ICS 13.060.50 SLOVENSKÁ TECHNICKÁ NORMA December 2021

STN	**Kvalita vody Stanovenie rozpustenej frakcie vybraných aktívnych farmaceutických zložiek, produktov premeny a iných organických látok vo vode a vyčistenej odpadovej vode Metóda vysokoúčinnej kvapalinovej chromatografie a hmotnostnej spektrometrickej detekcie (HPLC-MS/MS alebo -HRMS) po priamej injekcii (ISO 21676: 2018)**	**STN EN ISO 21676** 75 7517

Water quality - Determination of the dissolved fraction of selected active pharmaceutical ingredients, transformation products and other organic substances in water and treated waste water - Method using high performance liquid chromatography and mass spectrometric detection (HPLC-MS/MS or -HRMS) after direct injection (ISO 21676:2018)

Táto norma obsahuje anglickú verziu európskej normy.
This standard includes the English version of the European Standard.

Táto norma bola oznámená vo Vestníku ÚNMS SR č. 11/21

Obsahuje: EN ISO 21676:2021, ISO 21676:2018

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 21676

August 2021

ICS 13.060.50

English Version

Water quality - Determination of the dissolved fraction of selected active pharmaceutical ingredients, transformation products and other organic substances in water and treated waste water - Method using high performance liquid chromatography and mass spectrometric detection (HPLC-MS/MS or -HRMS) after direct injection (ISO 21676:2018)

Qualité de l'eau - Détermination de la fraction dissoute des ingrédients pharmaceutiques actifs sélectionnés, des produits de la transformation et d'autres substances organiques dans l'eau et dans l'eau résiduaire - Méthode par chromatographie en phase liquide à haute performance et détection par spectrométrie de masse (CLHP-MS/MS ou -HRSM) après l'injection directe (ISO 21676:2018)

Wasserbeschaffenheit - Bestimmung ausgewählter Arzneimittelwirkstoffe, Transformationsprodukte und weiterer organischer Stoffe gelöst in Wasser und gereinigtem Abwasser - Verfahren mittels Hochleistungs-Flüssigkeitschromatographie und massenspektrometrischer Detektion (HPLC-MS/MS oder -HRMS) nach Direktinjektion (ISO 21676:2018)

This European Standard was approved by CEN on 18 July 2021.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

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COMITÉ EUROPÉEN DE NORMALISATION
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CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

Ref. No. EN ISO 21676:2021 E

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European foreword

The text of ISO 21676:2018 has been prepared by Technical Committee ISO/TC 147 "Water quality" of the International Organization for Standardization (ISO) and has been taken over as EN ISO 21676:2021 by Technical Committee CEN/TC 230 "Water analysis" the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by February 2022, and conflicting national standards shall be withdrawn at the latest by February 2022.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

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Endorsement notice

The text of ISO 21676:2018 has been approved by CEN as EN ISO 21676:2021 without any modification.

INTERNATIONAL STANDARD

ISO 21676

First edition
2018-10

Water quality — Determination of the dissolved fraction of selected active pharmaceutical ingredients, transformation products and other organic substances in water and treated waste water — Method using high performance liquid chromatography and mass spectrometric detection (HPLC-MS/MS or -HRMS) after direct injection

Qualité de l'eau — Détermination de la fraction dissoute des ingrédients pharmaceutiques actifs sélectionnés, des produits de la transformation et d'autres substances organiques dans l'eau et dans l'eau résiduaire — Méthode par chromatographie en phase liquide à haute performance et détection par spectrométrie de masse (CLHP-MS/MS ou -HRSM) après l'injection directe

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 147, *Water quality*, Subcommittee SC 2, *Physical, chemical and biochemical methods*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Pharmaceutical ingredients are essential for human and animal health. Through application or improper disposal, active pharmaceutical ingredients enter the water cycle unchanged or transformed. This can happen via municipal waste water, treated at treatment plants. There, some active pharmaceutical ingredients and transformation products cannot be removed completely from the waste water by conventional treatment techniques. Active pharmaceutical ingredients and their transformation products also travel through sludge to the soil and subsequently enter water bodies via leachate, depending on the nature of the ground and the active ingredients. Active pharmaceutical ingredients and their transformation products are therefore found in treated waste water, as well as in surface and ground water. This document specifies a liquid chromatography method with mass spectrometric detection for the determination of selected active pharmaceutical ingredients and their transformation products in the dissolved fraction.

INTERNATIONAL STANDARD ISO 21676:2018(E)

Water quality — Determination of the dissolved fraction of selected active pharmaceutical ingredients, transformation products and other organic substances in water and treated waste water — Method using high performance liquid chromatography and mass spectrometric detection (HPLC-MS/MS or -HRMS) after direct injection

WARNING — Persons using this document should be familiar with normal laboratory practice. This document does not purport to address all of the safety problems, if any, associated with its use. It is the responsibility of the user to establish appropriate safety and health practices.

IMPORTANT — It is absolutely essential that tests conducted in accordance with this document be carried out by suitably qualified staff.

1 Scope

This document specifies a method for the determination of the dissolved fraction of selected active pharmaceutical ingredients and transformation products, as well as other organic substances (see Table 1) in drinking water, ground water, surface water and treated waste water.

The lower application range of this method can vary depending on the sensitivity of the equipment used and the matrix of the sample. For most compounds to which this document applies, the range is ≥ 0,025 µg/l for drinking water, ground water and surface water, and ≥ 0,050 µg/l for treated waste water.

The method can be used to determine further organic substances or in other types of water (e.g. process water) provided that accuracy has been tested and verified for each case, and that storage conditions of both samples and reference solutions have been validated. Table 1 shows the substances for which a determination was tested in accordance with the method. Table E.1 provides examples of the determination of other organic substances.

Table 1 — Substances for which a determination was tested in accordance with this method

Common name Chemical name (IUPAC[a])	Molecular formula	Molar mass g/mol	CAS-RN[b]
4-Acetylaminoantipyrine N-(2,3-Dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)acetamide	$C_{13}H_{15}N_3O_2$	245,28	83-15-8
N4-Acetyl sulfamethoxazole N-{4-[(5-Methyl-1,2-oxazol-3-yl)sulfamoyl]phenyl}-acetamide	$C_{12}H_{13}N_3O_4S$	295,32	21312-10-7
Diatrizoic acid (amidotricoic acid) 3,5-Bis(acetamido)-2,4,6-triiodobenzoic acid	$C_{11}H_9I_3N_2O_4$	613,91	117-96-4
Atenolol (RS)-2-[4-[2-Hydroxy-3-(1-methylethylamino) propoxy]phenyl] ethanamide	$C_{14}H_{22}N_2O_3$	266,34	29122-68-7
[a] IUPAC: International Union of Pure and Applied Chemistry.			
[b] CAS-RN: Chemical Abstracts System Registration Number.			

Table 1 *(continued)*

Common name Chemical name (IUPAC[a])	Molecular formula	Molar mass g/mol	CAS-RN[b]
Bezafibrate 2-{4-[2-(4-Chlorbenzamido)ethyl]phenoxyl}-2-methylpropanoic acid	$C_{19}H_{20}ClNO_4$	361,80	41859-67-0
Bisoprolol (RS)-1-[4-(2-Isopropoxyethoxymethyl)phenoxy]-3-isopropylamino-2-propanol	$C_{18}H_{31}NO_4$	325,45	66722-44-9
Carbamazepine 5H-Dibenzo[b,f]azepine-5-carbamide	$C_{15}H_{12}N_2O$	236,27	298-46-4
Clarithromycin (2R,3R,4S,5R,8R,9S,10S,11R,12R,14R)-11-[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy-5-ethyl-3,4-dihydroxy-9-[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyl-oxan-2-yl]oxy-12-methoxy-2,4,8,10,12,14-hexa-methyl-6-oxacyclotetradecane-1,7-dione	$C_{38}H_{69}NO_{13}$	747,95	81103-11-9
Clofibric acid 2-(4-Chlorophenoxy)-2-methylpropanoic acid	$C_{10}H_{11}ClO_3$	214,70	882-09-7
Dehydrato-Erythromycin (anhydro-erythromycin) (2R,3R,4S,5S,8R,9S,10S,11R,12R)-11-{[4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy}-5-ethyl-3-hydroxy-9-[(5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl)oxy]-2,4,8,10,12,14-hexame-thyl-6,15,16-trioxatricyclo[10.2.1.1{1,4}]hexadecane-7-one	$C_{37}H_{65}NO_{12}$	715,91	23893-13-2
Diazepam (RS)-7-Chlor-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepine-2-on	$C_{16}H_{13}ClN_2O$	284,74	439-14-5
Diclofenac 2-[2-[(2,6-Dichlorphenyl)amino]phenyl]acetic acid	$C_{14}H_{11}Cl_2NO_2$	296,15	15307-86-5
10,11-Dihydro-10,11-dihydroxy carbamazepine (5S,6S)-5,6-Dihydroxy-5,6-dihydrobenzo[b][1]benzazepie-11-carboxamide	$C_{15}H_{14}N_2O_3$	270,29	58955-93-4
Erythromycin 6-(4-Dimethylamino-3-hydroxy-6-methyl-oxan-2-yl)oxy-14-ethyl-7,12,13-trihydroxy-4-(5-hydroxy-4-methoxy-4,6-dimethyl-oxan-2-yl)-oxy-3,5,7,9,11,13-hexamethyl-1-oxacyclo-tetradecane-2,10-dione	$C_{37}H_{67}NO_{13}$	733,93	114-07-8
4-Formylaminoantipyrine N-(2,3-Dihydro-1,5-dimethyl-3-oxo-2-phenyl-1H-pyrazol-4-yl) formamide	$C_{12}H_{13}N_3O_2$	231,25	1672-58-8
Gemfibrozil 5-(2,5-Chlorophenoxy)-2,2-methylpropanoic acid	$C_{15}H_{22}O_3$	250,34	25812-30-0
Ibuprofen (RS)-2-[4-(2-Methylpropyl)phenyl]propanoic acid	$C_{13}H_{18}O_2$	206,28	15687-27-1

[a] IUPAC: International Union of Pure and Applied Chemistry.

[b] CAS-RN: Chemical Abstracts System Registration Number.

Table 1 *(continued)*

Common name Chemical name (IUPAC[a])	Molecular formula	Molar mass g/mol	CAS-RN[b]
Iomeprol (±)-N,N′-Bis-(2,3-dihydroxypropyl)-5-[(2-hydroxy-acetyl) methylamino]-2,4,6-triiodo isophthalamide	$C_{17}H_{22}I_3N_3O_8$	777,09	78649-41-9
Iopamidol (S)-N,N′-Bis[2-hydroxy-1-(hydroxymethyl)ethyl]-5-[(2-hydroxypropanoyl)amino]-2,4,6-triiodobenzene-1,3-dicarbamide	$C_{17}H_{22}I_3N_3O_3$	777,08	60166-93-0
Iopromide (±)-N,N′-Bis(2,3-dihydroxypropyl)-2,4,6-triiodo-5-(2-methoxyacetamido)-N-methylisophthalamide	$C_{18}H_{24}I_3N_3O_8$	791,12	73334-07-3
Metoprolol (RS)-1-(Isopropylamino)-3-[4-(2-methoxyethyl) phenoxy] propan-2-ol	$C_{15}H_{25}NO_3$	267,36	37350-58-6
Naproxen (S)-2-(6-Methoxy-2-naphthyl)propanoic acid	$C_{14}H_{14}O_3$	230,26	22204-53-1
Oxazepam (RS)-7-Chloro-3-hydroxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-on	$C_{15}H_{11}ClN_2O_2$	286,71	604-75-1
Phenazone 1,5-Dimethyl-2-phenyl-2,3-dihydro-1H-pyrazol-3-on	$C_{11}H_{12}N_2O$	188,23	60-80-0
Primidone 5-Ethyl-5-phenylhexahydropyrimidin-4,6-dione	$C_{12}H_{14}N_2O_2$	218,25	125-33-7
Propyphenazone 1,5-Dimethyl-4-(1-methylethyl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one	$C_{14}H_{18}N_2O$	230,31	479-92-5
Roxithromycin (3R,4S,5S,6R,7R,9R,11S,12R,13S,14R)-6-{[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl] oxy}-14-ethyl-7,12,13-trihydroxy-4-{[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy}-3,5,7,9,11,13-hexamethyl-10-(2,4,7-trioxa-1-azaoctan-1-ylidene)-1-oxacyclotetradecane-2-one	$C_{41}H_{76}N_2O_{15}$	837,05	80214-83-1
Sotalol (RS)-4′-(1-Hydroxy-2-isopropylaminoethyl) methanesulfonanilide	$C_{12}H_{20}N_2O_3S$	272,36	3930-20-9
Sulfamethoxazole 4-Amino-N-(5-methyl-1,2-oxazol-3-yl)benzene-sulfonamide	$C_{10}H_{11}N_3O_3S$	253,28	723-46-6
Temazepam (RS)-7-Chloro-3-hydroxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one	$C_{16}H_{13}ClN_2O_2$	300,74	846-50-4
Trimethoprim 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine	$C_{14}H_{18}N_4O_3$	290,32	738-70-5

[a] IUPAC: International Union of Pure and Applied Chemistry.

[b] CAS-RN: Chemical Abstracts System Registration Number.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 1042, *Laboratory glassware — One-mark volumetric flasks*

ISO 3696, *Water for analytical laboratory use — Specification and test methods*

ISO 4796-2, *Laboratory glassware — Bottles — Part 2: Conical neck bottles*

ISO 5667-4, *Water quality — Sampling — Part 4: Guidance on sampling from lakes, natural and man-made*

ISO 5667-5, *Water quality — Sampling — Part 5: Guidance on sampling of drinking water from treatment works and piped distribution systems*

ISO 5667-6, *Water quality — Sampling — Part 6: Guidance on sampling of rivers and streams*

ISO 5667-10, *Water quality — Sampling — Part 10: Guidance on sampling of waste waters*

ISO 5667-11, *Water quality — Sampling — Part 11: Guidance on sampling of groundwaters*

ISO 8466-1, *Water quality — Calibration and evaluation of analytical methods and estimation of performance characteristics — Part 1: Statistical evaluation of the linear calibration function*