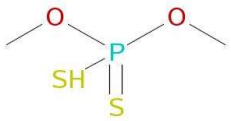
Miljøministeriet
Miljøstyrelsen

Fastsættelse af kvalitetskriterier for vandmiljøet

O,O-dimethyl hydrogen dithiophophat (MP1)

CAS nr. 756-80-9



Vandkvalitetskriterium	$VKK_{ferskvand}$	17,0 µg/l
Vandkvalitetskriterium	$VKK_{saltvand}$	1,7 µg/l
Korttidsvandkvalitetskriterium	$KVKK_{ferskvand}$	170,0 µg/l
Korttidsvandkvalitetskriterium	$KVKK_{saltvand}$	17,0 µg/l
Sedimentkvalitetskriterium	$SKK_{ferskvand}$	Ikke relevant
Sedimentkvalitetskriterium	$SKK_{saltvand}$	Ikke relevant
Biota-kvalitetskriterium, sekundær forgiftning	$BKK_{sek.\ forgiftn}$	Ikke relevant
Biota-kvalitetskriterium, sundhed	$BKK_{sundhed}$	Kan ikke beregnes

24. november 2021

Indholdsfortegnelse

Forord

Et kvalitetskriterium i vandmiljøet er det højeste koncentrationsniveau, ved hvilket der skønnes, at der ikke vil forekomme uacceptable negative effekter på vandøkosystemer.

Miljøstyrelsen (MST) udarbejder kvalitetskriterier for kemikalier i vandsøjlen (vandkvalitetskriterium), i sediment og i dyr og planter (biota).

Miljøstyrelsen bruger kvalitetskriterierne som det faglige grundlag til at kunne fastsætte miljøkvalitetskrav, hvorved der forstås den endelige koncentration af et bestemt forurenende stof i vand, sediment eller biota, som ikke må overskrides af hensyn til beskyttelsen af miljøet og menneskers sundhed.

Metodikken, der anvendes til udarbejdelse af miljøkvalitetskriterie, er harmoniseret i EU og baserer sig på vandrammedirektivet (EU, 2000), EU's vejledning til fastsættelse af kvalitetskriterier i vandmiljøet (EU, 2018) og Miljøstyrelsens vejledning til fastsættelse af vandkvalitetskriterier (Miljøstyrelsen, 2004). Metodikken er endvidere i overensstemmelse med EU's vejledning til risikovurdering under REACH forordningen (EU, 2008).

Miljøstyrelsen har haft mulighed for at kommentere et udkast til databladet inden den endelige udgave.

Den sidste litteratursøgning er foretaget den 07.09.2020.

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Faglig kvalitetssikring: John Jensen, Institut for Bioscience, Aarhus Universitet

Kvalitetssikring, DCE: Susanne Boutrup

English Summary and conclusions

This review is based on validated data from the e-CHEM portal and primarily ECHA (2020). There is complete base datasets for the compound but no chronic toxicity data, hence the high assessment factors applied in accordance with the EU TGD#27 (2018). Based on these data sources we discerned the following conclusions in light of the EU TGD#27 (2018) for O,O-dimethyl hydrogen dithiophosphate (MP1):

$AA\text{-}QS_{freshwater}$ = 17.0 µg/L

$AA\text{-}QS_{saltwater}$ = 1.7 µg/L

$MAC\text{-}QS_{freshwater}$ = 170.0 µg/L

$MAC\text{-}QS_{saltwater}$ = 17.0 µg/L

$QS_{sediment,\ freshwater}$ = Not relevant

$QS_{sediment,\ saltwater}$ = Not relevant

$QS_{biota,\ secondary\ poisoning}$ = Not relevant

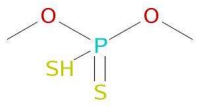
$QS_{biota,\ human\ health}$ = Cannot be assessed

Moreover, MP1 has the following self-classification hazard statements: H290 (May be corrosive to metals); H226 (Flammable liquid and vapour); H302 (Acute tox 4 - Harmful if swallowed); H332 (Harmful if inhaled); H314 (Causes severe skin burns and eye damage); H361 (Suspected of damaging fertility or the unborn child); H412 (Chronic tox 3 - Harmful to aquatic life with long-lasting effects).

1 Indledning

Identiteten af MP1 fremgår af tabel 1.1. Der er søgt efter data på stoffet baseret på review data fra ECHA (2020) og e-CHEM portal (2020) samt den videnskabelige litteratur.

Tabel 1.1. Identitet af MP1

IUPAC navn	O,O-dimethyl sulfanylphosphonothioate
Strukturformel	
CAS nr.	756-80-9
EINECS nr.	212-053-9
Kemisk formel	$C_2H_7O_2PS_2$
SMILES	COP(S)(=S)OC

MP1 anvendes som intermediat i produktion (ECHA, 2020). Salgsdata for MP1 er konfidentielle, men ifølge SPIN-databasen har der intet salg været af MP1 i Danmark siden 2007 (http://www.spin2000.net/spinmyphp/?pid=756809).

2 Fysisk kemiske egenskaber

De fysisk kemiske egenskaber for MP1 fremgår af tabel 2.1.

Tabel 2.1. Fysisk kemiske egenskaber for MP1.

Parameter	**Værdi**	**Reference**
Molekylevægt, M_w ($g \cdot mol^{-1}$)	158,17[2]	USEPA, 2020: https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID5027306#properties
Smeltepunkt, T_m (°C)	<-20	ECHA, 2020
Kogepunkt, T_b (°C)	48,5	ECHA, 2020
Damptryk, P_v (Pa)	133 [1]	ECHA, 2020
Henry's konstant, H ($atm \cdot m^3 \cdot mol^{-1}$)	$7{,}54 \cdot 10^{-8}$ [2]	USEPA, 2020: https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID5027306#properties
Vandopløselighed, S_w ($g \cdot L^{-1}$)	226 [3]	ECHA, 2020
Dissociationskonstant, pK_a	NA	NA
Octanol/vand fordelingskoefficient, log K_{ow}	-0,7 [4]	ECHA, 2020
Log K_{oc} ($L \cdot kg^{-1}$)	1,067 [2]	EPI Suite (MCI metode)

[1] Ved 48,5 °C

[2] Estimeret

[3] Ved 20 °C

[4] Ved 22 °C

3 Skæbne i miljøet

Der er søgt efter data i e-chem.org portal som indgang til globale datasæt for stoffet.

3.1 Nedbrydelighed

Stoffet er testet ifølge OECD test guideline nr. 301F i et manometrisk respirationsforsøg. Resultatet fra forsøget viste, at efter 28 dage var -2% af MP1 nedbrudt og stoffet kan derfor ikke betragtes som let bionedbrydeligt i vand. Stoffet er svært til slet ikke bionedbrydeligt ud fra disse data ifølge ECHA (2020) og dette understøttes ligeledes af QSAR-analyserne.

3.2 Bioakkumulering

MP1 har en log K_{ow} på -0,7, og derfor forventes stoffet ikke at bioakkumulere. Log BCF er estimeret til 0,498 i QSAR-programmet EPI Suite (se bilag A), og det konkluderes derfor, at bioakkumulerings potentialet for MP1 i akvatiske organiser er lavt.

3.3 Naturlig forekomst

MP1 er ikke naturligt forekommende.

4 Giftighedsdata

Der er søgt efter data i e-chem.org portal som indgang til globale datasæt for stoffet (https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID5027306#toxicity-values) - de mest valide og relevante data er fra ECHA, se nedenfor.

4.1 Giftighed over for vandlevende organismer

Der er få eksperimentelle giftighedsdata for MP1. I tabel 4.1, 4.2 og 4.3 er opsummeret effektværdier fra dossieret (ECHA, 2020), hvor der er data for syv forskellige arter fordelt på tre trofiske og taksonomiske grupper. Der forefindes ikke nogen fyldestgørende studierapporter, hvorfor udvælgelsen er baseret på ECHA's Klimisch vurderinger.

Tabel 4.1: Akutte ferskvandsgiftighedsværdier

Art (ferskvand)	Periode (timer)	Værdi akut EC_{50} (mg/L)	Troværdighed
Fisk: *Oncorhynchus mykiss*	96	19	4
Fisk*: Lepomis macrochirus*	96	60	4
Fisk*: Poecilia reticulate*	24	230	2
Fisk: *Umbra pygmaea*	96	17	2
Invertebrat*: Daphnia magna*	48	45,5	3

Tabel 4.2: Akutte saltvandsgiftighedsværdier

Art (saltvand)	Periode (timer)	Værdi akut EC_{50} (mg/L)	Troværdighed
Invertebrat: *Acartia tonsa*	48	1554	2
Alge*: Skeletonema costatum*	72	>1960	2

Tabel 4.3: Kronisk saltvandsgiftighedsværdi

Art (saltvand)	Periode (timer)	Værdi kronisk EC_{10} (mg/L)	Troværdighed
Alge*: Skeletonema costatum*	72	595	2

Data viser at marine alger og invertebrater er mindst følsomme, mens ferskvands fisk og invertebrater er lidt mere følsomme. Den mest følsomme art er den ferskvandslevende fisk Lille hundefisk (*Umbra pygmea*) (som er en ikkehjemmehørende art i Danmark). Der er ingen statistisk signifikant forskel mellem datasættene for salt og ferskvandsarter (p = 0,15) og datasættene kan derfor kombineres (EU TGD s. 37, 2018).

4.2 Giftighed over for sedimentlevende organismer

Der er ingen tilgængelige data for MP1's giftighed over for sedimentlevende organismer.

4.3 Giftighed over for pattedyr og fugle

Der er kun én oral giftighedsværdi for pattedyr i MP1 dossieret: Akut LD_{50} over for mus = 996 mg/kg lgv. (Klimisch score = 2). Akut (4 timer) inhalationsgiftighed over for rotter er målt til 1,96 mg/L, dette studie er dog fra 1981 og vurderes til Klimisch 4 og kan derfor ikke bruges (EU Dossieret 2020). Dette placerer MP1 i toksicitets-kategori IV ifølge ECHA (2020) indikerende en lav giftighed (https://www.epa.gov/sites/production/files/2015-03/documents/chap-07-jul-2014.pdf). Der er findes desuden et 14 ugers reproduktionsstudie fra 1984-1985 rotteforsøg der konkludere at stoffet er reproduktions toksisk hvor han rotterene fertilitet blev nedsat. Ved den højeste dosis (0,2 mg/l) blev han rotterne sterile og ved lavere dosis tog deres reproduktionsorganer skade. Det konkluderes at stoffet er reproduktions toksisk (EU Dossieret 2020). Det eneste andet nyere og relevante studie, der findes for MP1 er af Heydens og Kronenberg (1989), som fandt læsioner på hanrotters testikler i et inhalationsforsøg med mellem 4 og 25 mg MP1/m^3 – som bekræfter det ældre studie. Der er ingen data på fugle. Der findes ældre data og oversatte studier i HSDB som ikke er medtaget da de forventes at have lav troværdighed (https://pubchem.ncbi.nlm.nih.gov/compound/12959#section=Toxicity).

4.4 Giftighed over for mennesker

Der er ikke fundet nogen toksicitetsværdier eller daglig dosis værdier (TDI eller ADI) for mennesker.

5 Andre effekter

Ifølge EU's forordning for klassificering, mærkning og emballering af stoffer (CLP-forordning) er MP1 selvklassificeret med følgende sætninger: Met. Corr 1; H290 (Kan ætse metaller), Flam. Liquid 3; H226 (Brandfarlig væske og damp), Acute tox 4; H302 (Farlig ved indtagelse); H332 (Farlig ved indånding), Skin Corr. 1B; H314 (Forårsager svære ætsninger af huden og øjenskader), Repr. 2; H361 (Mistænkt for at skade forplantningsevnen eller det ufødte barn), Aquatic Chronic 3; H412 (Chronic tox 3 - Skadeligt for vandlevende organismer, med langvarige virkninger). For andre effekter henvises desuden til QSAR i bilag A.

6 Udledning af vandkvalitetskriterium

6.1 Vandkvalitetskriterium (VKK)

Der er ingen kroniske toksicitetsstudier for fisk eller invertebrater, og kun et kronisk studie for alger, og dette kan ikke alene repræsentere kronisk gifthed. Derfor beregnes VKK ud fra det akutte datasæt, som repræsenterer de tre trofiske niveauer alge, invertebrat og fisk. Da der kun er akutte ferskvandsdata, bliver usikkerhedsfaktoren (UF) på 1000 anvendt på den laveste giftighedsværdi for fisken (*Umbra pygmaea*) med en effektkoncentration på 17 mg/L. Derfor bestemmes $VKK_{ferskvand}$ som følger:

17 mg/L / 1000 = 0,017 mg/L = 17 µg/L.

For saltvand benyttes ligeledes fisk (*Umbra pygmaea)* værdien, dog med en yderligere usikkerhedsfaktor på 10 (Tab 4 EU TGD no 27, 2018). Derfor bestemmes $VKK_{saltvand}$ ud fra:

17 mg/L / 10.000 = 0,0017 mg/L = 1,7 µg/L.

6.2 Korttidsvandkvalitetskriterium (KVKK)

Korttidsvandkvalitetskriteriet for ferskvand, $KVKK_{ferskvand}$, udledes ud fra den akutte effektkoncentration for *Umbra pygmaea* på 17 mg/L. Da standardafvigelsen på de log10 transformerede akutte giftighedsdata overstiger 0,5, benyttes en UF på 100 (EU TGD, 2018, Tab. 5). KVKK for ferskvand udledes således:

17 mg/L /100 = 0,17 mg/L = 170 µg/L.

$KVKK_{saltvand}$, er baseret på den akutte giftighed for over for *Umbra pygmaea* med en akut EC_{50} effektkoncentration på 17,0 mg/L. Da standardafvigelsen på de log10 transformerede akutte giftighedsdata overstiger 0,5, benyttes en UF på 1000 (EU TGD#27, 2018, Tab. 6). Derfor bestemmes $KVKK_{saltvand}$ ud fra:

17 mg/L /1000 = 0,017 mg/L = 17,0 µg/L.

6.3 Kvalitetskriterium for sediment (SKK)

Da log K_{oc} er mindre end 3 for MP1 (Log K_{oc} = 1,067), skal der i overensstemmelse med det tekniske guidance-dokument (TGD) ikke beregnes et SKK for MP1 (EU, 2018).

6.4 Kvalitetskriterium for biota (BKK)

Der er i overensstemmelse med TGD (EU, 2018) ikke beregnet et BKK for sekundær forgiftning for MP1, da BCF for MP1 er 0,498 L/kg (EPI Suite, 2020) og tærskelværdien ifølge EU TGD (2018) er BCF >100 eller log K_{ow} > 3.

6.5 Kvalitetskriterium for human konsum af vandlevende organismer (HKK)

MP1 er klassificeret som Rep. 2 med faresætningen: mistænkt for at skade forplantningsevnen eller det ufødte barn. Klassificeringen Rep. 2 udløser behovet for udledning af HKK ifølge TGD (EU, 2018, afsnit 2.4.3.2). Der findes ikke nogen NOEC eller NOAEL værdier for stoffet, men der findes en akut LD_{50} værdi for rotter på 996 mg/kg. Dette studie har en troværdighedsscore af 2, er fra 1973 og er lavet uden nogen guideline og derfor i bedste fald anvendeligt med visse restriktioner. På baggrund af disse usikre data og betydelig ekstrapolationsusikkerhed anbefales det ikke at udlede en HKK inden der er et mere robust datamateriale.

7 Konklusion

Der er fundet følgende miljøkvalitetskriterier for MP1 baseret på review data fra ECHA (2020) og e-CHEM portal (2020), samt den videnskabelige litteratur og metoder beskrevet i EU 2018 TGD#27;

$VKK_{ferskvand}$ = 17,0 µg/L

$VKK_{saltvand}$ = 1,7 µg/L

$KVKK_{ferskvand}$ = 170 µg/L

$KVKK_{saltvand}$ = 17,0 µg/L

$SKK_{ferskvand}$ = Ikke relevant

$SKK_{saltkvand}$ = Ikke relevant

$BKK_{sek\ forgiftn}$ = Ikke relevant

$BKK_{sundhed}$ = Kan ikke beregnes

8 Referencer

ECETOC (2003): Derivations of assessment factors for human health risk. Technical report 86.

EFSA (2012): Guidance on Default assumptions used by the EFSA Scientific Panels and Committee, and EFSA Units in the absence of actual measured data: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2012.2579.

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EU (2000). Europa-Parlamentets og Rådets Direktiv 2000/60/EF om fastsættelse af en ramme for fællesskabets vandpolitiske foranstaltninger af 23. oktober 2000.

EU (2008). ECHA: Guidance on information requirements and chemical safety assessment Chapter R.10: Characterisation of dose [concentration]-response for environment (https://echa.europa.eu/documents/10162/13632/information_requirements_r10_en.pdf/bb902be7-a503-4ab7-9036-d866b8ddce69)

EU (2018). Common Implementation Strategy for the Water Framework Directive (2000/60/EC). Guidance Document No. 27. Technical Guidance Document for Deriving Environmental Quality Standards.

Heydens, W. F., Kronenberg, J. M. (1989). Inhalation Fertility and Reproduction Studies with *O,O'*-Dimethylphosphorodithioate in Sprague-Dawley Rats. *Toxicological Sciences*, Volume 12, Issue 1, January 1989, Pages 62–69, https://doi.org/10.1093/toxsci/12.1.62

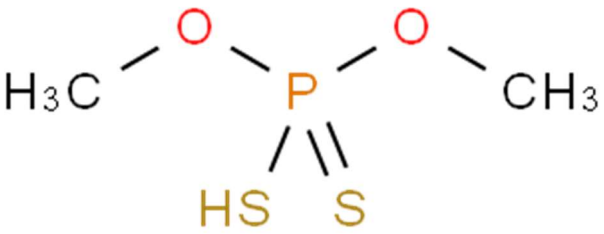
Miljøstyrelsen (2004). Principper for fastsættelse af vandkvalitetskriterier for stoffer i overfladevand. Vejledning fra Miljøstyrelsen nr. 4, 2004.

Bilag A. QSAR data

Danish (Q)SAR Database, http://qsar.food.dtu.dk Date: 30-06-2021

(Q)SAR predicted profile

8.1 Structure (as used for QSAR prediction):



SMILES (used for QSAR prediction): COP(=S)(S)OC

8.2 ID

REACH EC Number (pre-registration, by 2013)	212-053-9	REACH EC Number (registration, by Dec. 2019)	212-053-9
Registry Number	756-80-9	PubChem CID	
EU CLP Harmonized Classification*		DK-EPA / DTU QSAR-based CLP Advisory Classification	Acute Tox. 4; Aquatic Acute 1
REACH registration cumulated minimum annual tonnage			
Molecular Formula	C2 H7 O2 P1 S2	Molecular weight (g/mole)	158.17
Chemical Name	O,O-dimethyl hydrogen dithiophosphate		

(Annex VI to CLP up to and including the 9th ATP, and including Nordic Council of Minister SPIN list for group entries)

8.3 Melting point, Boiling point and Vapour pressure

Melting Point (deg C)	-82.36	Melting Point Experimental (deg C)	
Boiling Point (deg C)	197.38	Boiling Point Experimental (deg C)	48 @ 2.03 mm Hg
Vapour Pressure (atm)	EPI.Estimated_VP_atm	Vapour Pressure Experimental (atm)	EPI.Exp_VP_atm
Vapour Pressure (mm Hg)	0.411	Vapour Pressure Experimental (mm Hg)	
Vapour Pressure (Pa)	54.8	Vapour pressure Subcooled Liquid (Pa)	

EPI MPBPVP models

8.4 Henry's Law Constant

HLC Bond Method (atm-m3/mole)	0.0002105	HLC Group Method (atm-m3/mole)	
HLC Via VP/WSol (atm-m3/mole)	1.459E-005	HLC Via VP/WSol (Pa-m3/mole)	1.479
Henrys Law Const. Exp db (Pa-m3/mole)		Henrys Law Const. Exp db (atm-m3/mole)	

EPI HENRYWIN models

8.5 Water Solubility

Water solubility from Kow (mg/L)	5862	Water solubility from Fragments (mg/L)	8744.6
Water solubility Exp (mg/L)		Water solubility Exp Ref	

EPI WATERNT model

8.6 Hydrolysis

Hydrolysis Ka half-life pH 7		Hydrolysis Kb half-life pH 7	
Hydrolysis Ka half-life pH 8		Hydrolysis Kb half-life pH 8	

EPI HYDROWIN model

8.7 pKa

pKa Acid	-0.1
- Standard deviation (±)	0.4
pKa Base	-999
- Standard deviation (±)	0

ACDLabs model

pKa estimate 999: no acidic moiety found. pKa estimate -999: no basic moiety found.

8.8 Partition coefficients

pH	1	4	5	6	7	8	9
LogD	0.56	-2.11	-2.37	-2.4	-2.41	-2.41	-2.41

ACDLabs models

LogD: Log octanol-water partition coefficient, which for ionizable compounds varies with the pH-dependent amounts of neutral and ionized species

Log Koa	3.326	Log Kaw	-2.066

EPI KOAWIN models

Koa: octanol-air partition coefficient. Kaw: air-water partition coefficient.

Log Kow	1.26		
Log Kow Exp		Log Kow Exp Ref	

EPI WSKOW model

LogKow: log octanol-water partition coefficient

Kp (m3/ug) Mackay-based	5.98E-008	Kp (m3/ug) Koa-based	5.2E-010
Phi Junge-Pankow-based	2.16E-006	Phi Mackay-based	4.79E-006
Phi Koa-based	4.16E-008		

EPI AEROWIN models

Kp: particle-gas partition coefficient. Phi: fraction of substance sorbed to atmospheric particulates

Koc from MCI (L/kg)	11.67	Log Koc from MCI	1.067
Koc from Kow (L/kg)	33.91	Log Koc from Kow	1.5303

EPI KOCWIN models

Koc: soil adsorption coefficient of organic compounds. Kow: octanol-water partition coefficient. MCI: first order Molecular Connectivity Index

8.9 Level III Fugacity Environmental Partitioning, emission to air, water and soil

	Air	Water	Soil	Sediment
Mass Amount (%)	1.74	44.5	53.6	0.103
Half-Life (hr)	4.38	360	720	3240
Emissions (kg/hr)	1000	1000	1000	0

EPI Level III Fugacity Model

Persistence time (hr)	211
Persistence time (days)	8.791667

EPI Level III Fugacity Model

8.10 Level III Fugacity Environmental Partitioning, emission only to water

	Air	Water	Soil	Sediment
Mass Amount (%)	0.68	99.1	0.0068	0.23
Half-Life (hr)	4.38	360	720	3240
Emissions (kg/hr)	0	1000	0	0

EPI Level III Fugacity Model

Persistence time (hr)	247
Persistence time (days)	10.29167

EPI Level III Fugacity Model

8.11 Sewage Treatment Plant (STP) overall chemical mass balance using 10,000 hr

	Total removal	Biodegradation	Sludge Adsorption	Volatilization
(%)	10.94	0.09	1.68	9.17

EPI STPWIN model

8.12 Atmospheric oxidation (25 deg C)

	OH	Ozone
Half-Life (d)	0.1826	0
Half-Life (hr)	2.191	
Overall Rate Const. (OH: E-12 cm3/molecule-sec and OZ: E-17 cm3/molecule-sec)	58.576	

EPI AOPWIN models

8.13 Biodegradation

Biowin1 (linear model) Probability of Rapid Biodegradation	0.6722
Biowin2 (non-linear model) Probability of Rapid Biodegradation	0.6819
Biowin3 Expert Survey Ultimate Biodegradation	2.8496
Biowin3 Expert Survey Ultimate Timeframe	weeks
Biowin4 Expert Survey Primary Biodegradation	3.6195
Biowin4 Exp. Survey Primary Timeframe	days-weeks
Biowin5 (MITI linear model) Biodegradation Probability	0.2424
Biowin6 (MITI non-linear model) Biodegradation Probability	0.119
Biowin7 (Anaerobic Linear) Biodegradation Probability	0.6769
Petroleum Hydrocarbon Biodegradation Half-Life (days)	

EPI BIOWIN models

Biowin1 and Biowin2: ≥0.5: "Rapid" <0.5: "Slow"
Biowin3 and Biowin4: 5 ~ hours; 4 ~ days; 3 ~ weeks; 2 ~ months; 1 ~ years.
Biowin5 and Biowin6: ≥0.5: "Readily", <0.5: "Not readily".
Biowin7: ≥0.5: "Fast", <0.5: "Slow"

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Not Ready Biodegradability (POS=Not Ready)		POS_IN	POS_IN	POS_OUT	POS_IN

DTU-developed models

8.14 Bioaccumulation

BCF (L/kg wet-wt)	3.148
Log BCF (L/kg wet-wt)	0.498
Whole Body Primary Biotransformation Fish Half-Life (days)	0.08603
BCF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	2.34
BCF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	2.837
BAF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	2.34
BAF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	2.866

EPI BCFBAF models

BCF: Bioconcentration factor, BAF: Bioaccumulation factor

8.15 Aquatic toxicity

Exp	Battery	Leadscope	SciQSAR
Fathead minnow 96h LC50 (mg/L)		27.3977	121.6254
Domain	OUT	OUT	OUT
Daphnia magna 48h EC50 (mg/L)		8.139808	0.1635592
Domain	OUT	OUT	OUT
Pseudokirchneriella s. 72h EC50 (mg/L)		49.73752	33.9957
Domain	OUT	OUT	OUT

DTU-developed models

	Fish 96h	Daphnid 48h	Green Algae 96h
LC50 (Fish) or EC50 (Daphnid and Algae) for Most Toxic Class (mg/L)	2.165	0.002	32.538
Max. Log Kow for Most Toxic Class	5	5	6.4
Most Toxic Class	Esters, Dithiophosphates	Esters, Dithiophosphates	Esters, Dithiophosphates
Note			

EPI ECOSAR models

ECOSAR Classes: Esters, Dithiophosphates

8.16 Oral absorption

Lipinski's Rule-of-five score (bioavailability)	0
Absorption from gastrointestinal tract for 1 mg dose (%)	90
Absorption from gastrointestinal tract for 1000 mg dose (%)	90

Leadscope model on Lipinski's Rule-of-five. Equation from literature on GI abs.

Lipinski scores of 0 or 1: The substance may be bioavailable. Lipinski scores of 2, 3 or 4: The substance may not be bioavailable.

8.17 Skin absorption

Dermal absorption (mg/cm2/event)	0.0156

EPI DERMWIN model

8.18 Brain/blood Distribution

Log brain/blood partition coefficient	0.1314

Equation from literature

Partitioning between the two tissues at equilibrium. >1: high, >0 to <1: medium, >-1 to <0, fair, <-1: low.

8.19 Metabolism

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
CYP2C9 substrates (Human clinical data)		INC_OUT	INC_OUT	NEG_OUT	NEG_OUT
CYP2D6 substrates (Human clinical data)		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN

DTU-developed models

8.20 Acute toxicity in Rodents

	LD50 (mg/kg/d)	Reliability Index
Rat Oral	990	0.71
Rat Intraperitoneal	180	0.43
Mouse Oral	400	0.46
Mouse Intraperitoneal	160	0.37
Mouse Intravenous	220	0.4
Mouse Subcutaneous	220	0.43

ACDLabs models

Reliability index: <0.3 = Not reliable prediction quality; 0.3-0.5 = borderline prediction quality; 0.5-0.75 = moderate prediction quality; >0.75 = high prediction quality.

8.21 MRDD in Humans

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
MRDD in Humans ≤ 2.69 mg/kg-bw/d		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN

DTU-developed models

Model based on data on pharmaceuticals. Maximum recommended daily dose in pharmaceutical clinical trials employing primarily oral route of exposure and daily treatments, usually for 3-12 months.

8.22 Irritation and Sensitization

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Severe Skin Irritation in Rabbit		INC_OUT	NEG_IN	POS_OUT	POS_IN
Allergic Contact Dermatitis in Guinea Pig and Human*	N/A	INC_OUT	INC_OUT	INC_OUT	POS_OUT
Respiratory Sensitisation in Humans		INC_OUT	POS_OUT	POS_OUT	INC_OUT

DTU-developed models

**Based on commercial training set*

Protein binding by OASIS, alerts in:	
- parent only	No alert found
- metabolites from skin metabolism simulator only	
- metabolites from auto-oxidation simulator only	
Protein binding by OECD, alerts in:	
- parent only	No alert found
- metabolites from skin metabolism simulator only	
- metabolites from auto-oxidation simulator only	
Protein binding potency Cys (DRPA 13%), alerts in:	
- parent only	DPRA less than 9% (DPRA 13%) >> No protein binding alert
- metabolites from skin metabolism simulator only	
- metabolites from auto-oxidation simulator only	
Protein binding potency Lys (DRPA 13%), alerts in:	
- parent only	DPRA less than 9% (DPRA 13%) >> No protein binding alert
- metabolites from skin metabolism simulator only	
- metabolites from auto-oxidation simulator only	
Keratinocyte gene expression, alerts in:	
- parent only	Not possible to classify according to these rules
- metabolites from skin metabolism simulator only	
- metabolites from auto-oxidation simulator only	
Protein binding potency GSH, alerts in:	
- parent only	Not possible to classify according to these rules (GSH)

OECD QSAR Toolbox v.4.1 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.23 Endocrine and Molecular Endpoints

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Estrogen Receptor α Binding, Full training set (Human *in vitro*)		INC_OUT	INC_OUT	NEG_OUT	POS_OUT
Estrogen Receptor α Binding, Balanced Training Set (Human *in vitro*)		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN
Estrogen Receptor α Activation (Human *in vitro*)		INC_OUT	INC_OUT	NEG_OUT	INC_OUT
Estrogen Receptor Activation, CERAPP data (*in vitro*)		N/A	N/A	INC_OUT	N/A
Androgen Receptor Inhibition (Human *in vitro*)		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN
Androgen Receptor Binding, CoMPARA data (*in vitro*)		N/A	N/A	INC_OUT	N/A
Androgen Receptor Inhibition, CoMPARA data (*in vitro*)		N/A	N/A	INC_OUT	N/A
Androgen Receptor Activation, CoMPARA data (*in vitro*)		N/A	N/A	INC_OUT	N/A
Thyroperoxidase (TPO) inhibition QSAR1 (Rat *in vitro*)		N/A	N/A	INC_OUT	N/A
Thyroperoxidase (TPO) inhibition QSAR2 (Rat *in vitro*)		N/A	N/A	INC_OUT	N/A
Thyroid Receptor α Binding (Human *in vitro*)					
- mg/L				1216.366	
- μM				7690.243	
- Positive for IC_{50} ≤ 10 μM					
- Positive for IC_{50} ≤ 100 μM					
- Domain				OUT	OUT
Thyroid Receptor β Binding (Human *in vitro*)					
- mg/L				16.8025	
- μM				106.2307	
- Positive for IC_{50} ≤ 10 μM					
- Positive for IC_{50} ≤ 100 μM					
- Domain				OUT	OUT
Arylhydrocarbon (AhR) Activation – Rational final model (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
Arylhydrocarbon (AhR) Activation – Random final model (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
Pregnane X Receptor (PXR) Binding (Human *in vitro*)	N/A	INC_OUT	INC_OUT	NEG_OUT	NEG_OUT
Pregnane X Receptor (PXR) Binding (Human *in vitro*) NEW		N/A	N/A	INC_OUT	N/A
Pregnane X Receptor (PXR) Activation (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
Pregnane X Receptor (PXR) Activation (Rat *in vitro*)		N/A	N/A	INC_OUT	N/A

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Constitutive Androstane Receptor (CAR) Activation at max. 20 µM (*in vitro*)		N/A	N/A	INC_OUT	N/A
Constitutive Androstane Receptor (CAR) Activation at max. 50 µM (*in vitro*)		N/A	N/A	INC_OUT	N/A
Constitutive Androstane Receptor (CAR) Inhibition at max. 20 µM (*in vitro*)		N/A	N/A	INC_OUT	N/A
Constitutive Androstane Receptor (CAR) Inhibition at max. 50 µM (*in vitro*)		N/A	N/A	INC_OUT	N/A

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
YP3A4 Induction (Human *in vitro*)		N/A	N/A	INC_OUT	N/A

DTU-developed models

Estrogen Receptor Binding, alerts in:	
- parent only	Non binder, non cyclic structure
- metabolites from *in vivo* Rat metabolism simulator only	Non binder, non cyclic structure
- metabolites from Rat liver S9 metabolism simulator only	Non binder, non cyclic structure
rtER Expert System - USEPA, alerts in:	
- parent only	No alert found
- metabolites from *in vivo* Rat metabolism simulator only	No alert found
- metabolites from Rat liver S9 metabolism simulator only	No alert found

OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.24 Developmental Toxicity

	Battery	CASE Ultra	Leadscope	SciQSAR
Teratogenic Potential in Humans	NEG_OUT	INC_OUT	INC_OUT	NEG_IN

DTU-developed models based on commercial training set

8.25 Genotoxicity - Structural Alerts for DNA Reactivity

	Battery	CASE Ultra	Leadscope	SciQSAR
Ashby Structural Alerts	POS_OUT	POS_OUT	POS_OUT	POS_IN

DTU-developed models based on commercial training set

DNA binding by OASIS, alerts in:	
- parent only	No alert found
DNA binding by OECD, alerts in:	
- parent only	No alert found

OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.26 *In vitro* Genotoxicity - Bacterial Reverse Mutation Test (Ames test)

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Ames test in S. typhimurium (*in vitro*)		INC_OUT	INC_OUT	NEG_OUT	NEG_OUT
*Direct Acting Mutagens (without S9)	N/A	POS_OUT	INC_OUT	INC_OUT	POS_IN
*Base-Pair Ames Mutagens	N/A	NEG_OUT	INC_OUT	INC_OUT	NEG_IN
*Frameshift Ames Mutagens	N/A	NEG_OUT	INC_OUT	NEG_OUT	NEG_IN
*Potent Ames Mutagens, Reversions ≥ 10 Times Controls	N/A	POS_OUT	POS_OUT	INC_OUT	POS_IN

DTU-developed models

* The four models (Direct Acting mutagens (without S9), Base-Pair Ames Mutagens, Frameshift Ames Mutagens, Potent Ames Mutagens) should not be used to determine if substances are Ames mutagens, but can be used for indication of mechanism or potency for cases where the main Ames model (Ames test in S. typhimurium (*in vitro*)) is POS_IN.

DNA alerts for AMES by OASIS, alerts in:	
- parent only	No alert found
In vitro mutagenicity (Ames test) alerts by ISS, alerts in:	
- parent only	No alert found

OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.27 Other *in vitro* Genotoxicity Endpoints

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells*	N/A	NEG_OUT	INC_OUT	INC_OUT	NEG_IN
Chromosome Aberrations in Chinese Hamster Lung (CHL) Cells		POS_OUT	POS_OUT	INC_OUT	POS_IN
Mutations in Thymidine Kinase Locus in Mouse Lymphoma Cells		INC_OUT	POS_OUT	POS_OUT	POS_OUT
Mutations in HGPRT Locus in Chinese Hamster Ovary (CHO) Cells		POS_OUT	POS_OUT	NEG_OUT	POS_IN
Unscheduled DNA Synthesis (UDS) in Rat Hepatocytes		INC_OUT	INC_OUT	NEG_OUT	NEG_OUT
Syrian Hamster Embryo (SHE) Cell Transformation		POS_OUT	INC_OUT	INC_OUT	POS_IN

DTU-developed models
**Based on commercial training set*

HGPRT: Hypoxanthine-guanine phosphoribosyltransferase

DNA alerts for CA and MNT by OASIS, alerts in:	
- parent only	No alert found
Protein binding alerts for Chromosomal aberration by OASIS, alerts in:	
- parent only	No alert found

OECD QSAR Toolbox v.4.2 profilers

CA: Chromosomal aberration, MNT: Micronucleus test
Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.28 *In vivo* Genotoxicity Endpoints

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Sex-Linked Recessive Lethal (SLRL) Test in Drosophila m.		NEG_OUT	INC_OUT	INC_OUT	NEG_IN
Micronucleus Test in Mouse Erythrocytes		INC_OUT	INC_OUT	INC_OUT	INC_OUT
Dominant Lethal Mutations in Rodents		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN
Sister Chromatid Exchange in Mouse Bone Marrow Cells		INC_OUT	INC_OUT	POS_OUT	INC_OUT
Comet Assay in Mouse		POS_OUT	POS_OUT	POS_OUT	POS_IN

DTU-developed models

In vivo mutagenicity (Micronucleus) alerts by ISS, alerts in:	
- parent only	No alert found

OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

8.29 Carcinogenicity

	E Ultra	Leadscope
FDA RCA Cancer Male Rat	INC_OUT	INC_OUT
FDA RCA Cancer Female Rat	INC_OUT	INC_OUT
FDA RCA Cancer Rat	INC_OUT	INC_OUT
FDA RCA Cancer Male Mouse	INC_OUT	INC_OUT
FDA RCA Cancer Female Mouse	INC_OUT	INC_OUT
FDA RCA Cancer Mouse	INC_OUT	INC_OUT
FDA RCA Cancer Rodent	INC_OUT	INC_OUT

Commercial models from CASE Ultra and Leadscope

FDA RCA: Data from US Food and Drug Administration as part of Research Cooperation Agreement

Carcinogenicity (genotox and nongenotox) alerts by ISS, alerts in:	
- parent only	No alert found
Oncologic Primary Classification, alerts in:	
- parent only	Organophosphorus Type Compounds

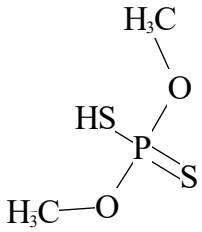
OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Liver Specific Cancer in Rat or Mouse		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN

DTU-developed models

EPI Suite Results For CAS 756-80-9



SMILES : COP(S)(=S)OC

CHEM : MP1

MOL FOR: C2 H7 O2 P1 S2

MOL WT : 158.17

---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:

Log Kow (octanol-water): ------

Boiling Point (deg C) : ------

Melting Point (deg C) : ------

Vapor Pressure (mm Hg) : ------

Water Solubility (mg/L): ------

Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):

Log Kow (KOWWIN v1.68 estimate) = 1.26

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):

Boiling Pt (deg C): 197.38 (Adapted Stein & Brown method)

Melting Pt (deg C): -82.36 (Mean or Weighted MP)

VP(mm Hg,25 deg C): 0.411 (Mean VP of Antoine & Grain methods)

VP (Pa, 25 deg C) : 54.8 (Mean VP of Antoine & Grain methods)

BP (exp database): 48 @ 2.03 mm Hg deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):

Water Solubility at 25 deg C (mg/L): 5862

log Kow used: 1.26 (estimated)

no-melting pt equation used

Water Sol Estimate from Fragments:

Wat Sol (v1.01 est) = 8744.6 mg/L

ECOSAR Class Program (ECOSAR v1.11):

Class(es) found:

Esters, Dithiophosphates

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:

Bond Method :   2.10E-004 atm-m3/mole (2.13E+001 Pa-m3/mole)

Group Method: Incomplete

For Henry LC Comparison Purposes:

User-Entered Henry LC: not entered

Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:

HLC: 1.459E-005 atm-m3/mole (1.479E+000 Pa-m3/mole)

VP: 0.411 mm Hg (source: MPBPVP)

WS: 5.86E+003 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:

Log Kow used: 1.26 (KowWin est)

Log Kaw used: -2.066 (HenryWin est)

Log Koa (KOAWIN v1.10 estimate): 3.326

Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):

Biowin1 (Linear Model)   :   0.6722

Biowin2 (Non-Linear Model)   :   0.6819

Expert Survey Biodegradation Results:

Biowin3 (Ultimate Survey Model):   2.8496 (weeks   )

Biowin4 (Primary Survey Model) :   3.6195 (days-weeks)

MITI Biodegradation Probability:

Biowin5 (MITI Linear Model)   :   0.2424

Biowin6 (MITI Non-Linear Model):   0.1190

Anaerobic Biodegradation Probability:

Biowin7 (Anaerobic Linear Model): 0.6769

Ready Biodegradability Prediction: NO

Hydrocarbon Biodegradation (BioHCwin v1.01):

Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:

Vapor pressure (liquid/subcooled): 50.1 Pa (0.376 mm Hg)

Log Koa (Koawin est): 3.326

Kp (particle/gas partition coef. (m3/ug)):

Mackay model   : 5.98E-008

Octanol/air (Koa) model: 5.2E-010

Fraction sorbed to airborne particulates (phi):

Junge-Pankow model   : 2.16E-006

Mackay model   : 4.79E-006

Octanol/air (Koa) model: 4.16E-008

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:

Hydroxyl Radicals Reaction:

OVERALL OH Rate Constant = 58.5760 E-12 cm3/molecule-sec

Half-Life = 0.183 Days (12-hr day; 1.5E6 OH/cm3)

Half-Life = 2.191 Hrs

Ozone Reaction:

No Ozone Reaction Estimation

Fraction sorbed to airborne particulates (phi):

3.47E-006 (Junge-Pankow, Mackay avg)

4.16E-008 (Koa method)

Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):

Koc : 11.67 L/kg (MCI method)

Log Koc: 1.067 (MCI method)

Koc : 33.91 L/kg (Kow method)

Log Koc: 1.530 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:

Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):

Log BCF from regression-based method = 0.498 (BCF = 3.148 L/kg wet-wt)

Log Biotransformation Half-life (HL) = -1.0654 days (HL = 0.08603 days)

Log BCF Arnot-Gobas method (upper trophic) = 0.369 (BCF = 2.34)

Log BAF Arnot-Gobas method (upper trophic) = 0.369 (BAF = 2.34)

log Kow used: 1.26 (estimated)

Volatilization from Water:

Henry LC: 0.00021 atm-m3/mole (estimated by Bond SAR Method)

Half-Life from Model River: 4.79 hours

Half-Life from Model Lake : 157.7 hours (6.571 days)

Removal In Wastewater Treatment:

Total removal: 10.94 percent

Total biodegradation: 0.09 percent

Total sludge adsorption: 1.68 percent

Total to Air: 9.17 percent

(using 10000 hr Bio P,A,S)

Level III Fugacity Model:

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	1.74	4.38	1000
Water	44.5	360	1000
Soil	53.6	720	1000
Sediment	0.103	3.24e+003	0

Persistence Time: 211 hr