any free cyanide present at neutral pH will volatilize to hydrogen cyanide ([Dionex Application note 173](#)).

Conclusion

The lowest LODs or LOQs found in the literature for (free) cyanide are 0.6 µg/l by [Meeussen et al. \(1989\)](#), 0.5 µg/l by the [US EPA method OIA-1677 \(1999\)](#), 1 µg/l by Dionex ([Dionex Application note 173](#)) for an ion chromatography method with a pulsed amperometric detector, and 2 µg/l using [ASTM D7237](#) by flow injection analysis (FIA) utilizing gas diffusion separation and amperometric detection. In addition, [Zheng et al. \(2003\)](#) report a MDL of approximately 1.5 µg/l for the ASTM microdiffusion-colorimetry method 4282. However, although the LODs in the method used by [Meeussen et al. \(1989\)](#) and the [US EPA method OIA-1677 \(1999\)](#) are low, they are not true free cyanide methods, as free cyanide is calculated through the correction of the total cyanide concentration. In conclusion, although the current routine analysis for free cyanides could reach a lowest LOQ of approximately 1-2 µg/l, it is still not sufficiently sensitive to assess compliance with the proposed PNEC for free cyanide.

References

American Public Health Association, American Water Works Association, and Water Environment Federation, Washington D.C., Standard Methods SM-4500-CN-F, **1998**.

ASTM D6888, American Society for Testing and Materials (ASTM), Standard test method for available cyanide with ligand displacement and flow injection analysis (FIA) utilizing gas diffusion separation and amperometric detection. URL: <http://www.astm.org/Standards/-D6888.htm>.

ASTM D7237, American Society for Testing and Materials (ASTM), Standard test method for free cyanide with flow injection analysis (FIA) utilizing gas diffusion separation and amperometric detection, URL: <http://www.astm.org/Standards/D7237.htm>

ASTM, **2010**. Total cyanide analysis of NPDES wastewater samples by ASTM D 7511-09e2. URL:<http://downloads.vertmarkets.com/files/downloads/70c8372c-42fe-473f-ac11-1555497db30d/3687wpaper.pdf>

ASTM D4282, **2010**. Standard test method for determination of free cyanide in water and wastewater by microdiffusion. URL: <http://www.astm.org/database.cart/historical/-D4282-02.htm>

Dionex Application note 173. Direct determination of cyanide in drinking water by ion chromatography with pulsed amperometric detection. Thermo Scientific; URL: http://www.dionex.com/en-us/webdocs/40397-AN173_LPN1787-R2.pdf

ISO 14403-2:**2012**. Water quality – Determination of total cyanide and free cyanide using flow analysis (FIA and CFA) – Part 2 : Method using continuous flow analysis (CFA).

Meeussen JCL, Temminghoff EJM, Keizer MG, Novozamsky I. **1989**. Spectrophotometric determination of total cyanide, iron – cyanide complexes, free cyanide and thiocyanate in water by a continuous-flow system. *Analyst* 114, 959 – 963.

NEMI, National Environmental Methods Index; URL: https://www.nemi.gov/methods/-method_summary/5708/

State of Oregon, Department of Environmental Quality Memorandum, www.deq.state.or.us/-wq/standards/docs/toxics/cyanide.pdf , **2012**

US EPA, **1978**. Method 335.3: Cyanide, total (colorimetric, automated UV).

US EPA, **1993**. Method 335.4: Determination of total cyanide by semi-automated colorimetry.

US EPA, **1999**. Method OIA-1677: Available cyanide by flow injection, ligand exchange, and amperometry. URL: http://water.epa.gov/scitech/methods/cwa/metals/cyanide/upload/-2007_07_10_methods_method_cyanide_1677final.pdf

US EPA. **2010**, Method 9016: Free cyanide in water, soils and solid wastes by microdiffusion. URL: <http://www.epa.gov/osw/hazard/testmethods/pdfs/9016.pdf>

Zheng, A., Dzombak, D.A., Luthy, R.G., Sawyer, B., Lazouskas, W., Tata, P., Delaney, M.F., Zilitinkevitch, L., Sebroski, J.R., Swartling, R.S., Drop, S.M., Flaherty, J.M. **2003**. Evaluation and testing of analytical methods for cyanide species in municipal and industrial contaminated waters. *Environ. Sci. Technol.* 37, 107-115.

6. Conclusions

Following extensive technical exchanges with experts from EU Member States and stakeholder groups, the 10 (groups of) substances proposed by the JRC for inclusion in the 1st WFD *Watch List* are diclofenac, 17-beta-estradiol (E2) and estrone (E1), 17-alpha-ethinylestradiol (EE2), oxadiazon, methiocarb, 2,6-ditert-butyl-4-methylphenol, tri-allate, neonicotinoid insecticides as a group (imidacloprid, thiacloprid, thiamethoxam, clothianidin, acetamiprid), macrolide antibiotics (erythromycin, clarithromycin, azithromycin), and 2-ethylhexyl-4-methoxycinnamate. The recommended monitoring matrix is in most cases water. For 2,6-ditert-butyl-4-methylphenol and 2-ethylhexyl-4-methoxycinnamate (EHMC) sediment would be respectively as or more appropriate. EHMC partitions quickly to sediment. The macrolide antibiotics could also be monitored in sediment. In the case of water analysis, all compounds can be analysed by LLE or SPE followed by LC-MS-MS or GC-MS. Large-volume SPE (extraction of more than 2 litres) is necessary to achieve the extremely low EQS for 17-alpha-ethinylestradiol. Sediment is extracted by SLE (solid liquid extraction) using techniques such as Soxhlet, pressurized liquid extraction (accelerated solvent extraction), or sonification. Multi-compound analytical methods are available for the proposed groups of substances (neonicotinoids and macrolide antibiotics). Trichlorfon and aminotriazole (amitrole) had to be excluded from the proposed list due to the non-availability of an appropriate analytical method. Also the analysis of free cyanide at the proposed PNEC value of 0.26 µg/l is difficult.

7. References

Carvalho, R.N., Ceriani, L., Ippolito, A., Lettieri, T. **2015**. Development of the 1st Watch List under the Environmental Quality Standards Directive. JRC Science and Policy Report.

European Union, **2000**. Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy.

European Union, **2008**. Directive 2008/105/EU of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council.

European Union, **2011**. Proposal for a Directive of the European Parliament and of the Council amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. COM(2011) 876 Final

<http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM:2011:0876:FIN>

European Union, **2013**. Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, as amended by Directive 2013/39/EU of the European Parliament and of the Council of 12 August 2013.

8. Internet pages used for the literature search

<http://www.sciencedirect.com/science/search>

<http://www.scopus.com/home.url>

<http://pubs.acs.org/journal/esthag> (Environmental Science & Technology)

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