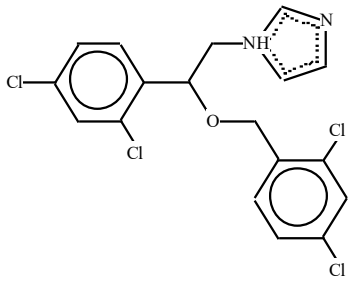
Miljøministeriet
Miljøstyrelsen

Fastsættelse af kvalitetskriterier for vandmiljøet

Miconazol

CAS nr. 22916-47-8



Vandkvalitetskriterium	$VKK_{ferskvand}$	Ikke muligt
Vandkvalitetskriterium	$VKK_{saltvand}$	Ikke muligt
Korttidsvandkvalitetskriterium	$KVKK_{ferskvand}$	Ikke muligt
Korttidsvandkvalitetskriterium	$KVKK_{saltvand}$	Ikke muligt
Sedimentkvalitetskriterium	$SKK_{ferskvand}$	Ikke muligt
Sedimentkvalitetskriterium	$SKK_{saltvand}$	Ikke muligt
Biota-kvalitetskriterium, sekundær forgiftning	$BKK_{sek.forgiftn.}$	Ikke muligt
Biota-kvalitetskriterium, human konsum	HKK	Ikke muligt

Juni 2024

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 human 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 12/02-2024.

English Summary and conclusions

Miconazole is a broad-spectrum fungicidal pharmaceutical belonging to the group of imidazoles.

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).

Experimental values for the toxicity of miconazole are available for short-term tests on two freshwater species; algae (*Pseudokirchneriella subcapitata*) and crustaceans (*Daphnia magna*) and two marine species; algae (*Skeletonema marinoi*) and crustaceans (*Artemia salina*). Furthermore, one experimental value is available for a long-term test on *Daphnia magna.* No long-term test data have been found for saltwater organisms.

For freshwater species, crustaceans are the most sensitive organism with an aggregated EC_{50} value for *Daphnia magna* of 0.35 mg/L. For marine species, algae are the most sensitive organism with an E_rC50 value for *Skeletonema marinoi* of 0.17 mg/L.

The toxicity of miconazole towards freshwater organisms has been estimated in the Danish QSAR database by the QSAR models Leadscope and SciQSAR (Danish (Q)SAR Database, 2024). The effect values are presented as a geometric mean of the two models. An LC_{50} of 0.014 mg/L for fish (*Pimephales promelas*), an EC_{50} of 0.067 mg/L for crustaceans (*Daphnia magna)* and an EC_{50} of 0.125 mg/L for algae (*Pseudokirchneriella subcapitata*) have been estimated (Danish (Q)SAR Database, 2024).

The dataset is listed in Appendix A.

AA-EQS for water

According to the TGD (EU, 2018), when not enough data is available to use the SSD (Species Sensitivity Distribution) method the deterministic approach using uncertainty factors, UF, shall be used for the derivation of EQS. Therefore, this approach is followed for derivation of the AA-EQS for miconazole.

There is only one available experimental datapoint on long-term tests and based on the experimental and estimated acute effect concentrations, it is not possible to derive the AA-EQS for water.

MAC-EQS for water

Based on the limited amount of data available the MAC-EQS for water cannot be derived.

QS for sediment

According to the TGD (EU, 2018) it is relevant to derive QS for sediment when log $K_{ow} \geq 3$ or log $K_{oc} \geq 3$. Miconazole has an estimated Log K_{ow} = 6,25 and a Log K_{oc} = 4.83 (EpiSuite, 2023). Thus, a QS for sediment should be derived. However, no data has been found on the toxicity of miconazole towards sediment living organisms and a QS for sediment cannot be derived.

QS for secondary poisoning

There are no valid values for the bioaccumulation potential (BMF or BCF (BAF)) of miconazole. Therefore, whether a QS for secondary poisoning ($QS_{sec.\ pois.}$) is relevant is determined using Log K_{ow}. According to the TGD (EU, 2018), it is relevant to derive $QS_{sec.\ pois.}$ for a substance when Log $K_{ow} \geq 3$. Miconazole has an estimated Log K_{ow} på 6,25 (EpiSuite, 2023). Thus, a QS for secondary poisoning should be derived. However, no data has been found on the toxicity of miconazole towards birds and mammals and a QS for secondary poisoning cannot be derived.

QS for human health

According to TGD (EU, 2018), a QS for human health of fishery products is relevant if the substance has relevant human hazard properties and has the potential to bioaccumulate. Miconazole has the self-classification harmful if swallowed (H302) and has the potential to bioaccumulate. Thus, a QS for human health should be derived. However, no data (data search on DNEL and ADI/TDI/PDE values) has been found on the toxicity of miconazole towards humans and a QS for human health cannot be derived.

QS_{water} based on $QS_{sec.\ pois.}$ and $QS_{human\ health}$

A QS for secondary poisoning and human health has not been derived since $Q_{Ssec.\ pois.}$ and $QS_{human\ health}$ are not available.

In conclusion, the following EQS for the aquatic environment have been derived for miconazole:

$AA\text{-}EQS_{freshwater}$	= Not possible
$AA\text{-}EQS_{saltwater}$	= Not possible
$MAC\text{-}EQS_{freshwater}$	= Not possible
$MAC\text{-}EQS_{saltwater}$	= Not possible
$QS_{sediment,\ freshwater}$	= Not possible
$QS_{sediment,\ saltwater}$	= Not possible
$QS_{sec.\ pois.}$	= Not possible
$QS_{human\ health}$	= Not possible

1 Indledning

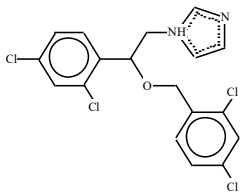
Nærværende datablad vedrører miconazol med CAS nr. 22916-47-8.

Identiteten af miconazol fremgår af Tabel 1.1.

Miconazol er et syntetisk bredspektret svampemiddel, som tilhører gruppen af imidazoler. Det er hyppigt anvendt til bl.a. behandling af candidiasis (svampeinfektion i fx slimhinder forårsaget af gærsvampen Candida). Miconazol er sædvanligvis tilgængelig som creme eller gel ved 1-2% koncentrationer (Mijaljica *et al.* 2022).
Det globale forbrug af miconazole er faldet siden 2008, og det daglige forbrug i 2018 var 0,000029 DDD[1]/1000 indbyggere/dag, hvilket er ca. 10% mindre end forbruget i 2008 (Pathadka *et al.* 2022).

Stoffet har ingen harmoniseret CLP-klassificering, men har to selvklassificeringer for miljøet; Aquatic Acute 1 (H400) og Aquatic Chronic 1 (H410) (52 C&L notifikationer). Stoffet har yderligere selvklassificeringen Acute Tox. 4 (H302), som er relevant for humant konsum (ECHA, 2024).

Tabel 1.1. Identitet af miconazol

IUPAC navn	1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]ethyl]imidazole
Strukturformel	
CAS nr.	22916-47-8
EINECS nr.	245-324-5
Kemisk formel	$C_{18}H_{14}Cl_4N_2O$
SMILES	n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
Harmoniseret klassificering	Ingen
Selvklassificering	Acute Tox. 4, H302 (farlig ved indtagelse) Aquatic Acute 1, H400 (meget giftig for vandlevende organismer) Aquatic Chronic 1, H410 (meget giftig med langvarige virkninger for vandlevende organismer)

[1] Defined Daily Dose

2 Fysisk kemiske egenskaber

De fysisk-kemiske egenskaber for miconazol fremgår af Tabel 2.1.

Tabel 2.1. Fysisk-kemiske egenskaber for miconazol

Parameter	**Værdi**	**Reference**
Molekylevægt, M_w ($g \cdot mol^{-1}$)	416,14	EPI Suite 2023, se Bilag B
Smeltepunkt, T_m (ºC)	215,55[1]	EPI Suite 2023, se Bilag B (vægtet værdi)
Kogepunkt, T_b (ºC)	506,31[1]	EPI Suite 2023, se Bilag B (metode adapteret efter Stein & Brown)
Damptryk, P_v (Pa)	$2{,}53 \times 10^{-6}$ [1]	EPI Suite 2023, se Bilag B
Henry's konstant, H ($Pa \cdot m^3 \cdot mol^{-1}$)	$2{,}48 \times 10^{-4}$ [1]	EPI Suite 2023, se Bilag B
Vandopløselighed, S_w ($g \cdot L^{-1}$)	$2{,}3975 \times 10^{-5}$ [1]	EPI Suite 2023, se Bilag B
Dissociationskonstant, pK_a	~6,50	Sanli *et al.* 2013
Octanol/vand fordelingskoefficient, log K_{ow}	6,25[1]	EPI Suite 2023, se Bilag B
Sediment/vand fordelingskoefficient, normaliseret til organisk karbon, K_{oc} ($L \cdot kg^{-1}$)	$6{,}829 \times 10^{4}$ [1]	EPI Suite 2023, se Bilag B

[1]Estimeret værdi for 25 °C

3 Skæbne i miljøet

3.1 Nedbrydelighed

Der er ikke fundet eksperimentelle data for let bionedbrydelighed af miconazol. Azol-svampemidler er ikke let-bionedbrydelige, primært grundet deres iboende egenskaber i at hæmme mikrobiel aktivitet (Chen *et al.,* 2013). Ved brug af BIOWIN v4.10 (EPI Suite) er miconazol vurderet som ikke let-bionedbrydelig under aerobe og anaerobe forhold (EPI Suite, 2023) (se Bilag B).

Yderligere er miconazol vurderet som værende persistent i jordmiljøet, da den estimerede halveringstid (DT_{50}) af miconazol i jord er 360 dage (EPI Suite, 2023) (se Bilag B). Resultatet understøttes af miconazols høje affinitet for organisk materiale i jord (K_{OC} $6{,}829\times10^{4}$), der indikerer, at stoffet er meget lidt mobilt i jord. Yderligere bliver miconazol akkumuleret i slam ved spildevandsrensningsanlæg grundet stoffets hydrofobiske egenskaber (Tran *et al.,* 2018).

Henry's lov konstant, H, på $2{,}48\times10^{-4}$ $Pa\cdot m^{3}\cdot mol^{-1}$ angiver en lav flygtighedsrate for miconazol og derved må det antages, at fordampning af miconazol ikke spiller en væsentlig rolle for stoffet i miljøet.

Samlet set kan miconazol således karakteriseres som ikke let-bionedbrydelig. Yderligere forventes miconazol at akkumulere i jord- og sedimentfasen, og en meget lille del vil derfor være til stede i vandfasen.

3.2 Bioakkumulering

Der er ikke fundet eksperimentelle data for bioakkumulering af miconazol. Stoffets affinitet for organiske stoffer er høj (estimeret log K_{OW} 6,25), og stoffet har potentiale for ophobning i organisk væv. EPI Suite beregning baseret på log K_{OW} 6,25 estimerer en BCF på 6192 L/kg vådvægt (EPI Suite, 2023) (se Bilag B). I Canada er miconazol målt i en koncentration op til 1,22 ng/g i muslinger i naturen og op til 1,71 ng/g i muslinger ved opdræt. Ligeledes er der i Kina fundet rester af miconazol i leveren af 12 forskellige fiskearter i koncentrationer op til 432 ng/g (Wroński *et al.,* 2024), hvilket understøtter vurderingen om, at stoffet har bioakkumulerende egenskaber.

3.3 Naturlig forekomst

Miconazol fremstilles ved kemisk syntese og findes ikke naturligt i miljøet.

Miconazol bruges hovedsageligt i creme eller gel og vil efter påføring blive vasket af og skyllet ud med vaskevandet til spildevandsbehandling. Forekomsten af miconazol i miljøet sker herved via udløb fra renseanlæg samt via akkumulering i renseanlæggets slam, der bliver spredt på landbrugsmarker (Chen & Ying, 2015).

4 Toksicitetsdata

De anvendte studier og deres troværdighed fremgår af bilag A. Troværdigheden af studierne er vurderet ved tildelingen af en Klimisch score fra 1 til 4 (Klimisch *et al.,* 1997). Score 1 angiver, at studiet kan anvendes uden forbehold, mens score 2 angiver at studiet kan anvendes med forbehold, f.eks. at der er tilstrækkelige oplysninger, selvom studiet ikke er udført i forhold til guideline. Studier, som ikke er tilstrækkeligt beskrevet, tildeles score 3 eller 4, hvor score 4 tildeles studier, hvor det ikke er muligt at vurdere kvaliteten og dermed troværdigheden. Estimerede værdier tildeles scoren 3, da de ikke bør anvendes direkte i udledningerne af miljøkvalitetskriterier jf. TGD (EU, 2018).

Der er kun fundet meget få eksperimentelle data for giftigheden af miconazol. Data er derfor suppleret med data fra den danske (Q)SAR-database (Danish (Q)SAR Database 2024). Resultater fra Danish (Q)SAR Database er vist i Bilag B.

4.1 Toksicitet over for vandlevende organismer

Der er fundet akutte eksperimentelle effektværdier for både ferskvands- og saltvandsorganismer. Ydermere er der fundet én eksperimentel kronisk effektværdi for ferskvandsorganismer. Effektkoncentrationer for organismer er sammenstillet i Bilag A.

Der er fundet troværdige akut toksicitetsdata for to forskellige trofiske grupper, hhv. alger (*Pseudokirchneriella subcapitata*) og krebsdyr (*Daphnia magna*) samt ét kronisk studie for krebsdyr (*Daphnia magna*). Dertil er der fundet et studie med troværdige akut toksicitetsdata for to saltvandsarter: alger (*Skeletonema marinoi*) og krebsdyr (*Artemia salina*). For ferskvandsorganismerne er krebsdyr den mest følsomme organisme med en aggregeret EC_{50}-værdi for *Daphnia magna* på 0,35 mg/L. For saltvandsorganismerne er alger den mest følsomme organisme med en E_rC_{50}-værdi for *Skeletonema marinoi* på 0,17 mg/L.

I den danske (Q)SAR-database er akut toksicitet over for ferskvandsorganismer estimeret ved hjælp af DTU-modellerne Leadscope og SciQSAR (Danish (Q)SAR Database, 2024). Resultaterne er vist i Bilag A og Bilag B, og effektværdierne er angivet som geometrisk gennemsnit af modellerne Leadscope og SciQSAR i Bilag A. Der er estimeret en LC_{50} for fisk (*Pimephales promelas*) på 0,014 mg/L, EC_{50} for krebsdyr (*Daphnia magna*) på 0,067 mg/L og EC_{50} for alger (*Pseudokirchneriella subcapitata*) på 0,125 mg/L (Danish (Q)SAR Database, 2024).

4.2 Toksicitet over for sedimentlevende organismer

Der er ikke fundet data for toksiciteten af miconazol over for sedimentlevende organismer.

4.3 Toksicitet over for pattedyr og fugle

Der er ikke fundet data, der kan beskrive toksiciteten af miconazol over for pattedyr eller fugle.

4.4 Toksicitet over for mennesker

Der er ikke fundet data, der kan beskrive toksiciteten af miconazol over for mennesker. Der er søgt efter DNEL samt ADI/TDI/PDE-værdier for miconazol for at undersøge toksicitet over for mennesker. Ligeledes er der søgt efter en MIC-værdi (Minimum Inhibitory Concentration) i publikationen fra Bengtsson & Larsson (2016), som har samlet MIC-værdier fra den offentligt tilgængeligt database European Committee on Antimicrobial Susceptibility Testing database (EUCAST). En MIC-værdi indikerer den laveste koncentration af antibiotika, hvor bakteriel eller svampevækst er fuldstændig hæmmet. Den relevante MIC-værdi angives som PNEC-MIC og forventes at være beskyttende for både mennesker og miljø. PNEC-MIC-værdien sammenlignes med vandkvalitetskriteriet (VKK), og den laveste værdi anvendes. Der er i publikationen ikke angivet en MIC-værdi for miconazol.

5 Andre effekter

Det er vurderet, at miconazol ikke har andre relevante effekter, da stoffet ikke er listet på aktuelle lister inklusiv Endocrine Disruptor-lister (CoRAP, EASIS, EDLIST, EDSP, PACT og TEDX)[2] samt ikke har en relevant klassificering, der antyder endokrine eller andre effekter end anført i databladet.

[2] CoRAP: Community Rolling Action Plan (https://echa.europa.eu/da/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table); EASIS: Endocrine Active Substances Information System (https://easis.jrc.ec.europa.eu/iuclid6-web/browser/raw/SUBSTANCE); EDLIST: Endocrine Disruptor List (https://edlists.org/the-ed-lists); EDSP: Endocrine Disruptor Screening Program (https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-estrogen-receptor-bioactivity); PACT: Public Activities Coordination Tool (https://echa.europa.eu/da/pact); TEDX: The Endocrine Disruption Exchange (https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list)

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 ikke tilstrækkelige data og taksonomiske grupper nok repræsenteret til at anvende SSD (Species Sensitivity Distribution) metoden, som jf. TGD (EU, 2018) kræver minimum 10 forskellige arter fordelt på minimum 8 taksonomiske grupper. Derfor skal den deterministiske metode anvendes med anvendelse af usikkerhedsfaktorer til udledning af vandkvalitetskriterier for miconazol.

Der er kun fundet ét eksperimentelt datapunkt for langtidstest på stoffet. Samtidig er tilgængelige akutte data ikke tilstrækkelige til at udgøre et basissæt bestående af test med organismer fra tre forskellige trofiske niveauer, så på baggrund af eksperimentelle og estimerede akutte effektkoncentrationer er det ikke muligt at fastsætte et vandkvalitetskriterium for hverken ferskvand eller saltvand. Read-across til det strukturelt lignende stof miconazol nitrat er heller ikke en mulighed, da der også er få tilgængelige data for dette stof. Dertil bør non-test data, herunder read-across, ikke anvendes som kritisk data jf. vejledningen (EU, 2018).

6.2 Korttidsvandkvalitetskriterium (KVKK)

På baggrund af den begrænsede mængde af anvendelige data, kan et korttidsvandkvalitetskriterie for ferskvand og saltvand ikke bestemmes.

6.3 Kvalitetskriterium for sediment (SKK)

Jævnført TGD (EU, 2018) er det relevant at udlede sedimentkvalitetskriterier for et stof, når log K_{ow} ≥ 3 eller log $K_{oc} \geq 3$. Miconazol har en estimeret Log K_{ow} = 6,25 og en Log K_{oc} = 4,83 (EpiSuite, 2023), hvorfor det er relevant at udlede et sedimentkvalitetskriterie. Der er dog ikke fundet data for toksiciteten af miconazol over for sedimentlevende organismer, og et kvalitetskriterie for sediment kan derfor ikke bestemmes.

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

Der foreligger ikke valide værdier for miconazols bioakkumulerbarhed (BMF eller BCF (BAF)), og hvorvidt et biotakriterie for sekundær forgiftning ($BKK_{sek.forgiftn.}$) er relevant afgøres derfor med anvendelse af Log K_{ow}. Jævnfør vejledningen (EU, 2018) er det relevant at udlede BKK for et stof, når Log $K_{ow} \geq 3$. Miconazol har en estimeret Log K_{ow} på 6,25 (EpiSuite, 2023), hvoraf det vurderes at udledning af $BKK_{sek.forgiftn.}$ er relevant. Der er dog ikke fundet data, der kan beskrive toksiciteten af miconazol over for pattedyr eller fugle, og et kvalitetskriterie for biota kan derfor ikke bestemmes.

6.5 Kvalitetskriterium for human konsum af vandlevende organismer (HKK)

Et kvalitetskriterie for human konsum af fiskeriprodukter (HKK) er i følge vejledningen (EU, 2018) relevant at udlede, hvis stoffet har relevante humane fareegenskaber og derudover har potentiale til at bioakkumulere (nærmere specificeret i vejledningen afsnit 2.4.3.2). Stoffer, som forårsager effekter på reproduktion, fertilitet og udvikling er af særlig vigtighed, da disse er langsigtede effekter på populationsniveau.

Miconazol har selvklassificeringen farlig ved indtagelse (H302) samt har potentiale til at bioakkumulere, hvorfor det er relevant at udlede et kvalitetskriterie for human konsum. Der er dog ikke fundet data, der kan beskrive toksiciteten af miconazol over for mennesker, og et kvalitetskriterie for human konsum kan ikke bestemmes.

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

Jævnfør TGD (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 human konsum af fiskeriprodukter. Det har dog ikke været muligt at bestemme $BKK_{sek.forgiftn.}$ og HKK, hvorfor en tilbageregning ikke kan laves.

7 Konklusion

Følgende kvalitetskriterier for vandmiljøet er udregnet for miconazol:

Vandkvalitetskriterium

$VKK_{ferskvand}$	Ikke muligt
$VKK_{saltvand}$	Ikke muligt

Korttidsvandkvalitetskriterium

$KVKK_{ferskvand}$	Ikke muligt
$KVKK_{saltvand}$	Ikke muligt

Sedimentkvalitetskriterium

$SKK_{ferskvand}$	Ikke muligt
$SKK_{saltvand}$	Ikke muligt

Biotakvalitetskriterium, sekundær forgiftning

$BKK_{sek.forgiftn.}$	Ikke muligt

Biotakvalitetskriterium, human konsum

HKK	Ikke muligt

8 Referencer

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Bilag A

Toksicitet over for vandorganismer (ECx, LCx, NOEC, osv.)
Ferskvandsorganismer
Akut toksicitet

	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Alger	Miconazol						
Pseudokirchneriella subcapitata		Nej	72 timer	E_rC_{50} (vækst)	1,35	Minguez *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines med tilstrækkelig information
Pseudokirchneriella subcapitata			72 timer	E_rC_{50} (vækst)	1,35	Villain *et al.,* 2016	2 – ikke guideline studie, men tilstrækkelige oplysninger
Pseudokirchneriella subcapitata		Nej	72 timer	EC_{50}	0,125	Danish (Q)SAR Database, 2024	3 – estimeret værdi (geometrisk gennemsnit af Leadscope og SciQSAR
Krebsdyr	Miconazol						
Daphnia magna Aggregeret værdi					0,35		
Daphnia magna		Nej	48 timer	EC_{50} (immobil)	0,4 [1]	Minguez *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines uden manglende information
Daphnia magna		Nej	48 timer	LC_{50}	0,3 [1]	Furuhagen *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines uden manglende information
Daphnia magna		Nej	48 timer	EC_{50}	0,067	Danish (Q)SAR Database, 2024	3 – estimeret værdi (geometrisk gennemsnit af Leadscope og SciQSAR
Fisk	Miconazol						
Pimephales promelas		Nej	96 timer	LC_{50}	0,014	Danish (Q)SAR Database, 2024	3 – estimeret værdi (geometrisk gennemsnit af Leadscope og SciQSAR

[1] Anvendt til beregning af aggregeret værdi

Ferskvandsorganismer
Kronisk toksicitet

	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Krebsdyr *Daphnia magna*	Miconazol	Nej	21 dage	LOEC (reproduktion)	0,022	Furuhagen *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines uden manglende information

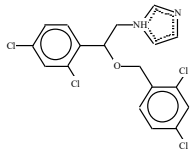
Saltvandsorganismer
Akut toksicitet

	Form/salt	Målt	Varighed	Effekt	Værdi mg/l	Reference	Troværdighed (1-4)
Alger *Skeletonema marinoi*	Miconazol	Nej	72 timer	E_rC_{50} (vækst)	0,17	Minguez *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines uden manglende information
Krebsdyr *Artemia salina*	Miconazol	Nej	48 timer	EC_{50} (immobil)	1,69	Minguez *et al.,* 2014	1 – ikke guideline studie, men udført efter guidelines uden manglende information

Bilag B

EpiSuite-beregninger for miconazol

EPI Suite Results For CAS 22916-47-8



```
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
------------------------------ 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) :   ------

KOWWIN Program (v1.68) Results:
===============================

Log Kow(version 1.69 estimate): 6.25

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
-------+-----+-----------------------------------------+---------+--------
TYPE   | NUM |        LOGKOW FRAGMENT DESCRIPTION      |  COEFF  |  VALUE
-------+-----+-----------------------------------------+---------+--------
Frag   |  2  |  -CH2-   [aliphatic carbon]             | 0.4911  |  0.9822
Frag   |  1  |  -CH     [aliphatic carbon]             | 0.3614  |  0.3614
Frag   |  1  |  -O-     [oxygen, aliphatic attach]     |-1.2566  | -1.2566
Frag   | 15  |  Aromatic Carbon                        | 0.2940  |  4.4100
Frag   |  4  |  -CL     [chlorine, aromatic attach]    | 0.6445  |  2.5780
Frag   |  2  |  Aromatic Nitrogen [5-member ring]      |-0.5262  | -1.0524
```

```
Const |     |  Equation Constant                          |         |  0.2290
-------+-----+---------------------------------------------+---------+--------
Log Kow   =   6.2516



MPBPVP (v1.43) Program Results:
===============================
Experimental Database Structure Match:  no data

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
----------------------- SUMMARY MPBPWIN v1.44 --------------------


Boiling Point:  506.31 deg C (Adapted Stein and Brown Method)

Melting Point:  349.84 deg C (Adapted Joback Method)
Melting Point:  181.97 deg C (Gold and Ogle Method)
Mean Melt Pt :  265.91 deg C (Joback; Gold,Ogle Methods)
Selected MP:  215.55 deg C (Weighted Value)

Vapor Pressure Estimations (25 deg C):
(Using BP: 506.31 deg C (estimated))
(Using MP: 215.55 deg C (estimated))
VP:  2.11E-012 mm Hg (Antoine Method)
:  2.81E-010 Pa  (Antoine Method)
VP:  1.77E-010 mm Hg (Modified Grain Method)
:  2.36E-008 Pa  (Modified Grain Method)
VP:  5.26E-010 mm Hg (Mackay Method)
:  7.01E-008 Pa  (Mackay Method)
Selected VP:  1.77E-010 mm Hg (Modified Grain Method)
:  2.36E-008 Pa (Modified Grain Method)
Subcooled liquid VP:  1.9E-008 mm Hg (25 deg C, Mod-Grain method)
:  2.53E-006 Pa  (25 deg C, Mod-Grain method)

-------+-----+--------------------+----------+---------
TYPE   | NUM |  BOIL DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
Group |  2  |  -CH2-             |   24.22  |   48.44
Group |  1  |  >CH-              |   11.86  |   11.86
Group |  1  |  -O- (nonring)     |   25.16  |   25.16
Group |  9  |  CH (aromatic)     |   28.53  |  256.77
Group |  6  |  -C (aromatic)     |   30.76  |  184.56
Group |  2  |  N (aromatic)      |   39.88  |   79.76
Group |  4  |  -Cl (to aromat)   |   36.79  |  147.16
Corr  |  1  |  Imidazole,N-sub   |   85.00  |   85.00
*   |     |  Equation Constant |          |  198.18
============+====================+==========+=========
RESULT-uncorr|  BOILING POINT in deg Kelvin  | 1036.89
RESULT- corr |  BOILING POINT in deg Kelvin  |  779.47
|  BOILING POINT in deg C       |  506.31
-------------------------------------------------------

-------+-----+--------------------+----------+---------
TYPE   | NUM |  MELT DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
```

```
Group |  2  |  -CH2-             |   11.27  |   22.54
Group |  1  |  >CH-              |   12.64  |   12.64
Group |  1  |  -O- (nonring)     |   22.23  |   22.23
Group |  9  |  CH (aromatic)     |    8.13  |   73.17
Group |  6  |  -C (aromatic)     |   37.02  |  222.12
Group |  2  |  N (aromatic)      |   68.40  |  136.80
Group |  4  |  -Cl (to aromat)   |   13.55  |   54.20
*   |     |  Equation Constant |          |  122.50
============+====================+==========+=========
RESULT    |  MELTING POINT in deg Kelvin  |  666.20
RESULT-limit|  MELTING POINT in deg Kelvin  |  623.00
|  MELTING POINT in deg C       |  349.84
-----------------------------------------------------
```

```
Water Sol from Kow (WSKOW v1.42) Results:
=========================================

Water Sol: 0.01114 mg/L

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
---------------------------------- WSKOW v1.43 Results -----------------------
Log Kow  (estimated)  :  6.25
Log Kow (experimental):  not available from database
Log Kow used by Water solubility estimates:  6.25

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW + Correction
(used when Melting Point NOT available)

Correction(s):         Value
--------------------   -----
No Applicable Correction Factors

Log Water Solubility  (in moles/L) :  -7.572
Water Solubility at 25 deg C (mg/L):  0.01114
```

```
WATERNT Program (v1.01) Results:
================================

Water Sol (v1.01 est): 0.023975 mg/L

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
-------+-----+-------------------------------------------+----------+---------
TYPE   | NUM |    WATER SOLUBILITY FRAGMENT DESCRIPTION   |  COEFF   |  VALUE
-------+-----+-------------------------------------------+----------+---------
Frag   |  2  |  -CH2-   [aliphatic carbon]                |-0.5370   | -1.0740
Frag   |  1  |  -CH     [aliphatic carbon]                |-0.5285   | -0.5285
Frag   |  1  |  -O-     [oxygen, aliphatic attach]        | 1.2746   |  1.2746
Frag   |  9  |  Aromatic Carbon  (C-H type)               |-0.3359   | -3.0228
```

```
Frag  |  4  |  -CL     [chlorine, aromatic attach]       |-0.4878   | -1.9512
Frag  |  6  |  Aromatic Carbon  (C-substituent type)     |-0.5400   | -3.2397
Frag  |  2  |  Aromatic Nitrogen [5-member ring]         | 0.5265   |  1.0530
Const |     |  Equation Constant                         |          |  0.2492
-------+-----+--------------------------------------------+----------+---------
Log Water Sol (moles/L) at 25 dec C  =   -7.2395
Water Solubility (mg/L) at 25 dec C  = 0.023975
ECOSAR Program (v1.11) Results:
================================
ECOSAR Version 1.11 Results Page

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
CAS Num:
ChemID1:
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
Log Kow: 6.252      (EPISuite Kowwin v1.68 Estimate)
Log Kow:            (User Entered)
Log Kow:            (PhysProp DB exp value - for comparison only)
Melt Pt:            (User Entered for Wat Sol estimate)
Melt Pt:            (deg C, PhysProp DB exp value for Wat Sol estimate)
Wat Sol: 0.01114    (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol:            (User Entered)
Wat Sol:            (PhysProp DB exp value)


--------------------------------------
Values used to Generate ECOSAR Profile
--------------------------------------
Log Kow: 6.252      (EPISuite Kowwin v1.68 Estimate)
Wat Sol: 0.01114    (mg/L, EPISuite WSKowwin v1.43 Estimate)


--------------------------------------
ECOSAR v1.11 Class-specific Estimations
--------------------------------------
Imidazoles
Predicted
ECOSAR Class                  Organism            Duration  End Pt   mg/L (ppm)
============================  ==================  ========  ======   ==========
Imidazoles                  : Fish                96-hr     LC50        0.044 *
Imidazoles                  : Daphnid             48-hr     LC50        0.128 *
Imidazoles                  : Green Algae         96-hr     EC50        0.049 *
Imidazoles                  : Fish                          ChV       0.00184
Imidazoles                  : Daphnid                       ChV         0.003
Imidazoles                  : Green Algae                   ChV         0.030 *!
Imidazoles                  : Mysid (SW)          96-hr     LC50        0.004

============================  ==================  ========  ======   ==========
Neutral Organic SAR         : Fish                96-hr     LC50        0.052 *
(Baseline Toxicity)         : Daphnid             48-hr     LC50        0.044 *
: Green Algae         96-hr     EC50        0.165 *
: Fish                          ChV         0.008
: Daphnid                       ChV         0.013 *
: Green Algae                   ChV         0.104 *

Note:  * = asterisk designates: Chemical may not be soluble enough to
measure this predicted effect. If the effect level exceeds the
```

water solubility by 10X, typically no effects at saturation (NES)
are reported.

NOTE: ! = exclamation designates: The toxicity value was estimated through application of acute-to-chronic ratios per methods outlined in the ECOSAR Methodology Document provided in the ECOSAR Help Menu.

Class Specific LogKow Cut-Offs

If the log Kow of the chemical is greater than the endpoint specific cut-offs presented below, then no effects at saturation are expected for those endpoints.

Imidazoles:

Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)

HENRYWIN (v3.20) Program Results:
==========

Bond Est : 2.45E-009 atm-m3/mole (2.48E-004 Pa-m3/mole)
Group Est: Incomplete

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14

HENRYWIN v3.21 Results

CLASS		BOND CONTRIBUTION DESCRIPTION	COMMENT	VALUE
HYDROGEN	5	Hydrogen to Carbon (aliphatic) Bonds		-0.5984
HYDROGEN	9	Hydrogen to Carbon (aromatic) Bonds		-1.3886
FRAGMENT	1	C-C		0.1163
FRAGMENT	2	C-Car		0.3239
FRAGMENT	2	C-O		2.1709
FRAGMENT	13	Car-Car		3.4295
FRAGMENT	4	Car-CL		-0.0964
FRAGMENT	4	Car-Nar		6.5129
FRAGMENT	1	Nar-C	ESTIMATE	-0.9700
FACTOR	1	Additional aromatic nitrogen(s)		-2.5000
RESULT		BOND ESTIMATION METHOD for LWAPC VALUE	TOTAL	7.000

HENRYs LAW CONSTANT at 25 deg C = 2.45E-009 atm-m3/mole
= 1.00E-007 unitless
= 2.48E-004 Pa-m3/mole

```
--------+-------------------------------------------------+------------+--------
|        GROUP CONTRIBUTION DESCRIPTION         |   COMMENT  |  VALUE
--------+-------------------------------------------------+------------+--------
|           1  CH2 (Car)(O)                     |  ESTIMATE  |  0.02
|           6  Car-H (Car)(Car)                 |            |  0.66
|           2  Car-H (Car)(Nar)                 |            |  0.22
|           2  Car (C)(Car)(Car)                |            |  1.40
|           4  Car (Car)(Car)(CL)               |            |  0.72
|           1  O (C)(C)                         |            |  2.93
|           1  Nar (Car)(Car)                   |            |  3.06
|              MISSING Value for:  Nar (Car)(C)(Car)
|              MISSING Value for:  CH2 (C)(Nar)
|              MISSING Value for:  CH (C)(O)(Car)
|              MISSING Value for:  CarH (Nar)(Nar)
--------+-------------------------------------------------+------------+--------
RESULT |  GROUP ESTIMATION METHOD for LOG GAMMA VALUE  | INCOMPLETE |  9.01
--------+-------------------------------------------------+------------+--------


For Henry LC Comparison Purposes:
Exper Database:  none available
User-Entered Henry LC:  not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC:  8.700E-009 atm-m3/mole  (8.815E-004 Pa-m3/mole)
VP:   1.77E-010 mm Hg (source: MPBPVP)
WS:   0.0111 mg/L (source: WSKOWWIN)



Log Octanol-Air (KOAWIN v1.10) Results:
=======================================

Log Koa: 13.249

SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
--------------------------- KOAWIN v1.10 Results -------------------------

Log Koa (octanol/air) estimate:  13.249
Koa (octanol/air) estimate:  1.775e+013
Using:
Log Kow:  6.25  (KowWin est)
HenryLC:  2.45e-009  atm-m3/mole (HenryWin est)
Log Kaw:  -6.999  (air/water part.coef.)

LogKow  : ----  (exp database)
LogKow  : 6.25 (KowWin estimate)
Henry LC: --- atm-m3/mole(exp database)
Henry LC: 2.45e-009 atm-m3/mole (HenryWin bond estimate)

Log Koa (octanol/air) estimate:  13.249 (from KowWin/HenryWin)


BIOWIN (v4.10) Program Results:
===============================
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
```

MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14

---------- BIOWIN v4.10 Results ----------

Biowin1 (Linear Model Prediction)   : Does Not Biodegrade Fast
Biowin2 (Non-Linear Model Prediction): Does Not Biodegrade Fast
Biowin3 (Ultimate Biodegradation Timeframe): Recalcitrant
Biowin4 (Primary Biodegradation Timeframe): Weeks-Months
Biowin5 (MITI Linear Model Prediction)   : Does Not Biodegrade Fast
Biowin6 (MITI Non-Linear Model Prediction): Does Not Biodegrade Fast
Biowin7 (Anaerobic Model Prediction): Does Not Biodegrade Fast
Ready Biodegradability Prediction: NO

TYPE	NUM	Biowin1 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.1824	-0.7297
Frag	1	Aliphatic ether [C-O-C]	-0.3474	-0.3474
MolWt	*	Molecular Weight Parameter		-0.1981
Const	*	Equation Constant		0.7475
RESULT		Biowin1 (Linear Biodeg Probability)		-0.5276

TYPE	NUM	Biowin2 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-2.0155	-8.0620
Frag	1	Aliphatic ether [C-O-C]	-3.4294	-3.4294
MolWt	*	Molecular Weight Parameter		-5.9091
RESULT		Biowin2 (Non-Linear Biodeg Probability)		0.0000

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

TYPE	NUM	Biowin3 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.2066	-0.8264
Frag	1	Aliphatic ether [C-O-C]	-0.0087	-0.0087
MolWt	*	Molecular Weight Parameter		-0.9196
Const	*	Equation Constant		3.1992
RESULT		Biowin3 (Survey Model - Ultimate Biodeg)		1.4445

TYPE	NUM	Biowin4 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.1653	-0.6614
Frag	1	Aliphatic ether [C-O-C]	-0.0097	-0.0097
MolWt	*	Molecular Weight Parameter		-0.6004
Const	*	Equation Constant		3.8477
RESULT		Biowin4 (Survey Model - Primary Biodeg)		2.5763

Result Classification: 5.00 -> hours 4.00 -> days 3.00 -> weeks
(Primary & Ultimate) 2.00 -> months 1.00 -> longer

TYPE	NUM	Biowin5 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.0392	-0.1567
Frag	1	Aliphatic ether [C-O-C]	-0.0106	-0.0106
Frag	1	Aromatic-CH2	0.0268	0.0268
Frag	1	Aromatic-CH	-0.1294	-0.1294
Frag	9	Aromatic-H	0.0004	0.0036
Frag	1	-CH2- [linear]	0.0255	0.0255
MolWt	*	Molecular Weight Parameter		-0.6562
Const	*	Equation Constant		0.5544
RESULT		Biowin5 (MITI Linear Biodeg Probability)		-0.3426

TYPE	NUM	Biowin6 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.7609	-3.0436
Frag	1	Aliphatic ether [C-O-C]	-0.2020	-0.2020
Frag	1	Aromatic-CH2	-0.0366	-0.0366
Frag	1	Aromatic-CH	-0.5554	-0.5554
Frag	9	Aromatic-H	0.0342	0.3077
Frag	1	-CH2- [linear]	0.2345	0.2345
MolWt	*	Molecular Weight Parameter		-7.1992
RESULT		Biowin6 (MITI Non-Linear Biodeg Probability)		0.0001

A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable
A Probability Less Than 0.5 indicates --> NOT Readily Degradable

TYPE	NUM	Biowin7 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic chloride [-CL]	-0.4023	-1.6091
Frag	1	Aliphatic ether [C-O-C]	-0.2573	-0.2573
Frag	1	Aromatic-CH2	-0.0073	-0.0073
Frag	1	Aromatic-CH	0.0331	0.0331
Frag	9	Aromatic-H	-0.0954	-0.8589
Frag	1	-CH2- [linear]	0.0260	0.0260
Const	*	Equation Constant		0.8361
RESULT		Biowin7 (Anaerobic Linear Biodeg Prob)		-1.8374

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

Ready Biodegradability Prediction: (YES or NO)

Criteria for the YES or NO prediction: If the Biowin3 (ultimate survey model) result is "weeks" or faster (i.e. "days", "days to weeks", or "weeks" AND the Biowin5 (MITI linear model) probability is >= 0.5, then the prediction is YES (readily biodegradable). If this condition is not

satisfied, the prediction is NO (not readily biodegradable). This method is based on application of Bayesian analysis to ready biodegradation data (see Help). Biowin5 and 6 also predict ready biodegradability, but for degradation in the OECD301C test only; using data from the Chemicals Evaluation and Research Institute Japan (CERIJ) database.

BioHCwin (v1.01) Program Results:
==========
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
---------- BioHCwin v1.01 Results ----------

NO Estimate Possible ... Structure NOT a Hydrocarbon
(Contains atoms other than C, H or S (-S-))

AEROWIN Program (v1.00) Results:
==========
Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 2.53E-006 Pa (1.9E-008 mm Hg)
Log Koa (Koawin est): 13.249
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 1.18
Octanol/air (Koa) model: 4.36
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 0.977
Mackay model : 0.99
Octanol/air (Koa) model: 0.997

AOP Program (v1.92) Results:
==========
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
---------- SUMMARY (AOP v1.92): HYDROXYL RADICALS (25 deg C) --------
Hydrogen Abstraction = 21.4020 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
**Addition to Aromatic Rings = 38.3367 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 59.7387 E-12 cm3/molecule-sec
HALF-LIFE = 0.179 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 2.149 Hrs
..... ** Designates Estimation(s) Using ASSUMED Value(s)
---------- SUMMARY (AOP v1.91): OZONE REACTION (25 deg C) ----------

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches

```
Fraction sorbed to airborne particulates (phi):
0.983 (Junge-Pankow, Mackay avg)
0.997 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation



KOCWIN Program (v2.00) Results:
==============================
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
--------------------------  KOCWIN v2.01 Results  --------------------------

Koc Estimate from MCI:
----------------------
First Order Molecular Connectivity Index  ........... : 12.025
Non-Corrected Log Koc (0.5213 MCI + 0.60)  .......... :  6.8684
Fragment Correction(s):
1   Ether, aliphatic  (-C-O-C-)  ..........  : -0.8716
1   Aromatic ring with 2 nitrogens  .......  : -0.5964
*   Poly-Chlorinated Aromatic .............  :  0.3438
Corrected Log Koc  ................................. :  5.7441

Estimated Koc:  5.548e+005  L/kg   <===========

Koc Estimate from Log Kow:
--------------------------
Log Kow  (Kowwin estimate)  ......................... :  6.25
Non-Corrected Log Koc (0.55313 logKow + 0.9251)  .... :  4.3822
Fragment Correction(s):
1   Ether, aliphatic  (-C-O-C-)  ..........  : -0.0906
1   Aromatic ring with 2 nitrogens  .......  :  0.3984
*   Poly-Chlorinated Aromatic .............  :  0.1444
Corrected Log Koc  ................................. :  4.8344

Estimated Koc:  6.829e+004  L/kg   <===========


HYDROWIN Program (v2.00) Results:
=================================
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
--------------------------- HYDROWIN v2.00 Results ---------------------------


Currently, this program can NOT estimate a hydrolysis rate constant for
the type of chemical structure entered!!

ONLY Esters, Carbamates, Epoxides, Halomethanes (containing 1-3 halogens),
Specific Alkyl Halides & Phosphorus Esters can be estimated!!

When present, various hydrolyzable compound-types will be identified.
For more information, (Click OVERVIEW in Help  or  see the User's Guide)

*****   CALCULATION NOT PERFORMED   *****
```

```
BCFBAF Program (v3.01) Results:
==============================
SMILES : n1(CC(c3c(CL)cc(CL)cc3)OCc2c(CL)cc(CL)cc2)cncc1
CHEM   :
MOL FOR: C18 H14 CL4 N2 O1
MOL WT : 416.14
---------------------------------- BCFBAF v3.01 --------------------------------
Summary Results:
Log BCF (regression-based estimate):  3.79  (BCF = 6.19e+003 L/kg wet-wt)
Biotransformation Half-Life (days) :  37.3  (normalized to 10 g fish)
Log BAF (Arnot-Gobas upper trophic):  5.50  (BAF = 3.17e+005 L/kg wet-wt)

Log Kow (experimental):  not available from database
Log Kow used by BCF estimates:  6.25

Equation Used to Make BCF estimate:
Log BCF = 0.6598 log Kow - 0.333 + Correction

Correction(s):                    Value
No Applicable Correction Factors

Estimated Log BCF =  3.792  (BCF = 6192 L/kg wet-wt)

============================================================
Whole Body Primary Biotransformation Rate Estimate for Fish:
============================================================
------+-----+-------------------------------------------+---------+---------
TYPE | NUM | LOG BIOTRANSFORMATION FRAGMENT DESCRIPTION |  COEFF  |  VALUE
------+-----+-------------------------------------------+---------+---------
Frag |  4  |  Aromatic chloride   [-CL]                |  0.3778 |  1.5114
Frag |  1  |  Aliphatic ether  [C-O-C]                 | -0.0232 | -0.0232
Frag |  1  |  Aromatic-CH2                             | -0.3365 | -0.3365
Frag |  1  |  Aromatic-CH                              | -0.4629 | -0.4629
Frag |  9  |  Aromatic-H                               |  0.2664 |  2.3974
Frag |  1  |  -CH2-  [linear]                          |  0.0242 |  0.0242
Frag |  2  |  Benzene                                  | -0.4277 | -0.8555
L Kow|  *  |  Log Kow =   6.25 (KowWin estimate)       |  0.3073 |  1.9214
MolWt|  *  |  Molecular Weight Parameter               |         | -1.0671
Const|  *  |  Equation Constant                        |         | -1.5371
============+===========================================+=========+=========
RESULT   |        LOG Bio Half-Life (days)             |         |  1.5720
RESULT   |            Bio Half-Life (days)             |         |   37.33
NOTE     |  Bio Half-Life Normalized to 10 g fish at 15 deg C   |
============+===========================================+=========+=========

Biotransformation Rate Constant:
kM (Rate Constant):  0.01857 /day (10 gram fish)
kM (Rate Constant):  0.01044 /day (100 gram fish)
kM (Rate Constant):  0.005872 /day (1 kg fish)
kM (Rate Constant):  0.003302 /day (10 kg fish)

Arnot-Gobas BCF & BAF Methods (including biotransformation rate estimates):
Estimated Log BCF (upper trophic) =  3.870  (BCF = 7410 L/kg wet-wt)
Estimated Log BAF (upper trophic) =  5.502  (BAF = 3.175e+005 L/kg wet-wt)
Estimated Log BCF (mid trophic)   =  4.004  (BCF = 1.01e+004 L/kg wet-wt)
Estimated Log BAF (mid trophic)   =  5.427  (BAF = 2.671e+005 L/kg wet-wt)
Estimated Log BCF (lower trophic) =  4.040  (BCF = 1.096e+004 L/kg wet-wt)
```

Estimated Log BAF (lower trophic) = 5.375 (BAF = 2.372e+005 L/kg wet-wt)

Arnot-Gobas BCF & BAF Methods (assuming a biotransformation rate of zero):
Estimated Log BCF (upper trophic) = 4.315 (BCF = 2.068e+004 L/kg wet-wt)
Estimated Log BAF (upper trophic) = 6.654 (BAF = 4.51e+006 L/kg wet-wt)

Volatilization From Water
==========

Chemical Name:

Molecular Weight : 416.14 g/mole
Water Solubility : -----
Vapor Pressure : -----
Henry's Law Constant: 2.45E-009 atm-m3/mole (estimated by Bond SAR Method)

RIVER		LAKE
Water Depth	(meters):	1	1
Wind Velocity	(m/sec):	5	0.5
Current Velocity	(m/sec):	1	0.05

HALF-LIFE (hours) :	4.875E+005	5.318E+006
HALF-LIFE (days) :	2.031E+004	2.216E+005
HALF-LIFE (years) :	55.61	606.7

STP Fugacity Model: Predicted Fate in a Wastewater Treatment Facility
==========
(using 10000 hr Bio P,A,S)
PROPERTIES OF:

Molecular weight (g/mol)		416.14
Aqueous solubility (mg/l)		0
Vapour pressure (Pa)		0
(atm)	0	
(mm Hg)	0	
Henry 's law constant (Atm-m3/mol)		2.45E-009
Air-water partition coefficient		1.00198E-007
Octanol-water partition coefficient (Kow)		1.77828E+006
Log Kow		6.25
Biomass to water partition coefficient		355657
Temperature [deg C]		25

Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L MLSS (h):

-Primary tank	0.00	9985.96	10000.00
-Aeration tank	0.00	9985.96	10000.00
-Settling tank	0.00	9985.96	10000.00

STP Overall Chemical Mass Balance:
---

g/h	mol/h	percent	
Influent	1.00E+001	2.4E-002	100.00
Primary sludge	5.91E+000	1.4E-002	59.07
Waste sludge	3.31E+000	8.0E-003	33.13
Primary volatilization	1.85E-008	4.4E-011	0.00
Settling volatilization	4.11E-008	9.9E-011	0.00
Aeration off gas	1.01E-007	2.4E-010	0.00

Primary biodegradation	1.73E-002	4.2E-005	0.17
Settling biodegradation	4.23E-003	1.0E-005	0.04
Aeration biodegradation	5.57E-002	1.3E-004	0.56
Final water effluent	7.03E-001	1.7E-003	7.03
Total removal	9.30E+000	2.2E-002	92.97
Total biodegradation	7.73E-002	1.9E-004	0.77

Level III Fugacity Model (Full-Output): MCI Method
==========

Chem Name :
Molecular Wt: 416.14
Henry's LC : 2.45e-009 atm-m3/mole (Henrywin program)
Vapor Press : 1.77e-010 mm Hg (Mpbpwin program)
Liquid VP : 1.36e-008 mm Hg (super-cooled)
Melting Pt : 216 deg C (Mpbpwin program)
Log Kow : 6.25 (Kowwin program)
Soil Koc : 5.55e+005 (KOCWIN MCI method)

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	0.0154	4.3	1000
Water	1.32	4.32e+003	1000
Soil	49.2	8.64e+003	1000
Sediment	49.5	3.89e+004	0

Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)	
Air	4.04e-014	748	46.4	24.9	1.55
Water	6.09e-015	63.7	397	2.12	13.2
Soil	3.62e-016	1.18e+003	0	39.5	0
Sediment	1.64e-014	265	297	8.82	9.9

Persistence Time: 1e+004 hr
Reaction Time: 1.33e+004 hr
Advection Time: 4.05e+004 hr
Percent Reacted: 75.3
Percent Advected: 24.7

Water Compartment Percents:

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	0.0154	4.3	1000
Water	1.32	4.32e+003	1000
water	(0.689)		
biota	(0.0613)		
suspended sediment	(0.573)		
Soil	49.2	8.64e+003	1000
Sediment	49.5	3.89e+004	0

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 4.296
Water: 4320
Soil: 8640
Sediment: 3.888e+004
Biowin estimate: 1.444 (recalcitrant)

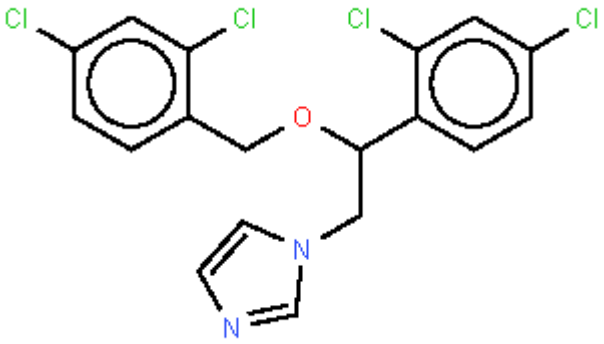
```
Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004

Level III Fugacity Model (Full-Output): EQC Default
=====================================================
Chem Name   :
Molecular Wt: 416.14
Henry's LC  : 2.45e-009 atm-m3/mole (Henrywin program)
Vapor Press : 1.77e-010 mm Hg  (Mpbpwin program)
Liquid VP   : 1.36e-008 mm Hg  (super-cooled)
Melting Pt  : 216 deg C (Mpbpwin program)
Log Kow     : 6.25  (Kowwin program)
Soil Koc    : 7.29e+005  (EQC Model Default)

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       0.015           4.3          1000
Water     1.18            4.32e+003    1000
Soil      47.7            8.64e+003    1000
Sediment  51.1            3.89e+004    0

Fugacity    Reaction    Advection   Reaction    Advection
(atm)       (kg/hr)      (kg/hr)    (percent)   (percent)
Air       4.04e-014    748         46.4        24.9        1.55
Water     4.93e-015    58.6        366         1.95        12.2
Soil      2.76e-016    1.18e+003   0           39.5        0
Sediment  1.33e-014    282         316         9.4         10.5

Persistence Time: 1.03e+004 hr
Reaction Time:    1.36e+004 hr
Advection Time:   4.25e+004 hr
Percent Reacted:  75.7
Percent Advected: 24.3

Water Compartment Percents:
--------------------------
Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       0.015           4.3          1000
Water     1.18            4.32e+003    1000
water     (0.541)
biota     (0.0481)
suspended sediment (0.592)
Soil      47.7            8.64e+003    1000
Sediment  51.1            3.89e+004    0

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air:      4.296
Water:    4320
Soil:     8640
Sediment: 3.888e+004
Biowin estimate: 1.444  (recalcitrant)

Advection Times (hr):
Air:      100
Water:    1000
Sediment: 5e+004
```

Danish (Q)SAR Database beregninger for miconazol

Danish (Q)SAR Database, https://qsar.food.dtu.dk Date: 12-02-2024

(Q)SAR predicted profile

Structure (as used for QSAR prediction):



SMILES (used for QSAR prediction): c1(Cl)c(C(CN2C=CN=C2)OCc2c(Cl)cc(Cl)cc2)ccc(Cl)c1

ID

Registry Number	22916-47-8	PubChem CID	
REACH EC Number (pre-registration, by 2013)	245-324-5	REACH EC Number (registration, 2019 or 2022)	
REACH registration (2022)		REACH registration cumulated minimum annual tonnage (2022)	
EU CLP Harmonized Classification*		DK-EPA / DTU QSAR-based CLP Advisory Classification	Acute Tox. 4
EU Biocide active substances		EU Pesticide active substances	
EU EFSA Botanical substances		US TSCA (Oct. 2021)	
Tox21 (2019)	Yes	ToxCast (Oct. 2021)	
Molecular Formula	C18 H14 CL4 N2 O1	Molecular weight (g/mole)	416.14
Chemical Name	miconazole		

(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)	215.55	Melting Point Experimental (deg C)	
Boiling Point (deg C)	506.31	Boiling Point Experimental (deg C)	
Vapour Pressure (atm)		Vapour Pressure Experimental (atm)	
Vapour Pressure (mm Hg)	1.77E-010	Vapour Pressure Experimental (mm Hg)	
Vapour Pressure (Pa)	2.36E-008	Vapour pressure Subcooled Liquid (Pa)	2.53E-006

EPI MPBPVP models

Henry's Law Constant

HLC Bond Method (atm-m3/mole)	2.446E-009	HLC Group Method (atm-m3/mole)	
HLC Via VP/WSol (atm-m3/mole)	8.7E-009	HLC Via VP/WSol (Pa-m3/mole)	0.0008815
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)	0.01114	Water solubility from Fragments (mg/L)	0.023975
Water solubility Exp (mg/L)		Water solubility Exp Ref	

EPI WATERNT model

Partition coefficients

pH	1	4	5	6	7	8	9
LogD	2.08	3.62	4.59	5.48	5.95	6.05	6.06

Minimum LogD in the pH interval 4-9	3.62	Maximum LogD in the pH interval 4-9	6.06

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	13.249	Log Kaw	-6.999

EPI KOAWIN models

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

Log Kow	6.25		
Log Kow Exp		Log Kow Exp Ref	

EPI WSKOW model

LogKow: log octanol-water partition coefficient

Kp (m3/ug) Mackay-based	1.18	Kp (m3/ug) Koa-based	4.36
Phi Junge-Pankow-based	0.977	Phi Mackay-based	0.99
Phi Koa-based	0.997		

EPI AEROWIN models

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

Koc from MCI (L/kg)	554800	Log Koc from MCI	5.7441
Koc from Kow (L/kg)	68290	Log Koc from Kow	4.8344

EPI KOCWIN models

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

Bioaccumulation

BCF (L/kg wet-wt)	6192
Log BCF (L/kg wet-wt)	3.792
Whole Body Primary Biotransformation Fish Half-Life (days)	37.33
BCF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	7410
BCF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	20680
BAF Arnot-Gobas (upper trophic) Including Biotransformation (L/kg wet-wt)	317500
BAF Arnot-Gobas (upper trophic) Zero Biotransformation (L/kg wet-wt)	4510000

EPI BCFBAF models

BCF: Bioconcentration factor, BAF: Bioaccumulation factor

Aquatic toxicity

Exp	Battery	Leadscope	SciQSAR
Fathead minnow 96h LC50 (mg/L)		0.01783937	0.01160218
Domain	OUT	OUT	OUT
Daphnia magna 48h EC50 (mg/L)	0.0801653	0.03587067	0.1244599
Domain	IN	IN	IN
Pseudokirchneriella s. 72h EC50 (mg/L)	0.9849566	1.961944	0.007969654
Domain	IN	IN	IN

DTU-developed models

	Fish 96h	Daphnid 48h	Green Algae 96h
LC50 (Fish) or EC50 (Daphnid and Algae) for Most Toxic Class (mg/L)	0.044	0.044	0.049
Max. Log Kow for Most Toxic Class	5	5	6.4
Most Toxic Class	Imidazoles	Neutral Organic SAR	Imidazoles
Note	Chemical may not be soluble enough. Log Kow for this chemical exceeds the maximum Log Kow for Most Toxic Class.	Chemical may not be soluble enough. Log Kow for this chemical exceeds the maximum Log Kow for Most Toxic Class.	Chemical may not be soluble enough

EPI ECOSAR models

ECOSAR Classes: Imidazoles