Miljøministeriet
Miljøstyrelsen

Fastsættelse af kvalitetskriterier for vandmiljøet

O,O-diethyl hydrogen phosphorodithioate (EP-1)

CAS nr. 298-06-6

Vandkvalitetskriterium	$VKK_{ferskvand}$	0,54 µg/l
Vandkvalitetskriterium	$VKK_{saltvand}$	0,054 µg/l
Korttidsvandkvalitetskriterium	$KVKK_{ferskvand}$	05,4 µg/l
Korttidsvandkvalitetskriterium	$KVKK_{saltvand}$	0,54 µg/l
Sedimentkvalitetskriterium	$SKK_{ferskvand}$	Ikke beregnet
Sedimentkvalitetskriterium	$SKK_{saltvand}$	Ikke beregnet
Biota-kvalitetskriterium, sekundær forgiftning	$BKK_{sek.forgiftn.}$	Ikke beregnet
Biota-kvalitetskriterium, humant konsum	HKK	Ikke beregnet

December 2023

Indholdsfortegnelse

Forord

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

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

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 miljøkvalitetskrav 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).

Den sidste litteratursøgning er foretaget den 15. maj 2023.

English Summary and conclusions

Derivation of environmental quality standards (EQS) for the aquatic environment is following the EU Guidance Document No. 27. Technical Guidance Document (TGD) for Deriving Environmental Quality Standards (EU, 2018).

O,O-diethyl hydrogen phosphorodithioate (EP-1) is an intermediate in the synthesis of organophosphate insecticides and occurs also as a degradation product from certain organophosphate insecticides, e.g. disulfoton. Overall, limited information is available about the substance.

AA-EQS for water
Chronic data is only available for algae, and therefore acute data was used for calculation of the AA-EQS.

Acute data were available for three marine species (*Vibrio fischeri, Skeletonema costatum,* and *Acartia tonsa*) and two freshwater species (*Daphnia magna* and *Oncorhynchus mykiss*). In total, these species represent five taxonomic groups when different classes of crustaceans are considered (bacteria, algae, crustacean (branchiopoda, copepoda), fish). The lowest EC_{50} value was found for *D. magna* at 0.54 mg/l for immobilisation.

An assessment factor (AF) of 1,000 and the acute EC_{50} of 0.54 mg/l for *D. magna* were chosen for the calculation of AA-EQS for freshwater:

$AA\text{-}EQS_{freshwater}$ = EC_{50} / AF
= 0.54 mg/l / 1,000
= 0.54 µg/l

Correspondingly, an AF of 10,000 is applied for AA-EQS for saltwater:

$AA\text{-}EQS_{saltwater}$ = 0.54 mg/l / 10,000
= 0.054 µg/l

MAC-EQS for water
An AF of 100 and the acute EC_{50} of 0.54 mg/L for *D. magna* were chosen for the calculation of MAC-EQS for freshwater:

$MAC\text{-}EQS_{freshwater}$ = EC_{50} / AF
= 0.54 mg/l / 100
= 5.4 µg/l

Correspondingly, an AF of 1,000 is applied for MAC-EQS for saltwater:

MAC-EQS$_{saltwater}$ = 0.54 mg/l / 1,000
= 0.54 µg/l

QS for sediment
The QSAR-estimated K_{oc} < 1,000, and no sediment toxicity data are available. Therefore, no sediment QS was derived.

QS for secondary poisoning
The QSAR-estimated values are log K_{ow} < 3 and BCF < 100. Data indicating high intrinsic toxicity were not available. Therefore, no QS for secondary poisoning was derived.

QS for human health
There is no harmonised classification for EP-1. The hazard statements from self-classification and the low estimated bioaccumulation potential indicate that the substance does not pose a risk to human health through consumption by aquatic organisms. Therefore, no QS for human health was derived.

In conclusion, the following EQS for the aquatic environment have been derived for EP-1:

AA-EQS$_{freshwater}$ = 0.54 µg/l
AA-EQS$_{saltwater}$ = 0.054 µg/l
MAC-EQS$_{freshwater}$ = 5.4 µg/l
MAC-EQS$_{saltwater}$ = 0.54 µg/l

QS$_{sediment, freshwater}$ Not derived
QS$_{sediment, saltwater}$ Not derived

QS$_{sec. pois.}$ Not derived
QS$_{human health}$ Not derived

1 Indledning

Identiteten af O,O-diethyl hydrogen phosphorodithioate (EP-1) fremgår af Tabel 1.1.

Videnskabelig og grå litteratur om fysisk-kemiske egenskaber, økotoksikologiske og humantoksikologiske data blev søgt i forskellige databaser (herunder ECHA database, HSDB PubChem database, EuropePMC, GoogleScholar, US EPA Ecotox databasen, Danish QSAR database) og ved åben Google søgning under anvendelse af CAS nr. og navnene for stoffet.

EP-1 er registreret i henhold til REACH-forordningen som mellemprodukt og oplysninger om stoffet er angivet på ECHAs hjemmeside (ECHA substance Infocard) og i registreringsdossieret (ECHA, 2011). Tonnagen er ikke angivet. Ingen oplysninger om stoffets anvendelse er tilgængelige på ECHAs hjemmeside.

EP-1 nævnes som udgangsstof i syntesen af organofosfat insekticider (Comptox, 2023) og forekommer også som nedbrydningprodukt af organofosfat insekticider som f.eks. disulfoton (Gälli et al. 1994, Daughton et al. 1979, Capel et al. 1988).

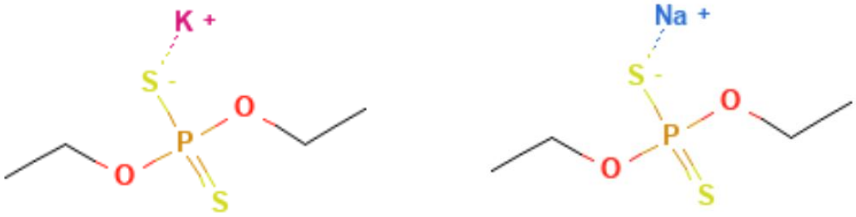
Der er modtaget to økotoksikologiske studier (DHI, 2005 og DHI 2005a) samt et nedbrydningsstudie (Sherburn and Large, 1998) fra Miljøstyrelsen. Der er også udarbejdet et QSAR-profil for stoffet, som er tilgængeligt fra den danske QSAR database (Danish QSAR database, 2023).

Tabel 1.1. Identitet af O,O-diethyl hydrogen phosphorodithioate (ECHA substance Infocard, HSDB)

IUPAC navn	Diethoxy-sulfanyl-sulfanylidene-λ5-phosphane
CAS navn	Phosphorodithioic acid, O,O-diethyl ester
Andre navne	0,0-diethyl phosphorodithiocic acid EP-1 (handelsnavn) O,O-Diethyl dithiophosphate
Strukturformel	
CAS nr.	298-06-6
EINECS nr.	206-055-9
Kemisk formel	$C_4H_{11}O_2PS_2$
SMILES	CCOP(=S)(OCC)S

Harmoniseret klassificering	Ingen harmoniseret klassificering
Selvklassificering	Flertallet af anmeldere (38 ud af 41) angiver: Acute Tox. 3, H301 (giftig ved indtagelse) Acute Tox. 3, H311 (giftig ved hudkontakt) Skin Corr. 1B, H314 (forårsager svære ætsninger af huden og øjenskader) Acute Tox. 2, H330 (livsfarlig ved indånding) Klassificering fra REACH lead-dossier (fælles registrering fra 2 anmeldere) angiver: Acute Tox. 4, H302 (farlig ved indtagelse) Skin Corr. 1B, H314 (forårsager svære ætsninger af huden og øjenskader) Acute Tox. 4, H332 (farlig ved indånding)

Det bemærkes at EP-1 også forekommer som kalium- eller natriumsalt, hvor brintatomet, som er bundet kovalent til svovlenheden, er erstattet med ionbundet kalium eller natrium, jf. nedenstående figur. Disse to stoffer er inddraget i litteratursøgningen.



CAS nr. 3454-66-8 CAS nr. 3338-24-7

Figur 1.1. Struktur af EP-1 som kalium- eller natriumsalt (fra HSDB).

2 Fysisk kemiske egenskaber

De fysisk kemiske egenskaber for EP-1 fremgår af Tabel 2.1.

Daughton et al. (1979) undersøgte adsorptionen i jorden samt fosfortilgængelighed for mikroorganismer for flere thiofosfater som angives at være nedbrydningsprodukter af organofosfat pesticider. Forfatterne angiver, at nedbrydningsprodukterne, herunder EP-1, generelt vil være tilgængelige for mikroorganismer i jord og sedimenter, pga. deres høje vandopløselighed og ringe evne til sorption. Forfatterne bemærker, at disse egenskaber står i kontrast til den lave vandopløselighed af organofosfat pesticider og deres større tilbageholdelse i jorden (Daughton et al., 1979). Værdier på vandopløselighed eller sediment/vand fordelingskoefficienter er dog ikke udviklet i dette studie.

Tabel 2.1. Fysisk kemiske egenskaber for EP-1.

Parameter	**Værdi**	**Reference**
Molekylevægt, M_w ($g \cdot mol^{-1}$)	186,2	ECHA, 2011
Smeltepunkt, T_m (ºC)	-33 <0 -59,92 [a]	ECHA, 2011 ECHA, 2011 Danish QSAR database
Kogepunkt, T_b (ºC)	65 235,63 [a]	ECHA, 2011 Danish QSAR database
Damptryk, P_v (Pa)	60 ved 57 °C	ECHA, 2011
Henry's konstant, H ($Pa \cdot m^3 \cdot mol^{-1}$)	37,6 [b] 2,316 [c]	Danish QSAR database
Vandopløselighed, Sw ($g \cdot L^{-1}$)	330 ved 25°C	ECHA, 2011
Dissociationskonstant, pK_a	-0,1 ± 0,4 [a]	Danish QSAR database
Octanol/vand fordelingskoefficient, log K_{ow}	2,24 (ikke ioniseret) [d] 1,4 ved pH 1 [e] -1,26 ved pH 4 [e] -1,56 ved pH 7 [e] -1,56 ved pH 9 [e]	Danish QSAR database
Sediment/vand fordelings-koefficient, normaliseret til organisk karbon, K_{oc} ($L \cdot kg^{-1}$)	38,8 – 118 [a]	Danish QSAR database

[a] Estimeret værdi
[b] Estimeret værdi (HLC Bond Method)
[c] Estimeret værdi (HLC Via VP/WSol)
[d] Estimeret værdi (EPI WSKOW model)
[e] Estimeret værdi (ACDLabs models)

3 Skæbne i miljøet

3.1 Nedbrydelighed

I registreringsdossieret refereres til et laboratoriestudie (Patil et al., 1997, i ECHA, 2011), som undersøger mekanismerne af hydrolyse af EP-1 i vandig opløsning i et medium fra 0,1 til 7,0 mol/dm^3 HCl (pH≤1) ved 98 °C. På baggrund af de særlige forsøgsbetingelser (høj temperatur, lav pH) vurderes studiet ikke at have miljømæssig relevans.

Der foreligger ikke andre oplysninger om abiotisk nedbrydning i registreringsdossieret.

Der beskrives et enkelt studie om biologisk nedbrydning i registreringsdossieret (Sherburn & Large, 1999), som er blevet troværdighedsvurderet med Klimisch score 2 af registranten. Fire bakteriestammer blev isoleret fra forurenede metalbearbejdningsvæsker og efterfølgende identificeret som *Aeromonas*, *Pseudomonas*, *Flavobacterium* og *Bacillus*. Bakteriestammer blev dyrket i med teststoffet natrium O,O-diethyldithiophosphat, og der blev udtaget prøver hvert 5. minut i en periode på 2 timer og undersøgt for nedbrydningsprodukter af teststoffet.
Ethanol, aldehyd og orthofosfat blev identificeret som nedbrydningsprodukter af teststoffet. Halveringstider blev ikke udledt. Der foreligger ikke informationer om forureningen af de i testen anvendte metalbearbejdningsvæsker, men det må antages at bakteriestammer har været tilpasset forureningen og studiet vurderes derfor til at have begrænset miljømæssig relevans til udledning af miljøkvalitetskriterier.

Estimater på nedbrydelighed er tilgængelige i QSAR databasen (Danish QSAR database, 2023) og listet i nedenstående Tabel 3.1. Estimater viser en hurtig nedbrydning ved anaerob nedbrydning, men langsom nedbrydning under aerobe forhold.

Tabel 3.1. Estimater på halveringstider og nedbrydelighed fra QSAR databasen (Danish QSAR database, 2023)

	Halveringstid	**Model anvendt i estimeringen**
Bionedbrydning, aerob	Langsom (”Slow”)	Biowin1 and Biowin2
	Flere uger (”weeks”)	Biowin3
	Dage-uger (”days-weeks”)	Biowin4
	Ikke let “Not readily”	Biowin5 (MITI linear model) Biodegradation Probability
	Ikke let (“Not readily”)	Biowin6 (MITI non-linear model) Biodegradation Probability
Bionedbrydning, anaerob	Hurtig (“Fast”)	Biowin7 (Anaerobic Linear)
Bionedbrydning	Ikke let (“Not readily”)	DTU-developed models (Battery, CASE Ultra, SciQSAR)
	Ikke let (“Not readily”)	Fra eksperiment

Derudover er der ikke identificeret oplysninger om nedbrydning.

3.2 Bioakkumulering

Eksperimentelle data er ikke blevet identificeret. Estimater på biokoncentrations- og bioakkumuleringsfaktorer (BCF og BAF) er tilgængelige i QSAR databasen (Danish QSAR database, 2023) og listet i nedenstående Tabel 3.2.

Den estimerede log K_{ow} er < 4 og de estimerede BCF'er er < 500. Det vurderes derfor at EP-1 har ringe potentiale for bioakkumulering.

Tabel 3.2. Biokoncentrations- og bioakkumuleringsfaktorer (BCF og BAF) fra QSAR databasen beregnet med EPI BCFBAF modeller (Danish QSAR database, 2023).

Faktor	**Værdi**
BCF (L/kg vådvægt)	14
Log BCF (L/kg vådvægt)	1,146
Primær biotransformation i hele kroppen, halveringstid for fisk (dage)	0,1633
BCF Arnot-Gobas (øverste trofiske niveau) inklusive biotransformation	14,03
BCF Arnot-Gobas (øverste trofiske niveau) uden biotransformation	19,54
BAF Arnot-Gobas (øverste trofiske niveau) inklusive biotransformation	14,03
BAF Arnot-Gobas (øverste trofiske niveau) uden biotransformation	20,19

3.3 Naturlig forekomst

Der foreligger ingen oplysninger om naturlig forekomst af EP-1.

4 Toksicitetsdata

4.1 Toksicitet over for vandlevende organismer

Oversigten over identificerede data kan ses i Bilag A.

Der er modtaget to økotoksikologiske studier (DHI, 2005 og DHI, 2005a) fra Miljøstyrelsen, hvis resultater også er rapporteret i registreringdossieret for EP-1 (ECHA, 2011). Disse to studier undersøger hhv. akut og kronisk toksicitet i saltvandsorganismerne *Acartia tonsa* (krebsdyr, copepoda) og *Skeletonema costatum* (kiselalge).

Via US EPA ECOTOX databasen (2023) er der identificeret to akutte studier på ferskvandsorganismerne *Daphnia magna* (krebsdyr, branchiopoda) og *Oncorhynchus mykiss* yngel (fisk), samt et Microtox assay ® med den marine bakterie *Vibrio fischeri* (Gälli et al., 1994, Fuerstenau, 1974).

QSAR-profilen for EP-1 indeholder estimeret akvatisk toksicitetsdata (Danish QSAR database, 2023), som vist i Bilag B. For tre af modellerne (DTU modeller) er stoffet uden for modellernes anvendelsesdomæne. Estimater fra EPI ECOSAR er beregnet for fisk (96 timer), dafnier (48 timer) og grønalger (96 timer) ud fra den mest toksiske kemikalieklasse "Estere, dithiophosphater" med log K_{ow} ≥5, hvilket ligger væsentlig over log K_{ow} for EP-1. Estimater ligger 2-3 størrelsesordener under de eksperimentelle værdier fra ECOTOX databasen. Estimaterne anses til at have begrænset værdi og medtages ikke i beregning af VKK.

Derudover er der ikke identificeret øvrige toksicitetsdata for vandlevende organismer.

4.2 Toksicitet over for sedimentlevende organismer

Der er ikke identificeret toksicitetsdata for sedimentlevende organismer.

4.3 Toksicitet over for pattedyr og fugle

Via PubChem, registreringsdossieret (ECHA, 2011) og NIOSH databasen er der identificeret enkelte akutte toksicitetsdata for rotte, mus og kanin, som vist i Tabel 4.1. En LD_{50} på 240 mg/kg lgv. i mus indikerer at EP-1 er toksisk for pattedyr ved oralt indtag, mens et tilsvarende rottestudie indikerer ingen toksicitet. Originallitteraturen har ikke været tilgængeligt, og det har derfor ikke været muligt at vurdere undersøgelsernes troværdighed.

Toksicitetsdata for fugle er ikke identificeret.

Tabel 4.1. Toksicitetsdata for pattedyr

Organisme	**Stof**	**Dosering og varighed**	**Effekt**	**Effektkoncentration**	**Reference**
Rotte	EP-1	Akut oral, varighed ikke angivet	Dødelighed, LD_{50}	4510 mg/kg lgv.	HSDB (Marhold 1986, originallitteratur ikke tilgængeligt)
Mus	EP-1	Akut oral, 14 dage	Dødelighed, LD_{50}	240 mg/kg lgv.	ECHA, 2011 (originalreference ikke tilgængeligt)
Rotte	EP-1	Akut inhalation, 4 timer	Dødelighed, LC_{50}	1640 mg /m3	HSDB database (National Technical Information Service, OTS0539075, originallitteratur ikke tilgængeligt)
Kanin	EP-1	24 timer	Øjenirritation	50 µg Alvorlig øjenirritation	NIOSH database, 2018 (Marhold 1986, originallitteratur ikke tilgængeligt)
Kanin	EP-1	Ikke angivet	Øjenirritation	0,1 mg Alvorlig øjenirritation	NIOSH database, 2018 (originalreference ikke tilgængeligt)
Kanin	EP-1	24 timer	Hudirritation	500 mg Mild hudirritation	NIOSH database, 2018 (originalreference ikke tilgængeligt)

4.4 Toksicitet over for mennesker

EP-1 har ingen harmoniseret klassificering jf. CLP-forordning (Forordning (EF) nr. 1272/2008). I selvklassificering angiver flere anmeldere akutte effekter ved oralt indtag (H301, H302), hudkontakt (H311) og inhalation (H330, H332), samt hud- og øjenirritation (H314), se Tabel 1.1.

Der er ikke identificeret sundhedsbaserede grænseværdier for mennesker.

5 Andre effekter

Der er ikke identificeret andre effekter med miljømæssig relevans.

6 Udledning af vandkvalitetskriterium

Kvalitetskriterierne er fastsat i overensstemmelse med EU's Guidance Document no. 27: Technical Guidance Document (TGD) for Deriving Environmental Quality Standards (EU, 2018).

6.1 Vandkvalitetskriterium (VKK)

Der er identificeret troværdige kroniske data for én saltvandsart, *Skeletonema costatum* (kiselalge).

Troværdige akutte data foreligger for tre saltvandsarter (*Acartia tonsa*, *Skeletonema costatum* og *Vibrio fischeri*) og to ferskvandsarter (*Daphnia magna* og *Oncorhynchus mykiss*), som tilsammen repræsenterer fem taksonomiske grupper.

Da EP-1 som stof er relateret til organofosfat insekticider, anses toksicitetsdata for insekter og krebsdyr som særlig relevante.

Fersk- og saltvandsdata for det organiske stof EP-1 betragtes samlet i udledning af VKK. Det spinkle datagrundlag tillader ikke en statistik relevant sammenligning af dataene. Kriterierne beregnes deterministisk vha. en usikkerhedsfaktor.

Jf. vejledningen (EU, 2018) kræves der akutte toksicitetsdata fra minimum tre taksonomiske grupper ('basissættet' fisk, invertebrater, fortrinsvis dafnier, og alger) eller en kronisk effektkoncentration for fisk eller krebsdyr for at kunne bestemme usikkerhedsfaktoren til beregning af $VKK_{ferskvand}$ (Tabel 3, s. 40 i EU, 2018).

Der anvendes en usikkerhedsfaktor (UF) på 1.000 på den laveste akutte effektkoncentration, EC_{50} på 0,54 mg/l for krebsdyret *Daphnia magna*, til beregning af $VKK_{ferskvand}$:

$VKK_{ferskvand}$ = EC_{50} / UF = 0,54 mg/l / 1.000 = 0,00054 mg/l = 0,54 µg/l

På baggrund af det akutte toksicitetsdata anvendes en UF 10.000 til beregning af $VKK_{saltkvand}$ (jf. Tabel 4, s. 43 i EU, 2018). $VKK_{saltvand}$ bliver således:

$VKK_{saltvand}$ = EC_{50} / UF = 0,54 mg/l / 10.000 = 0,000054 mg/l = 0,054 µg/l

6.2 Korttidsvandkvalitetskriterium (KVKK)

På baggrund af de akutte toksicitetsdata anvendes en UF på 100 til beregning af $KVKK_{ferskvand}$ (Tabel 5, s. 53 i EU, 2018). UF kan reduceres til 10, hvis data fra basissættet er tilgængeligt og standardafvigelsen for data ikke er større end en faktor 3 til begge sider, eller der foreligger viden

om mest følsomme arter eller virkemekanisme. Der ses her bort fra reduktionen af UF til 10, da standardafvigelsen er større end en faktor 3[1]. $KVKK_{ferskvand}$ beregnes således:

$KVKK_{ferskvand}$ = EC_{50} / UF = 0,54 mg/l / 100 = 0,0054 mg/l = 5,4 µg/l

På tilsvarende vis beregnes $KVKK_{saltvand}$ med en UF på 1.000 (jf. Tabel 6, s.55 i EU, 2018):

$KVKK_{saltvand}$ = EC_{50} / UF = 0,54 mg/l / 1.000 = 0,00054 mg/l = 0,54 µg/l

6.3 Kvalitetskriterium for sediment (SKK)

Den estimerede K_{oc} er < 1000 og de estimerede log K_{OW} er < 3 (Tabel 2.1) og der foreligger ingen data for sedimenttoksicitet. Jf. vejledningen (EU, 2018, s. 19) udledes SKK derfor ikke.

6.4 Kvalitetskriterium for biota, sekundær forgiftning ($BKK_{sek.forgiftn.}$)

Den estimerede log K_{ow} er < 3 og den estimerede BCF er < 100 (Tabel 2.1 og Tabel 3.2). Der foreligger ingen data, som indikerer høj toksicitet over for pattedyr og fugle. Jf. vejledningen (EU, 2018, s. 20) udledes $BKK_{sek.forgiftn.}$ derfor ikke.

6.5 Kvalitetskriterium for humant konsum af vandlevende organismer (HKK)

Kvalitetskriterier for humant konsum skal jf. vejledningen (EU, 2018) beregnes, hvis forekomsten af stoffet medfører en sundhedsrisiko for mennesker igennem konsum af vandlevende organismer.

Der findes ingen harmoniseret klassificering for EP-1. Faresætningerne fra selvklassificering og det ringe estimerede bioakkumuleringspotentiale indikerer at stoffet ikke medfører en sundhedsrisiko for mennesker igennem konsum af vandlevende organismer. HKK udledes derfor ikke.

6.6 Vandkvalitetskriterium baseret på $BKK_{sek.forgiftn.}$ og HKK

Jævnfør vejledningen (EU, 2018) skal der laves en tilbageregning fra biotakvalitetskriterierne ($BKK_{sek.forgiftn.}$ og HKK) til en vandkoncentration, for at se om vandkvalitetskriteriet fastsat for direkte effekter, også beskytter for sekundær forgiftning gennem fødekæden, samt beskytter mod forgiftning ved humant konsum af fiskeriprodukter.

Beregning af et vandkvalitetskriterium baseret på $BKK_{sek.forgiftn.}$ og HKK er ikke relevant for EP-1.

[1] Standardafvigelsen er beregnet med excelfunktionen STDEV.P med log10-transformerede værdier af følgende E/LC50 (mg/l): 0,54 for *D. magna*, 800 for *O. mykiss*, 3,13 for *V. fischeri*, 1800 for *S. costatum* og 1271 for *A. tonsa*. Standardafgivelsen er 1,48. Værdien er vejledende, fordi flere effektkoncentrationer er ikke angivet som bestemte koncentrationer (800-825 for *O. mykiss* og >1800 for *S. costatum*). Jf. vejledningen (tabelnote b s. 53 i EU 2018) kan AF reduceres, hvis standardafvigelsen er mindre end 0,5, hvilket ikke er tilfældet her.

7 Konklusion

Følgende kvalitetskriterier for vandmiljøet er udregnet for EP-1:

Vandkvalitetskriterium

$VKK_{ferskvand}$	0,54 µg/l
$VKK_{saltvand}$	0,054 µg/l

Korttidsvandkvalitetskriterium

$KVKK_{ferskvand}$	5,4 µg/l
$KVKK_{saltvand}$	0,54 µg/l

Sedimentkvalitetskriterium

$SKK_{ferskvand}$	Ikke beregnet
$SKK_{saltvand}$	Ikke beregnet

Biotakvalitetskriterium, sekundær forgiftning

$BKK_{sek.forgiftn.}$	Ikke beregnet

Biotakvalitetskriterium, humant konsum

HKK	Ikke beregnet

Referencer

Comptox Chemicals Dashboard (2023). U.S. Environmental Protection Agency. Diethyl dithiophosphoric acid. https://comptox.epa.gov/dashboard/chemical/details/DTXSID6027133 (02. maj, 2023).

Danish (Q)SAR Database, Division of Diet, Disease Prevention and Toxicology, National Food Institute, Technical University of Denmark, Registry Number 298-06-6. http://qsar.food.dtu.dk (02. maj 2023).

Capel, P. D., Giger, W., Reichert, P., & Wanner, O. (1988). Accidental input of pesticides into the Rhine River. Environmental science & technology, 22(9), 992-997.

Daughton, C. G., Cook, A. M., & Alexander, M. (1979). Phosphate and soil binding: factors limiting bacterial degradation of ionic phosphorus-containing pesticide metabolites. Applied and environmental microbiology, 37(3), 605-609.

DHI (2005). *Skeletonema costatum* growth inhibition test with ”EP-1 potassium salt”. Project No.: 53015. Ikke publiceret.

DHI (2005a). *Acartia tonsa* acute toxicity test with ”EP-1 potassium salt”. Project No.: 53015. Ikke publiceret.

ECHA (2011). Registreringsdossier O,O-diethyl hydrogen phosphorodithioate. https://echa.europa.eu/da/registration-dossier/-/registered-dossier/11749/1/2 (02. maj 2023).

ECHA Substance Infocard, Opslag på CAS nr. 20315-30-4. https://echa.europa.eu/da/information-on-chemicals (02. maj 2023).

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. (https://circabc.europa.eu/sd/a/ba6810cd-e611-4f72-9902-f0d8867a2a6b/Guidance%20No%2027%20-%20Deriving%20Environmental%20Quality%20Standards%20-%20version%202018.pdf)

Fuerstenau, M. C. (1974). The toxicity of selected sulfhydryl collectors to rainbow trout. Bureau of Mines Open File Report 11-75. Prepared for Department of the Interior Bureau of Mines.

Gälli, R., Rich, H. W., & Scholtz, R. (1994). Toxicity of organophosphate insecticides and their metabolites to the water flea Daphnia magna, the Microtox test and an acetylcholinesterase inhibition test. Aquatic toxicology, 30(3), 259-269.

HSDB, Hazardous Substances Data Bank (HSDB) (2023). Opslag på CAS nr. 298-06-6, 3454-66-8 og 3338-24-7. https://pubchem.ncbi.nlm.nih.gov National Library of Medicine (02. maj 2023).

Marhold, J. (1986). Prehled Prumyslove Toxikologie; Organicke Latky, Prague, Czechoslovakia, Avicenum (1175), 1986. Angivet i HSDB PubChem database.

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

NIOSH (The National Institute for Occupational Safety and Health, 2018). Registry of Toxic Effects of Chemical Substances (RTECS). Opslag på CAS nr. 298-06-6. https://www.cdc.gov/niosh-rtecs/TD7026F0.html (15. maj 2023).

Patil, R., Shinde, C. P. & Samadhia, A. (1997). Kinetics and Mechanism of Hydrolysis of Di-Ethyl Dithiophosphate in Acid Media. Asian Journal of Chemistry, Vol. 9, No. 3, 407-410.

Sherburn, R. E. & Large, P. J. (1999). The degradation of sodium O, O-diethyl dithiophosphate by bacteria from metalworking fluids. Letters in applied microbiology, 28(1), 61-65.

US EPA (United States Environmental Protection Agency, 2023). ECOTOXicology knowledgebase https://cfpub.epa.gov/ecotox/search.cfm (02. maj 2023).

Bilag A Toksicitetsdata

Toksicitet over for vandorganismer (EC_x, LC_x, NOEC, osv.)

Ferskvandsorganismer

Akut toksicitet

	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Krebsdyr, branchiopoda							
Daphnia magna	EP-1	Ja	24 timer	EC_{50}, immobilisation	0,54	Gälli et al. 1994	2
Fisk							
Oncorhynchus mykiss (yngel)	K-salt af EP-1 (CAS 3454-66-8)	Nej	96 timer	LC_{50}, dødelighed	800-825	Fuerstenau, 1974	2

Saltvandsorganismer

Akut toksicitet

	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Bakterier							
Vibrio fischeri (Photobacterium phosphoreum)	EP-1	Ja	30 min	EC_{50}, bioluminescence	3,13	Gälli et al. 1994	2
Alger, kiselalger							
Skeletonema costatum	K-salt af EP-1	Nej	72 timer	EC_{50}, vækst	>1800	DHI, 2005	2
Krebsdyr, Copepoda							
Acartia tonsa	K-salt af EP-1	Nej	48 timer	LC_{10}, dødelighed	529	DHI, 2005a	2
Acartia tonsa	K-salt af EP-1	Nej	48 timer	LC_{50}, dødelighed	1271	DHI, 2005a	2

Saltvandsorganismer
Kronisk toksicitet

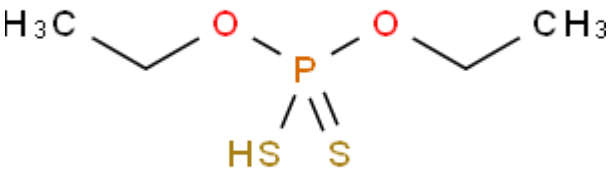
	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Alger, kiselalger							
Skeletonema costatum	K-salt af EP-1	Nej	72 timer	NOEC, vækst	1000	DHI, 2005	2
Skeletonema costatum	K-salt af EP-1	Nej	72 timer	EC_{10}, vækst	1026	DHI, 2005	2
Skeletonema costatum	K-salt af EP-1	Nej	72 timer	LOEC, vækst	1800	DHI, 2005	2
Skeletonema costatum	K-salt af EP-1	Nej	72 timer	EC_{50}, vækst	>1800	DHI, 2005	2

Bilag B QSAR-profil

Danish (Q)SAR Database, http://qsar.food.dtu.dk Date: 02-05-2023

(Q)SAR predicted profile

- **Structure (as used for QSAR prediction):**



SMILES (used for QSAR prediction): C(C)OP(=S)(S)OCC

- **ID**

Registry Number	298-06-6	PubChem CID	
REACH EC Number (pre-registration, by 2013)	206-055-9	REACH EC Number (registration, 2019 or 2022)	206-055-9
REACH registration (2022)	Yes	REACH registration cumulated minimum annual tonnage (2022)	
EU CLP Harmonized Classification*		DK-EPA / DTU QSAR-based CLP Advisory Classification	Aquatic Acute 1
EU Biocide active substances		EU Pesticide active substances	
EU EFSA Botanical substances		US TSCA (Oct. 2021)	Yes
Tox21 (2019)	Yes	ToxCast (Oct. 2021)	
Molecular Formula	C4 H11 O2 P1 S2	Molecular weight (g/mole)	186.23
Chemical Name	O,O-diethyl hydrogen phosphorodithioate		

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

- Melting point, Boiling point and Vapour pressure

Melting Point (deg C)	-59.92	Melting Point Experimental (deg C)	
Boiling Point (deg C)	235.63	Boiling Point Experimental (deg C)	
Vapour Pressure (atm)		Vapour Pressure Experimental (atm)	
Vapour Pressure (mm Hg)	0.0583	Vapour Pressure Experimental (mm Hg)	
Vapour Pressure (Pa)	7.773	Vapour pressure Subcooled Liquid (Pa)	

EPI MPBPVP models

- Henry's Law Constant

HLC Bond Method (atm-m3/mole)	0.0003709	HLC Group Method (atm-m3/mole)	
HLC Via VP/WSol (atm-m3/mole)	2.286E-005	HLC Via VP/WSol (Pa-m3/mole)	2.316
Henrys Law Const. Exp db (Pa-m3/mole)		Henrys Law Const. Exp db (atm-m3/mole)	

EPI HENRYWIN models

- Water Solubility

Water solubility from Kow (mg/L)	625	Water solubility from Fragments (mg/L)	868.19
Water solubility Exp (mg/L)	0.064	Water solubility Exp Ref	CHEMICALS INSPECTION AND TESTING INSTITU (1992)

EPI WATERNT model

- 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

- 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.

- **Partition coefficients**

pH	1	4	5	6	7	8	9
LogD	1.4	-1.26	-1.52	-1.56	-1.56	-1.56	-1.56

Minimum LogD in the pH interval 4-9	-1.56	Maximum LogD in the pH interval 4-9	-1.26

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	4.059	Log Kaw	-1.819

EPI KOAWIN models

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

Log Kow	2.24		
Log Kow Exp		Log Kow Exp Ref	

EPI WSKOW model

LogKow: log octanol-water partition coefficient

Kp (m3/ug) Mackay-based	4.06E-007	Kp (m3/ug) Koa-based	2.81E-009
Phi Junge-Pankow-based	1.47E-005	Phi Mackay-based	3.25E-005
Phi Koa-based	2.25E-007		

EPI AEROWIN models

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

Koc from MCI (L/kg)	38.75	Log Koc from MCI	1.5883
Koc from Kow (L/kg)	118.1	Log Koc from Kow	2.0724

EPI KOCWIN models

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

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

	Air	Water	Soil	Sediment
Mass Amount (%)	1.1	36.8	61.9	0.127
Half-Life (hr)	2.8	360	720	3240
Emissions (kg/hr)	1000	1000	1000	0

EPI Level III Fugacity Model

Persistence time (hr)	221
Persistence time (days)	9.208333

EPI Level III Fugacity Model

- **Level III Fugacity Environmental Partitioning, emission only to water**

	Air	Water	Soil	Sediment
Mass Amount (%)	0.58	99.1	0.00592	0.341
Half-Life (hr)	2.8	360	720	3240
Emissions (kg/hr)	0	1000	0	0

EPI Level III Fugacity Model

Persistence time (hr)	228
Persistence time (days)	9.5

EPI Level III Fugacity Model

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

	Total removal	Biodegradation	Sludge Adsorption	Volatilization
(%)	16.58	0.09	2.18	14.32

EPI STPWIN model

- **Atmospheric oxidation (25 deg C)**

	OH	Ozone
Half-Life (d)	0.1167	0
Half-Life (hr)	1.401	
Overall Rate Const. (OH: E-12 cm3/molecule-sec and OZ: E-17 cm3/molecule-sec)	91.6286	

EPI AOPWIN models

- **Biodegradation**

Biowin1 (linear model) Probability of Rapid Biodegradation	0.6589
Biowin2 (non-linear model) Probability of Rapid Biodegradation	0.5901
Biowin3 Expert Survey Ultimate Biodegradation	2.7876
Biowin3 Expert Survey Ultimate Timeframe	weeks
Biowin4 Expert Survey Primary Biodegradation	3.5791
Biowin4 Exp. Survey Primary Timeframe	days-weeks
Biowin5 (MITI linear model) Biodegradation Probability	0.2578
Biowin6 (MITI non-linear model) Biodegradation Probability	0.1243
Biowin7 (Anaerobic Linear) Biodegradation Probability	0.7289
Petroleum Hydrocarbon Biodegradation Half-Life (days)	

EPI BIOWIN models

SkinBiowin1 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	POS_IN	POS_IN	POS_OUT	POS_IN

DTU-developed models

- **Bioaccumulation**

BCF (L/kg wet-wt)	14
Log BCF (L/kg wet-wt)	1.146
Whole Body Primary Biotransformation Fish Half-Life (days)	0.1633
BCF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	14.03
BCF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	19.54
BAF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	14.03
BAF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	20.19

EPI BCFBAF models

BCF: Bioconcentration factor, BAF: Bioaccumulation factor

- **Aquatic toxicity**

Exp	Battery	Leadscope	SciQSAR
Fathead minnow 96h LC50 (mg/L)		11.33756	54.31874
Domain	OUT	OUT	OUT
Daphnia magna 48h EC50 (mg/L)		3.99475	0.1042725
Domain	OUT	OUT	OUT
Pseudokirchneriella s. 72h EC50 (mg/L)		33.77766	15.34792
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)	0.826	0.00163	9.044
Max. Log Kow for Most Toxic Class	5	5	6.4
Most Toxic Class	Esters, Dithiophosphates	Esters, Dithiophosphates	Esters, Dithiophosphates
Note	Chemical may not be soluble enough		Chemical may not be soluble enough

EPI ECOSAR models

ECOSAR Classes: Esters, Dithiophosphates

- Oral absorption

Lipinski's Rule-of-five score (bioavailability)	0
Absorption from gastrointestinal tract for 1 mg dose (%)	95
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.

- Skin absorption

Dermal absorption (mg/cm2/event)	0.00623

EPI DERMWIN model

- Brain/blood Distribution

Log brain/blood partition coefficient	0.3274

Equation from literature

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

- Metabolism

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

DTU-developed models

- Acute toxicity in Rodents

	LD50 (mg/kg/d)	Reliability Index
Rat Oral	1300	0.71
Rat Intraperitoneal	180	0.46
Mouse Oral	430	0.45
Mouse Intraperitoneal	89.17	0.15
Mouse Intravenous	180	0.42
Mouse Subcutaneous	210	0.44

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.

- **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.

- **Irritation and Sensitization**

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Severe Skin Irritation in Rabbit	NEG	NEG_IN	NEG_IN	POS_OUT	NEG_IN
Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based (open data only)				INC_OUT	
Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based (open data and REACH-registrations)	N/A			INC_OUT	
Skin sensitisation GHS/CLP at least Cat. 1, LLNA-based, only negative predictions (open data only)				N/A	
Skin sensitisation GHS/CLP Cat. 1A, LLNA-based (open data only)				INC_OUT	
Skin sensitisation GHS/CLP Cat. 1A, LLNA-based (open data and REACH-registrations)	N/A			INC_OUT	
Skin sensitisation GHS/CLP Cat. 1A, LLNA-based, only positive predictions (open data and REACH-registrations)	N/A			N/A	
Allergic Contact Dermatitis in Guinea Pig and Human*	N/A	INC_OUT	INC_OUT	INC_OUT	POS_OUT
Respiratory Sensitisation in Humans		INC_OUT	INC_OUT	POS_OUT	NEG_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	No alert found
- metabolites from auto-oxidation simulator only	
Protein binding by OECD, alerts in:	
- parent only	No alert found
- metabolites from skin metabolism simulator only	No alert found
- 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	DPRA less than 9% (DPRA 13%) >> Mercaptoalcohols
- 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	DPRA less than 9% (DPRA 13%) >> No protein binding alert
- 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	Not possible to classify according to these rules
- 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

- **Endocrine and Molecular Endpoints**

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Estrogen Receptor α Binding, Full training set (Human *in vitro*)		POS_OUT	INC_OUT	NEG_OUT	POS_IN
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	POS_OUT
Estrogen Receptor Activation, CERAPP data (*in vitro*)		N/A	N/A	INC_OUT	N/A
Androgen Receptor Inhibition (Human *in vitro*)		INC_OUT	INC_OUT	NEG_OUT	POS_OUT
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
Sodium/iodide symporter (NIS), higher		N/A	N/A	INC_OUT	N/A

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
sensitivity					
Sodium/iodide symporter (NIS), higher specificity		N/A	N/A	INC_OUT	N/A
Thyroid Receptor α Binding (Human *in vitro*)					
- mg/L			29788.57	1228.654	139.4279
- µM			159955.8	6597.51	748.6865
- Positive for IC_{50} ≤ 10 µM					
- Positive for IC_{50} ≤ 100 µM					
- Domain		OUT	OUT	OUT	OUT
Thyroid Receptor β Binding (Human *in vitro*)					
- mg/L			6026.288	14.11886	175.772
- µM			32359.38	75.8141	943.8435
- Positive for IC_{50} ≤ 10 µM					
- Positive for IC_{50} ≤ 100 µM					
- Domain		OUT	OUT	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	INC_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
CYP3A4 Induction (Human *in vitro*)		N/A	N/A	INC_OUT	N/A
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

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

- **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

- **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

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

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Ames test in S. typhimurium (*in vitro*)		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN
*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	POS_OUT	POS_IN

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR

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.

	VEGA	Mut. / Non-mut. scores	Used models
Mutagenicity consensus	NEG	0 / 0.2	4

Mutagenicity (Ames) consensus model version 1.0.2 contained in VEGA version 1.1.4 with calculation core version 1.2.4

Prediction: POS = Mutagenic, NEG = Non-mutagenic.

VEGA

ISS	CAESAR	SarPy	KNN
NEG_Low	NEG_Low	NEG_Low	NEG_Low

Four individual models in mutagenicity consensus model version 1.0.2 contained in VEGA version 1.1.4 with calculation core version 1.2.4

Prediction: POS = Mutagenic, NEG = Non-mutagenic, SUSP.POS = Suspected mutagenic, POSS.NEG = Possible Non-mutagenic, Exp = experimental value, Good = Good reliability, Mod = Moderate reliability, Low = Low reliability.

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

- **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	NEG_OUT	NEG_IN
Chromosome Aberrations in Chinese Hamster Lung (CHL) Cells		POS_OUT	INC_OUT	INC_OUT	POS_IN
Mutations in Thymidine Kinase Locus in Mouse Lymphoma Cells		INC_OUT	INC_OUT	POS_OUT	POS_OUT
Mutations in HGPRT Locus in Chinese Hamster Ovary (CHO) Cells		POS_OUT	INC_OUT	NEG_OUT	POS_IN
Unscheduled DNA Synthesis (UDS) in Rat Hepatocytes		NEG_OUT	INC_OUT	NEG_OUT	NEG_IN

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
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

- ***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	POS_OUT	INC_OUT	INC_OUT
Dominant Lethal Mutations in Rodents		POS_OUT	INC_OUT	NEG_OUT	POS_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

- **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

- Abbreviations

INC: inconclusive. A definite call within the defined applicability domain could not be made.

NEG: negative

POS: positive

IN: inside applicability domain

OUT: outside applicability domain

Exp: Experimental values, from EpiSuite experimental databases or DK DTU QSAR models training sets.

N/A: Not applicable, either because training set data cannot be released for commercial or proprietary models / training sets, or because the model was not developed in a given QSAR software (i.e. a given prediction is not available as the model version does not exist).

- Important notes

This is an automatically generated report from the Danish (Q)SAR Database, http://qsar.food.dtu.dk.

For predictions from CASE Ultra, Leadscope, SciQSAR as well as the Acute toxicity in rodent from ACDLabs information on the software versions can be found in the QMRFs. For the other predicted properties the software versions are:

EPI MPBPWIN v1.43

EPI HENRYWIN v3.20

EPI WSKOW v1.42

EPI WATERNT v1.01

EPI KOAWIN v1.10

EPI AEROWIN v1.00

EPI KOCWIN v2.00

EPI Level III Fugacity Model (EPI Suite v4.11)

EPI STPWIN (EPI Suite v4.11)

EPI AOPWIN v1.92

EPI BIOWIN v4.10

EPI BCFBAF v3.01

EPI ECOSAR v1.11

EPI DERMWIN v2.02

ACD/ ToxSuite 2.95.1 Ionization\pKa

ACD/ ToxSuite 2.95.1 Ionization\ LogD

ACD/ ToxSuite 2.95.1

It is recommended to run the latest version of the EPI Suite Programs in preference of the predictions given in this document when these endpoints are of importance and new versions have been released from the United States Environmental Protection Agency in comparisons. EPI Suite can be downloaded from the US EPA homepage: http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

For further information on the applied systems, see the following homepages:

Case Ultra: http://www.multicase.com/case-ultra

Leadscope: http://www.leadscope.com/

SciQSAR: http://lhasa-llc.com/

ToxSuite: http://www.acdlabs.com/

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