Committee for Risk Assessment

RAC

Annex 1

Background document

to the Opinion proposing harmonised classification and labelling at EU level of

cis-Tricos-9-ene (Muscalure)

EC number: 248-505-7

CAS number: 27519-02-4

ECHA/RAC/CLH-O-0000001670-80-02/A1

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

30 November 2012

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

Substance Name: *cis*-Tricos-9-ene

EC Number: **248-505-7**

CAS Number: **27519-02-4**

Index Number:

Contact details for dossier submitter:

Umweltbundesamt GmbH

on behalf of

AT Competent Authority

Federal Ministry of Agriculture, Forestry, Environment and Water Management

Version number: 3 **Date: 15 June 2012**

CONTENTS

Part A.

Part B.

Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	cis-Tricos-9-ene
EC number:	248-505-7
CAS number:	27519-02-4
Annex VI Index number:	n.a.
Degree of purity:	min. 80.1 %w/w
Impurities:	The manufacturer has requested that all impurities remain confidential since it may provide an indication on the possible method of manufacturing. Information on impurities is provided in the confidential Annex.

The minimum degree of purity is derived from the results of a 5-batch-analysis. The value is calculated according to the following formula:

mean value – 3 x SD

Details of the 5-batch analysis are given in the confidential annex.

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation	**Directive 67/548/EEC (Dangerous Substances Directive; DSD)**
Current entry in Annex VI, CLP Regulation	Not currently in Annex VI (table 3.1) of CLP Regulation	Not currently in Annex VI (table 3.2) of CLP Regulation
Current proposal for consideration by RAC	Skin Sens. 1B; H317: May cause an allergic skin reaction	R43 – May cause sensitisation by skin contact
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Skin Sens. 1B; H317: May cause an allergic skin reaction	R43 – May cause sensitisation by skin contact

1.1 Proposed harmonised classification and labelling based on CLP Regulation and/or DSD criteria

Table 3: Proposed classification according to the CLP Regulation (including criteria according to 2nd ATP of CLP)

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.2.	Flammable gases	n.a.	n.a.	currently not classified	Data lacking
2.3.	Flammable aerosols	n.a.	n.a.	currently not classified	Data lacking
2.4.	Oxidising gases	n.a.	n.a.	currently not classified	Data lacking
2.5.	Gases under pressure	n.a.	n.a.	currently not classified	Data lacking
2.6.	Flammable liquids	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.7.	Flammable solids	n.a.	n.a.	currently not classified	Data lacking
2.8.	Self-reactive substances and mixtures	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.9.	Pyrophoric liquids	n.a.	n.a.	currently not classified	Data lacking
2.10.	Pyrophoric solids	n.a.	n.a.	currently not classified	Data lacking
2.11.	Self-heating substances and mixtures	n.a.	n.a.	currently not classified	Data lacking
2.12.	Substances and mixtures which in contact with water emit flammable gases	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.13.	Oxidising liquids	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.14.	Oxidising solids	n.a.	n.a.	currently not classified	Data lacking
2.15.	Organic peroxides	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
2.16.	Substance and mixtures corrosive to metals	n.a.	n.a.	currently not classified	Data lacking
3.1.	Acute toxicity - oral	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
	Acute toxicity - dermal	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification

Table 3: Proposed classification according to the CLP Regulation

Contd.

	Acute toxicity - inhalation	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.2.	Skin corrosion / irritation	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.3.	Serious eye damage / eye irritation	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.4.	Respiratory sensitisation	n.a.	n.a.	currently not classified	Data lacking
3.4.	Skin sensitisation	Skin Sens. 1B H317: May cause an allergic skin reaction.	n.a.	currently not classified	n.a.
3.5.	Germ cell mutagenicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.6.	Carcinogenicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.7.	Reproductive toxicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.8.	Specific target organ toxicity –single exposure	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.9.	Specific target organ toxicity – repeated exposure	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
3.10.	Aspiration hazard	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
4.1.	Hazardous to the aquatic environment	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
5.1.	Hazardous to the ozone layer	n.a.	n.a.	currently not classified	Data lacking

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Signal word: Warning

Hazard statements:
H317: May cause an allergic skin reaction.

Precautionary statements:
P261: Avoid breathing dust/fume/gas/mist/vapours/spray.
P272: Contaminated work clothing should not be allowed out of the workplace.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P302+P352: IF ON SKIN: Wash with plenty of soap and water.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.
P363: Wash contaminated clothing before reuse.

Proposed notes assigned to an entry: none

Table 4: Proposed classification according to DSD

Hazardous property	Proposed classification	Proposed SCLs	Current classification [1)]	Reason for no classification [2)]
Explosiveness	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Oxidising properties	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Flammability	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Other physico-chemical properties	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Thermal stability	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Acute toxicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Acute toxicity – irreversible damage after single exposure	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Repeated dose toxicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Irritation / Corrosion	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Sensitisation	R43 May cause sensitisation by skin contact.	n.a.	currently not classified	n.a.
Carcinogenicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Mutagenicity – Genetic toxicity	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Toxicity to reproduction – fertility	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Toxicity to reproduction – development	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Toxicity to reproduction – breastfed babies. Effects on or via lactation	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification
Environment	n.a.	n.a.	currently not classified	conclusive but not sufficient for classification

[1)] Including SCLs
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Indication of danger: Xi – irritant

R-phrases: R43 - may cause sensitisation by skin contact

S-phrases: S36/37 - wear suitable protective clothing and gloves

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

There is no current classification for *cis*-Tricos-9-ene according to Annex I of Council Directive 67/548/EEC.

No REACH registration dossier was available for this substance on 23 September 2011.

2.2 Short summary of the scientific justification for the CLH proposal

Human toxicology:

Skin Sens. 1B; H317: May cause an allergic skin reaction: GPMT induced moderate sensitisation: intradermal induction of a 5% mixture in corn oil and Freund Adjuvance; 7 from 20 animals (35%) were positive with irritation score 1 from 4.

Environment:

Aquatic acute toxicity: $L(E)C_{50}$ values are only available for fish (>100 mg/L (nominal, corresponding to>71 mg/l, mean measured) and daphnia (>10 mg/L, nominal, corresponding to >0.25 mg/L mean measured); in both cases the $L(E)C_{50}$ values are > water solubility of $7x10^{-3}$ mg/L. The EC_{50} value for daphnids was chosen with >0.25 mg/L, since this was the highest concentration tested, without physical effects on mobility. But also at 0.83 mg/L mean measured (=100 mg/L, nominal) the observed effects on mobility were attributed to physical burden. Therefore it is considered, that an EC_{50} based on toxicological effects would be higher and in any case exceed 1mg/L.

Aquatic chronic toxicity: no data available

Fate & behaviour: assumed to be rapidly biodegradable based on QSAR calculation and on inherent testing; log P_{ow} >8.2; BCF estimations range from 794.3 to 19952; weight of evidence decision;

2.3 Current harmonised classification and labelling

2.3.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

No current classification and labelling.

2.3.2 Current classification and labelling in Annex VI, Table 3.2 in the CLP Regulation

No current classification and labelling.

2.4 Current self-classification and labelling

2.4.1 Current self-classification and labelling based on the CLP Regulation criteria

No current classification and labelling.

2.4.2 Current self-classification and labelling based on DSD criteria

Indication of danger: Xi - irritant
R-phrases: R43 - may cause sensitisation by skin contact
S-phrases: S36/37 - wear suitable protective clothing and gloves

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Biocides: No need for justification.

Also conclusion for non-classification for the various endpoints is of utmost importance for European harmonisation. RMS proposals for classification and non-classification were not discussed in detail within the European Biocides Technical Meetings.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

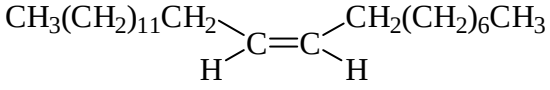
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 5: Substance identity

EC number:	248-505-7
EC name:	cis-tricos-9-ene
CAS number (EC inventory):	27519-02-4
CAS number:	27519-02-4
CAS name:	cis-Tricos-9-ene; 9-Tricosene, (9Z)-
IUPAC name:	*cis*-Tricos-9-ene; (9Z)-Tricos-9-ene
CLP Annex VI Index number:	not applicable
Molecular formula:	$C_{23}H_{46}$
Molecular weight range:	322.6 g/mol

Structural formula:



1.2 Composition of the substance

See confidential Annex. (concerns Table 6-8)

Current Annex VI entry: No current Annex VI entry.

1.2.1 Composition of test material

See confidential Annex.

1.3 Physico-chemical properties

Table 9: Summary of physico - chemical properties

Property	Purity/Specification	Results	Reference
Melting point	96.0% Muscalure 84.7% Muscalure	-2°C (271 K, 1009 hPa) -4°C (269 K, 1009 hPa)	**Doc. III-A 3;** **Study A 3.1.1/01** **Study A 3.1.1/02**
Boiling point	96.0% Muscalure 84.7% Muscalure	380°C (653K, 1009 hPa) 376°C (649K, 1009 hPa)	**Doc. III-A 3;** **Study A 3.1.1/01** **Study A 3.1.1/02**
Density	98.2% Muscalure	0.803 kg/L (20°C)	**Doc. III-A 3;** **Study A 3.1.3**
Vapour pressure	96.0% Muscalure	6.4×10^{-2} Pa (20°C) 0.119 ± 0.003 Pa (25°C)	**Doc. III-A 3;** **Study A 3.2**
Henry´s Law Constant	n.a.	2.95×10^{3} Pa x m^3/mol (calculated)	**Doc. III-A 3;** **Study A 3.2.1**
Physical state	84.7% Muscalure 98.2% Muscalure	Liquid Liquid	**Doc. III-A 3;** **Study A 3.3/01** **Study A 3.3/02**
Colour	84.7% Muscalure 98.2% Muscalure	Colourless Light yellow (Munsell 5Y 9/4)	**Doc. III-A 3;** **Study A 3.3/01** **Study A 3.3/02** **Study A 3.3/03**
Odour	84.7% Muscalure 98.2% Muscalure	No characteristic odour at 19.5°C No characteristic odour at 19.5°C	**Doc. III-A 3;** **Study A 3.3/01** **Study A 3.3/02**
Absorption spectra: UV/VIS	98.2% Muscalure	UV/VIS spectrum in hexane: One absorbance maximum at 230 nm, molar absorption coefficient 15.0 L/(mol x cm)	**Doc. III-A 3;** **Study A 3.4/01**

Property	Purity/Specification	Results	Reference
Absorption spectra: IR	96.0% Muscalure	C=C stretching: 3004cm^{-1} C=H stretching: 2920 cm^{-1} and 2852 cm^{-1} C-H bending: 1466 cm^{-1} C-H bending: 1378 cm^{-1} CH2 rocking:720 cm^{-1}	**Doc. III-A 3; Study A 3.4/02**
Absorption spectra: NMR	98.2% Muscalure	^{1}H spectrum: Chemical shift 5.4 ppm (triplet) 2.0 ppm (multiplet) 1.3 ppm (multiplet) 0.9 ppm (triplet)	**Doc. III-A 3; Study A 3.4/03**
Absorption spectra: MS	96.0% Muscalure	m/z (C23H46+) 322; Fragmentation and m/z is in accordance with the structure and Wiley library	**Doc. III-A 3; Study A 3.4/04**
Water solubility	98.2% Muscalure Batch No.20031118	< 7 x 10-6 g/L (20°C, pH 4) < 7 x 10-6 g/L (20°C, pH 7) < 7 x 10-6 g/L (20°C, pH 10)	**Doc. III-A 3; Study A 3.5**
Dissociation constant	n.a.	Since the water solubility of Muscalure is < 7 µg/L, Perrin´s calculation method was used. Result: Muscalure has no acid or basic groups and therefore no pKa value	**Doc. III-A 3; Study A 3.6**
Solubility in organic solvents, including the effects of temperature on stability	87.2% Muscalure	Solubility (g/L) (20°C) Result: Solubility (g/L) Hexane: 465.3 g/L Toluene: 608.8 g/L Dichlormethane: 932.3 g/L Methylal: 431.2 g/L Methanol: 161.3 g/L Propyleneglycol: 212.2 g/L Acetone: 159.7 g/L Acetonitril: 157.2 g/L Dimethylsulfoxide : 220.8 g/L	**Doc. III-A 3; Study A 3.7**
Stability in organic solvents used in b.p. and identity of relevant breakdown products		Not required according to the TNsG on Data Requirements, because the a.s. as manufactured does not contain any organic solvent.	**Doc. III-A 3.8; Justification**
Partition coefficient n-octanol/water	98.2% Muscalure	log Pow >8.2 (20°C, pH 4, 7 and 10)	**Doc. III-A 3; Study A 3.9/01**
Thermal stability identity of relevant breakdown products		Thermically stable, boils at 380°C without decomposition.	**Doc. III-A 3; Study A 3.10**

Property	Purity/Specification	Results	Reference
Flammability, including autoflammability and identity of combustion products	84.7% Muscalure	Pyrophoric properties: The molecular structures of Muscalure technical do not contain any chemical groups that might lead to spontaneous ignition within a short time after coming into contact with air at 20°C Auto-ignition temperature: 250°C	**Doc. III-A 3;** **Study A 3.11/01** **Study A 3.11/02**
Flash point	84.7% Muscalure	Result: 161.5°C	**Doc. III-A 3;** **Study A 3.12**
Surface tension		Not required for substances with a water solubility < 1 mg/L.	**Doc. III-A 3.13;** **Justification**
Viscosity	84.7% Muscalure	Result: 15 mPa x s (20°C) Result: 10-11 mPa x s (40°C)	**Doc. III-A 3;** **Study A 3.14**
Explosive properties	84.7% Muscalure	The molecular structures of the test substance do not contain any chemical instable or highly energetic groups that might lead to explosions.	**Doc. III-A 3;** **Study A 3.15**
Oxidizing properties	84.7% Muscalure	Examination of the molecular structures of the test substance establish beyond reasonable doubt that the substance are incapable of showing a positive result in test EC A.21.The substance does not contain any group that might act as oxidizing agent.	**Doc. III-A 3;** **Study A 3.16**
Reactivity towards container material	83.8% Muscalure	Container material: PE and PET No corrosive properties (7 days at 54°C)	**Doc. III-A 3;** **Study A 3.17/01** **Study A 3.17/02**

2 MANUFACTURE AND USES

2.1 Manufacture

Biocides: Does not need to be specified for the CLH proposal.

2.2 Identified uses

Attractant, product type 19

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Table 10: Summary table for relevant physico-chemical studies

Property	Purity/Specification	Results	Reference
Thermal stability identity of relevant breakdown products		Thermically stable, boils at 380°C without decomposition.	**Doc. III-A 3; Study A 3.10**
Flammability, including autoflammability and identity of combustion products	84.7% Muscalure	Pyrophoric properties: The molecular structures of Muscalure technical do not contain any chemical groups that might lead to spontaneous ignition within a short time after coming into contact with air at 20°C Auto-ignition temperature: 250°C	**Doc. III-A 3; Study A 3.11/01 Study A 3.11/02**
Flash point	84.7% Muscalure	Result: 161.5°C	**Doc. III-A 3; Study A 3.12**
Explosive properties	84.7% Muscalure	The molecular structures of the test substance do not contain any chemical instable or highly energetic groups that might lead to explosions.	**Doc. III-A 3; Study A 3.15**
Oxidizing properties	84.7% Muscalure	Examination of the molecular structures of the test substance establish beyond reasonable doubt that the substance are incapable of showing a positive result in test EC A.21.The substance does not contain any group that might act as oxidizing agent.	**Doc. III-A 3; Study A 3.16**
Reactivity towards container material	83.8% Muscalure	Container material: PE and PET No corrosive properties (7 days at 54°C)	**Doc. III-A 3; Study A 3.17/01 Study A 3.17/02**

3.1 *[Insert hazard class when relevant and repeat section if needed]*

No classification is proposed based on available data.

3.1.1 Summary and discussion of

No classification is proposed based on available data.

3.1.2 Comparison with criteria

No classification is proposed based on available data.

3.1.3 Conclusions on classification and labelling

No classification is proposed based on available data.

RAC evaluation of [physical hazards]
Summary of the Dossier submitter's proposal No classification is proposed **Comments received during public consultation** No Comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4 HUMAN HEALTH HAZARD ASSESSMENT

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

4.1.1 Non-human information

No study data are available, for justification see 6.1.3.

4.1.2 Human information

In case the substance reaches systemic availability it may be expected that it is oxidised by cytochrome P450 enzymes to various alcohols. Enzyme systems exist in liver, fibroblasts and brain that convert fatty alcohols to fatty acids. In some tissues fatty acids can be reduced back to alcohols. Evidence suggests that long chain fatty acids and alcohols up to at least C24 are reversibly inter-converted in the endoplasmatic reticulum by means of a fatty alcohol dehydrogenase and a fatty aldehyde dehydrogenase, a complex that requires NAD+ and releases long chain fatty acids. Further ß-oxidation of long chain fatty acids predominantly occurs after uptake into the peroxisomes and it is assumed that it proceeds to the 18-20C level and then may continue in the peroxisomes or the substrates may be shuttled to mitochondria for complete oxidation. Alternatively the alcohols may be conjugated with glucuronide and excreted via the kidneys (Hargrove et al. 2004).

4.1.3 Summary and discussion on toxicokinetics

According to the available guidance for waiving[1] for Muscalure as dipterian pheromone a reduced data set is acceptable, mainly based on the consideration of the mode of action and natural occurrence as well as low exposure.

According to this guidance document data on toxicokinetics and metabolism are only required when triggered by adverse effects or toxicological concerns arising form other data points for health risk.

The available information on the toxicology of Muscalure does not give rise to concern for the human health except for a moderate skin sensitization property estimated from the results of a Guinea Pig Maximisation Test. Waiving of toxicokinetic and metabolism studies as well as repeated dose toxicity studies is based on the following considerations:

- No adverse effects in the acute oral and dermal toxicity tests with doses of 5000 and 2000 mg/kg bw, respectively.
- No severe concerns from the acute inhalation toxicity test and a LC_{50} of > 5710 mg/m^3
- Within the dermal and eye irritation tests submitted no dermal irritation and only minimal eye irritation that is reversible till 24 hours
- No structural alerts for specific toxic effects - Muscalure is a higher linear mono-alkene
- Negative bacterial mutation tests and a negative in vitro chromosomal aberration test
- Within the OECD/EPA SIDS HPV program a category approach was chosen grouping the higher olefins (alkenes) based on the observation that the location of the double bond or the addition of branching to the structure do not appear to affect the toxicity

[1] Guidance for Waiving of Data Requirements for Pheromones for Inclusion in Annex I/IA of Directive 98/8/EC, 2005, Addendum to the Technical Notes on Data Requirements, ECB, 2008. OECD Monograph 12 (OECD ENV/JM/MONO(2001)12) was taken into consideration for the development of this guidance.

- The reference to the EPA robust study summaries dossier 2005 (American Chemistry Council) for higher olefins indicating minimal oral absorption and NOAELs above 1000 mg/kg bw for 28 day studies (OECD 407), 90 day studies (OECD 408) and oral reproduction/developmental toxicity screening studies (OECD 421) as well as negative findings within the genotoxicty tests (AMES, in vitro chromosome aberration, in vitro gene mutation with *Saccharomyces cerevisiae*, in vivo micronucleus). However, the original studies neither are available to the RMS nor were submitted by the applicant. Therefore these data were not evaluated by the RMS, which means that they can serve only as supplementary information within this report and cannot build up the core argument for waiving.
- The tier 1 primary exposure estimates (for application of the product) are slightly below the short term AEL that is based on intake rates of the structurally related higher-mono-alkenes (C17:1-C30:1) as natural food component of various sources like apples, citrus-juices, honey, olive- and hazelnut-oil (see Doc. II-A.3.6).
- The tier 2 secondary exposure estimates (for sojourning in in-use areas) are below the long term AEL that is based on the "Threshold of Toxicological Concern" of 1800 µg/day (as supported e.g. by ILSI 2005, International Life Sciences Institute) and below the long term intake rates of the structurally related higher-mono-alkenes (C17:1- C30:1) as natural food component (see Doc. II-A.3.6).
- The moderate skin sensitizing property of Muscalure (35% positive response in GPMT with intradermal induction of a 5% mixture in corn oil and Freund Adjuvance) requires minimizing exposure in line with classification and labelling rules: Products with concentrations leading to a classification (≥1%) must not be put on the market. Furthermore with the actual representative product and intended use exposure is estimated to remain below the long term AEL (0.024 mg/kg bw/day) which is derived from natural food contents of the group of higher linear mono-alkenes. This non-standard derivation of the AEL provides some support for its scientific acceptability also as sensitization threshold.

In the absence of dermal absorption studies, the dermal absorption rate is considered to be 100%, though this is very likely an overestimation since Muscalure has a log Po/w far above 4, is not soluble in water (<7 x 10-6 g/L) and has a molecular weight of 322.6 g/mol.

Also oral and inhalation absorption is considered to be 100% in the absence of respective studies.

In case the substance reaches systemic availability it may be expected that it is oxidised by cytochrome P450 enzymes to various alcohols. Enzyme systems exist in liver, fibroblasts and brain that convert fatty alcohols to fatty acids. In some tissues fatty acids can be reduced back to alcohols. Evidence suggests that long chain fatty acids and alcohols up to at least C24 are reversibly inter-converted in the endoplasmatic reticulum by means of a fatty alcohol dehydrogenase and a fatty aldehyde dehydrogenase, a complex that requires NAD+ and releases long chain fatty acids. Further ß-oxidation of long chain fatty acids predominantly occurs after uptake into the peroxisomes and it is assumed that it proceeds to the 18-20C level and then may continue in the peroxisomes or the substrates may be shuttled to mitochondria for complete oxidation. Alternatively the alcohols may be conjugated with glucuronide and excreted via the kidneys (Hargrove et al. 2004).

4.2 Acute toxicity

4.2.1 Non-human information

4.2.1.1 Acute toxicity: oral

Table 11a: Summary table of relevant acute toxicity studies

Route	Method Guideline	Species Strain Sex no/group	dose levels duration of exposure and post-exposure	Value LD50/LC50	Remarks	Reference
Oral	OECD 401	Rat, Wistar, male/female 5/sex/dose	5000 mg/kg bw single gavage application, 14 days post exposure	> 5000 mg/kg bw	GLP study from 1990	**A6.1.1**

4.2.1.2 Acute toxicity: inhalation

Table 11b: Summary table of relevant acute toxicity studies

Route	Method Guideline	Species Strain Sex no/group	dose levels duration of exposure and post-exposure	Value LD50/LC50	Remarks	Reference
Inhalation	OECD 403	Rat, Wistar, male/female 5/sex/dose	4910 and 5710 mg/m^3 4 hours exposure, 18 days post-exposure	> 5710 mg/m^3	GLP study from 1991	**A6.1.3**

4.2.1.3 Acute toxicity: dermal

Table 11c: Summary table of relevant acute toxicity studies

Route	Method Guideline	Species Strain Sex no/group	dose levels duration of exposure and post-exposure	Value LD50/LC50	Remarks	Reference
Dermal	OECD 402	Rat, Wistar, male/female 5/sex/dose	2000 mg/kg bw 24 hours application, 14 days post exposure	> 2000 mg/kg bw	GLP study from 1990	**A6.1.2**

4.2.1.4 Acute toxicity: other routes

No information available.

4.2.2 Human information

Not available.

4.2.3 Summary and discussion of acute toxicity

As reported in the table below a complete acute toxicity data package with GLP standard is available indicating no concern for the endpoints acute oral, dermal, inhalation toxicity. The acute oral and acute dermal toxicity study did not show any effects with doses of 5000 and 2000 mg/kg bw, respectively. The endpoints analysed were clinical signs, body weight and macroscopic analysis. In the acute inhalation test only slight (restlessness, red nasal discharge, visually increased breathing) to moderate (wet head, wet fur) clinical signs were observed at concentrations of 4910 (lower dose) and 5710 mg/ m3 (higher dose). Weight decrease was observed between days 7 and 14 in the higher dose group which recovered till day 18. One animal died in the lower dose group at the first day after exposure, though it did not show severe symptoms. One animal was lethargic in the lower dose group between days 2 and 4. One animal showed a small eye and corneal opacity on day 1 to 9 and 12 to 13. However the relative humidity of the test atmosphere was just 1% instead of 30 to 70% as recommended by the draft OECD guideline 436, which may have negatively affected the study outcome. In summary the acute inhalation toxicity test does not indicate severe concerns at 5710 mg/m3 which results in doses above 1000 mg/kg bw and in a LC50 of > 5710 mg/m3.

4.2.4 Comparison with criteria

The acute oral toxicity study did not show any effects with doses of 5000 mg/kg bw, which is above the LD50 range that may lead to classification in category 4 (300 to 2000 mg/kg bw) or DSD category 3 (200 to 2000 mg/kg bw).

The acute dermal toxicity study did not show any effects with doses of 2000 mg/kg bw, which is above the LD50 range that may lead to classification in category 4 (1000 to 2000 mg/kg bw) or DSD category 3 (400 to 2000 mg/kg bw).

The acute inhalation toxicity test does not indicate severe concerns at 5.710 mg/L which results in doses above 1000 mg/kg bw and in a LC50 of > 5.710 mg/L, which is above the LD50 range that may lead to classification in category 4 (dust, mist 1 to 5 mg/L) or DSD category 3 (1 to 5 mg/L).

4.2.5 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of acute toxicity
Summary of the Dossier submitter's proposal No classification is proposed **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4.3 Specific target organ toxicity – single exposure (STOT SE)

No classification necessary.

RAC evaluation of specific target organ toxicity – single exposure (STOT SE)
Summary of the Dossier submitter's proposal No classification is proposed **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4.4 Irritation

4.4.1 Skin irritation

4.4.1.1 Non-human information

No concern arises from the skin irritation test according to OECD TG 404.

Erythema scores were zero (0) to all animals at all time points. Oedema scores were zero (0) to all animals at all time points. No staining (colouration) of the treated skin was observed. There was no

evidence of a corrosive effect on the skin. Scaliness was observed in three of the six animals only at 72 hours. No symptoms of systemic toxicity were observed and no mortality occurred.

4.4.1.2 Human information

Not available.

4.4.1.3 Summary and discussion of skin irritation

No concern arises from the skin irritation test.

Table 12: Summary table of relevant skin irritation studies

Species	Method	Average score 24, 48, 72 h		Reversibility yes/no	Result	Remarks	Reference
		Erythema	Edema				
Rabbit	OECD 404	0	0	Not applicable	Not irritating	GLP study from 1990	A6.1.4

4.4.1.4 Comparison with criteria

Erythema and Oedema scores were 0 for all animals at all time points.

4.4.1.5 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of skin corrosion/irritation
Summary of the Dossier submitter's proposal No classification is proposed **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4.4.2 Eye irritation

4.4.2.1 Non-human information

No concern arises from the eye irritation test according to OECD 405.

Lacrimation was observed in all animals at time point '1 hour'. This subsided before the 24 hour time point.

Chemosis grade 1 for eyelids was observed in 3 of 6 animals at time point '1 hour'. This subsided before the 24 hour time point.

Treatment of the eyes with 2% fluorescein, 24 hours after test substance instillation revealed no corneal epithelial damage in any of the animals.

No staining by the test substance was observed.

There was no evidence of ocular corrosion.

No toxic symptoms were observed in the animals during the test period and no mortality occurred.

At the observation time points 24, 48 and 72 hours, all irritation effects (cornea, iris, conjunctivae and discharge) were scored "0".

Based on the 1 hour observations the Draize score is calculated to be "3".

4.4.2.2 Human information

Not available.

4.4.2.3 Summary and discussion of eye irritation

Table 13: Summary table of relevant eye irritation studies

Species	**Method**	**Average Score 24, 48, 72 h**				**Reversibility yes/no**	**Result**	**Remarks**	**Reference**
		Cornea	Iris	Redness Conjunctiva	Chemosis				
Rabbit	OECD 405	0	0	0	0	Slight chemosis in 3 of 6 animals at 1h time point reversible till 24 hour time point	Not irritating	GLP study from 1990	**A6.1.4**

4.4.2.4 Comparison with criteria

The cornea, iris and conjunctiva scores were 0 for all animals at the time points of 24, 48 and 72 hours.

4.4.2.5 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of eye corrosion/irritation
Summary of the Dossier submitter's proposal No classification is proposed **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4.4.3 Respiratory tract irritation

No specific information available.

RAC evaluation of respiratory sensitisation
Summary of the Dossier submitter's proposal No information available **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

4.5 Corrosivity

No irritation and no corrosion observed, see chapter 4.4.

4.6 Sensitisation

4.6.1 Skin sensititsation

4.6.1.1 Non-human information

A guinea pig maximisation test indicates moderate skin sensitising properties: With intradermal induction of a 5% mixture in corn oil and Freund Adjuvance, 7 from 20 animals (35%) scored positive (all animals with irritation score 1 from 4).

Often reaction to clear sensitizers is most prominent during the first 24 hours after challenge, with subsequently decreasing intensity. However in this study all positive readings were observed only at the second day after challenge (no response in the first 24 hours) with animals showing minimal irritation scores of 1 from maximal 4. There is no plausible explanation for such unusual behavior.

4.6.1.2 Human information

Not available.

4.6.1.3 Summary and discussion of skin sensitisation

Table 15: Summary table of relevant skin sensitisation studies

Species	Method	Number of animals sensitized/total	Result	Remarks	Reference
Guinea pig	OECD 406, maximization test Intradermal induction with 5% a.s. in corn oil and Freund Adjuvance; epidermal induction with undiluted a.s.; epidermal challenge with 25%, 10%, 5% a.s. in corn oil	Test: 7/20 negative control: 0/10 positive control formaldehyde: 0%, 0.1%, 0.25%, 0.5% induced sensitization in 0, 10%, 20%, 95% of animals	Sensitizing, CLP category 1B; all positive animals with irritation score 1 (red spots, scattered reaction) from maximal 4.	GLP study from 1991	**A6.1.5**

The positive guinea pig maximisation test indicates moderate skin sensitising properties

4.6.1.4 Comparison with criteria

The guinea pig maximisation test indicates moderate skin sensitising properties: With intradermal induction of a 5% mixture in corn oil and Freund Adjuvance, 7 from 20 animals (35%) scored positive (all animals with irritation score 1 from 4). This represents a reaction that is stronger than the criterion indicated in the CLP Regulation table 3.4.4. for category 1B, that is $\geq$ 30% response at > 1% intradermal induction dose. The reaction is less strong than the criteria indicated in CLP Regulation table 3.4.4. for category 1A ($\geq$ 60% response at intradermal induction dose of > 0.1% to $\leq$ 1% or $\geq$ 30% response at intradermal induction dose of $\leq$ 0.1%).

The DSD criteria are less differentiated (for adjuvant test a response of at least 30% of the animals is required). However according to the DSD criteria classification with R43 is required.

4.6.1.5 Conclusions on classification and labelling

Muscalure has to be classified as sensitizing, CLP category 1B, H317 and according to the DSD criteria with R43.

RAC evaluation of skin sensitisation

Summary of the Dossier submitter's proposal

The dossier submitter proposed the harmonised classification for cis-tricos-9-ene to be The dossier submitter (DS) proposed the harmonised classification of cis-tricos-9-ene to be Skin Sens. 1B, H317 (May cause an allergic skin reaction) in accordance with CLP (DSD; R43 - May cause skin sensitisation by skin contact). In the CLH report, one key study was presented, namely, an OECD 406 Maximisation test (data unpublished, data owner Denka Int., 1991). In that study, the intradermal induction of a 5% mixture of cis-tricos-9-ene in corn oil and Freund Adjuvant resulted in 7/20 animals (35%) which scored positive following epidermal induction (challenge) with undiluted cis-tricos-9-ene (positive animals presented an irritation score ranging from 1 to 4).

Comments received during public consultation

During the public consultation, Germany noted that while the criteria for Cat. 1B are formally fulfilled, all positive readings were observed only at the second day after challenge with animals showing minimal irritation scores ranging from 1 to 4. However, in their experience, reaction to clear sensitizers is most prominent throughout the first 24 hours after challenge, and subsequently, with decreasing intensity. Germany specified that, on the basis of the data provided, there is no plausible explanation for such unusual behaviour.

Additional key elements

-

Assessment and comparison with the classification criteria

RAC agreed with DS's proposal to classify and label muscalure; cis-tricos-9-ene according the CLP criteria as sensitising, under CLP category 1B, H317.

Classification/labelling for skin sensitization according to CLP Regulation 1272/2008/EC

A guinea pig maximization test indicated that muscalure; cis-tricos-9-ene has moderate skin sensitizing properties: with intradermal induction of a 5% mixture in corn oil and Freund Adjuvant, 7 out of 20 animals (35%) scored positive.

Often reaction to typical sensitizers is indeed most prominent during the first 24 hours after challenge, with subsequent decreasing intensity. However in this study all positive readings were observed only on the second day after challenge (no response in the first 24 hours) with animals showing irritation (red spots, scattered reaction) scores ranging from 1 to 4. There is no plausible explanation for such unusual behaviour because CIS-TRICOS-9-ene is not a skin irritant.

The reaction (35% response at 5% intradermal induction dose) fits with the criterion indicated in the CLP Regulation Table 3.4.4., for category 1B, that represents ≥ 30% response at > 1% intradermal induction dose. The reaction is less strong than that indicated in CLP Regulation table 3.4.4., for category 1A (≥ 60% response at intradermal induction dose of > 0.1% to ≤ 1% or ≥ 30% response at intradermal induction dose of

≤ 0.1%).

The RAC concluded that muscalure; cis-tricos-9-ene should be classified as sensitising, under CLP category 1B, H317 (may cause an allergic skin reaction).

Classification/labeling for skin sensitization according to Directive 67/548/EEC

The DSD criteria are less differentiated (for adjuvant test method, a response of at least 30% of the animals is required). However, according to the DSD criteria classification, R43 is required.

The RAC concluded that muscalure; cis-tricos-9-ene should be classified as sensitising according to the DSD criteria with R43.

Supplemental information - In depth analyses by RAC

-

4.6.2 Respiratory sensitisation

No information available.

RAC evaluation of respiratory sensitisation

Summary of the Dossier submitter's proposal

No information available

Comments received during public consultation

No comments received

Additional key elements

-

Assessment and comparison with the classification criteria

This endpoint was not assessed by the RAC, as no classification was proposed by the dossier submitter and no comments were submitted during public consultation.

Supplemental information - In depth analyses by RAC

-

4.7 Repeated dose toxicity

4.7.1 Non-human information

No study data available.

4.7.2 Human information

No information available.

4.7.3 Other relevant information

No other information available.

4.7.4 Summary and discussion of repeated dose toxicity

According to the 'Guidance for waiving' data on sub-acute, sub-chronic, chronic toxicity are normally only required if there is a significant exposure potential in terms of level, frequency and duration or if there is a concern from the toxicological profile.

The available information on the toxicology of Muscalure and the precautious AEL estimation support the absence of concern for human health with low exposure. The respective data and information are summarized as bullet points in chapter 4.1.

Therefore no repeated dose toxicity tests were submitted and the waiving was accepted.

4.8 Specific target organ toxicity (CLP Regulation) – repeated exposure (STOT RE)

See chapter 4.7.

RAC evaluation of repeated dose toxicity (DSD) and specific target organ toxicity (CLP) – repeated exposure (STOT RE)
Summary of the Dossier submitter's proposal No information available **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by RAC, as the CLH report did not contain data on this hazard class following the application of the Guidance on Data Requirements for active substances in biocidal products under Directive 98/8/EC (ECB, 2000, 2008). No comments were submitted during public consultation. The technical note on data requirements is available at

http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/guidance-documents

Supplemental information - In depth analyses by RAC

-

4.9 Germ cell mutagenicity (Mutagenicity)

4.9.1 Non-human information

4.9.1.1 In vitro data

The results from the new GLP studies on bacterial mutagenicity and on in vitro chromosomal aberration (CHO cells) are negative in the absence and presence of metabolic activation

4.9.1.2 In vivo data

Not available.

4.9.2 Human information

Not available.

4.9.3 Other relevant information

Not available.

4.9.4 Summary and discussion of mutagenicity

See chapter 4.9. Muscalure as a higher linear mono-alkene does not contain structural alerts for genotoxicity and exposure is expected to be below the intake as natural food component of various sources like apples, citrus-juices, honey, olive- and hazelnut-oil (several micrograms per day). The purity of Muscalure is described in the confidential Annex. No substance with known genotoxicity or structural alerts for genotoxicity is present.

Moreover the results from the new GLP studies on bacterial mutagenicity and on in vitro chromosomal aberration (CHO cells) are negative in the absence and presence of metabolic activation.

It can be concluded that Muscalure does not pose a hazard with regard to genotoxicity.

Table 18: Summary table of relevant in vitro and in vivo mutagenicity studies

Test system Method Guideline	organism/ strain(s)	concentra-tions tested (give range)	Result		Remark	Reference
			+ S9	- S9		
			+/-/+	+/-/+		
Ames test, OECD 471	Salmonella typhimurium: strains TA1535, TA1537,	10 - 1000 µg/plate	-	-	GLP study from 2006 Precipitate with 1000 µg/plate	A6.6.1

	TA98, TA100					
Ames test, OECD 471	Escherichia coli: Strains WP2uvrA	10 - 1000 µg/plate	-	-	GLP study from 2006 Precipitate with 1000 µg/plate	A6.6.1
Chromosomal aberration OECD 473	Cultured Chinese Hamster Ovary (CHO) cells	62.5 – 500 µg/ml	-	-	GLP study from 2008 Clear flocculation with 500 and 250 µg/ml Slight flocculation with 125 and 62.5 µg/ml	A 6.6.2

4.9.5 Comparison with criteria

The results from the new GLP studies on bacterial mutagenicity and on in vitro chromosomal aberration (CHO cells) are negative in the absence and presence of metabolic activation

4.9.6 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of germ cell mutagenicity

Summary of the Dossier submitter's proposal
No classification is proposed

Comments received during public consultation
No comments received

Additional key elements
-

Assessment and comparison with the classification criteria
This endpoint was not assessed by the RAC, as the CLH report does not contain data about this endpoint and no comments were submitted during public consultation.

Supplemental information - In depth analyses by RAC
-

4.10 Carcinogenicity

4.10.1 Non-human information

No study data available.

4.10.2 Human information

No information available.

4.10.3 Other relevant information

No information available.

4.10.4 Summary and discussion of carcinogenicity

According to the 'Guidance for waiving' carcinogenicity studies, teratogenicity studies and fertility studies would be required in case of adverse effects in mutagenicity or short term studies or significant long-term exposure.

The available information on the toxicology of Muscalure and the precautious AEL estimation support the absence of concern for human health with low exposure. The respective data and information are summarized as bullet points in chapter 4.1.

Therefore no carcinogenicity and no reproductive toxicity studies were submitted and the waiving was accepted.

4.10.5 Comparison with criteria

See chapter 4.10.

4.10.6 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of carcinogenicity
Summary of the Dossier submitter's proposal No information available **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by RAC, as the CLH report did not contain data on this hazard class following the application of the Guidance on Data Requirements for active substances in biocidal products under Directive 98/8/EC (ECB, 2000, 2008). No comments were submitted during public consultation. The technical note on data requirements is available at http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/guidance-documents **Supplemental information - In depth analyses by RAC** -

4.11 Toxicity for reproduction

4.11.1 Effects on fertility

No study data available.

4.11.2 Developmental toxicity

No study data available.

4.11.3 Other relevant information

No other information available.

4.11.4 Summary and discussion of reproductive toxicity

According to the 'Guidance for waiving' carcinogenicity studies, teratogenicity studies and fertility studies would be required in case of adverse effects in mutagenicity or short term studies or significant long-term exposure.

The available information on the toxicology of Muscalure and the precautious AEL estimation support the absence of concern for human health with low exposure. The respective data and information are summarized as bullet points in chapter 4.1.

Therefore no carcinogenicity and no reproductive toxicity studies were submitted and the waiving was accepted.

4.11.5 Comparison with criteria

See chapter 4.11.

4.11.6 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of reproductive toxicity

Summary of the Dossier submitter's proposal
No information available
Comments received during public consultation
No comments received
Additional key elements
-
Assessment and comparison with the classification criteria
This endpoint was not assessed by RAC, as the CLH report did not contain data on this hazard class following the application of the Guidance on Data Requirements for active substances in biocidal products under Directive 98/8/EC (ECB, 2000, 2008). No comments were submitted during public consultation.

The technical note on data requirements is available at

http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/guidance-documents

Supplemental information - In depth analyses by RAC
-

4.12 Other effects

4.12.1 Non-human information

4.12.1.1 Neurotoxicity

Not relevant.

4.12.1.2 Immunotoxicity

Not relevant.

4.12.1.3 Specific investigations: other studies

Not available.

4.12.1.4 Human information

Not available.

4.12.2 Summary and discussion

No data available.

4.12.3 Comparison with criteria

Not relevant.

4.12.4 Conclusions on classification and labelling

No classification necessary.

RAC evaluation of aspiration toxicity
Summary of the Dossier submitter's proposal No information available **Comments received during public consultation** No comments received **Additional key elements** - **Assessment and comparison with the classification criteria** This endpoint was not assessed by the RAC, as the CLH report does not contain data about this endpoint and no comments were submitted during public consultation. **Supplemental information - In depth analyses by RAC** -

5 ENVIRONMENTAL HAZARD ASSESSMENT

The results of key studies as well as the references to key studies are highlighted bold throughout this chapter.

Muscalure belongs to the group of alkenes consisting of a twenty-three unbranched aliphatic structure having a chain of twenty-three carbon and containing one double bound. Muscalure is a sex pheromone produces by the female house fly and acts by a non-toxic mode of action aiming to modify the behaviour of other individuals of the same species (target specificity).

This evaluation was carried out under the consideration of the Guidance for waiving of data requirements for pheromones for inclusion in Annex I/IA of Directive 98/8/EC[2]. As stated in the Guidance sufficient information has to be provided to enable the evaluation of any risk arising to the environment from the use of this pheromone. However a waiver for core data requirement was accepted in the light that emissions to the environment are very low and the mode of action is highly target specific.

Muscalure is used in pheromone traps placed exclusively indoors (cf. Doc. II-B, chapter 3) and loaded with 1.25 mg a.s/m^2 floor released from the trap over a period of approximately 4 to 6 weeks. Thus justifications for non submission of studies for initial degradation studies, anaerobic degradation, adsorption/desorption, growth inhibition on algae, inhibition to microbial activity were accepted.

[2] Guidance document for waiving of data requirements for pheromones for inclusion in Annex I/IA of Directive 98/8/EC, http://ecb.jrc.ec.europa.eu/biocides/.

OECD Monograph 12 (OECD ENV/JM/MONO(2001)12) was taken into consideration for the development of this guidance.

5.1 Degradation

Table 21: Summary of relevant information on degradation - See single subsections.

5.1.1 Stability

Hydrolysis and photolysis in water

Abiotic degradation due to hydrolysis and photolysis in water was not investigated. The applicant provided a justification for non-submission of initial degradation studies based on limited exposure due to the intended indoor use.

The HYDROWIN model v1.67 is not applicable to this kind of chemcial and therefore no rate constant could be estimated (Doc IV- A 7.1.1).

The Henry's law constant of Muscalure for the system water/air is calculated to be >2.95 x 10^3 Pa x m^3/mol (cf. Doc. IV-A 3.2.1/01 and Doc III-A 3), indicating that if Muscalure reaches the water surface it is not dissolved in water, but partitions to the atmosphere at a rapid rate (log Henry´s Law Constant >2).

Regarding aqueous phototransformation, Muscalure does not display chromophore properties at wavelengths above 290 nm and thus does not absorb light in the range of 290 to 800 nm (Doc. IV-A 3.4, Doc. III-A 3).

Based on the exposure assessment the justifications for non-submission of data are acceptable.

Phototransformation in air

In the air compartment, Muscalure is susceptible to photochemical degradation in the gas phase as proven by the estimation according to the methodology described in the TGD (EC 2003, part II, p. 51). The specific degradation rate constant at 25°C with OH-radicals was estimated to be kOH = 83 x 10^{-12} cm³/molecule/s (**cf. Doc IV-A 7.1.1 and Doc. III-A 7.3.1**). By relating k_{OH} to the average OH-radical concentration in the atmosphere $c(OH)_{air}$, the pseudo-first order rate constant for degradation in air k deg, air can be derived:

$$k_{deg,\,air} = k_{OH} \times c(OH)_{air} \times 24 \times 3600 \qquad [d^{-1}]$$

The half-life is 4.7 h (cf. table 4.1.2.1-1). Based on this result, accumulation or long-range transport of Muscalure in air is not expected. Also reaction with other photooxidative species in the atmosphere, such as O_3 is possible and, more shown in table 4.1.1.2-1, results in even faster degradation than by reaction with OH-radicals. Grosjean and Grosjean 1997 concluded that the ozone-alkene reaction plays a major role in the formation of photochemical oxidants such as carbonyls and biradicals.

Also reactions with NO_3-radicals may occur.

Table 21a: Phototransformation in air

Guideline / Test method	Molecule / radical	Rate constant	Molecule/Radical concentration	k deg, air	Half-life (t1/2)	Reference
Estimation indirect photolysis	OH	83 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1}	5 x 10^5 molecule cm^{-3}	3.5 d^{-1}	4.7h	Doc. III-A7.3.1
	Ozone	13 x 10^{-17} cm^3 $molecule^{-1}$ s^{-1}	7 x 10^{11} molecule cm^{-3}	-	2.1h	

5.1.2 Biodegradation

The applicant provided a justification for non submission of data (Doc. III-A 7.1.1) and a QSAR estimation on ready biodegradability (**cf. Doc. IV-A 7.1.1, Doc. III-A 7.1.1.2.1**). The predictions from the models Biowin1, 2, 3, 5 and 6 (Linear Model Prediction, Non-Linear Model Prediction, Ultimate Biodegradation Timeframe, MITI Linear Model Prediction, MITI Non-Linear Model Prediction) indicate that Muscalure is readily biodegradable. Several higher alkanes were used to derive the linear/non linear, the ultimate as well as the MITI model (Eicosan (C20) and Docosane (C22)). Thus the predictivity is enhanced because these alkanes were used to derive the used BIOWIN model (v4.10) from the EPI SUITE software. According to Fuchs et al., 2006 the aerobic microbial degradation mechanism for alkanes can be applied for alkenes as well. In addition all probability cut off points as suggested in ECHA (2008)[3] regarding ready biodegradability of the used QSAR model were met. BIOWIN predictions concerning not ready biodegradability seem to be more certain according to the ECHA (2008).

In addition indications exist that higher alkenes (C24-30 alkenes, branched and linear) do not meet in standard ready test system the pass level, whereas C20-24 branched and linear alkenes did (Doc. IV-B 6). However this summary information submitted by the American Chemistry Council (ACC) for the US EPA HPV Chemical Program were not evaluated so far by the respective authority and may serve as additional information only. USEPA, 1994 concluded that Muscalure as a member of the alkenes would be expected to persist in the environment.

According to the work for the OECD HPV programme, OECD SIDS, 2004 also refers to the study submitted by the ACC for the US EPA HPV Chemical program. The initial assessment report states, “There is no clear correlation between carbon number and degree of biodegradation for alpha olefins. The internal olefins may exhibit increasing biodegradation with increasing carbon number, up to C24.

Testing in an OECD 301B test with a C20-C24 branched and linear material (>70% branched) resulted in 92% degradation in 28 days. Both substrate and benzoate showed unusually high percent biodegradation (92 and nearly 100%, respectively), suggesting some bias in the test. However, since both substrate and benzoate were biased the same way, the test still supports ready biodegradability of the substrate.”

According to Leahy and Colwell, 1990 several factors play a major role for the microbial degradation of hydrocarbons in the environment. Aliphatic fraction of the oil is considered as the most susceptible for degradation. Also low concentrations, dispersion and emulsification enhance the degradability. Carvo-Laureau et al. 2007 reported the isolation of a novel long-chain alkenes and fatty acid degrading bacterium.

In conclusion it is feasible to assume that Muscalure will be degraded in environmental compartments. In addition based on the intended indoor use no significant exposure to environmental compartments is expected.

For anaerobic biodegradation a justification for non-submission of data was accepted due to the fact that Muscalure will enter manure only in very low quantities, when used in traps in stables (see Doc. III-A 7.1.2.1.2).

5.1.2.1 Biodegradation estimation

See chapter 5.1.2

5.1.2.2 Screening tests

See chapter 5.1.2.

5.1.2.3 Simulation tests

See chapter 5.1.2.

[3] ECHA, 2008: Guidance on information requirements and chemical safety assessment, R.7 b: Endpoint Specific Guidance.

5.1.3 Summary and discussion of degradation

Based on model estimations on ready biodegradability and on its role in intraspecies communication it can be concluded that Muscalure will dissipate in environmental compartments due to volatilisation and biodegradation.

Abiotic degradation due to hydrolysis and photolysis in water was not investigated. From its UV/VIS absorption spectrum its susceptibility for photolytic breakdown can be considered as low.

Muscalure is decomposed in the atmosphere by photooxidation with half-lives of 4.7 hours by OH-radicals and of 2.1 hours by ozone radicals. Because of degradation and physico-chemical properties no abiotic effects on the atmospheric environment are likely.

5.2 Environmental distribution

5.2.1 Adsorption/Desorption

No data available

5.2.2 Volatilisation

Table 21b Vapour pressure

Property	Purity/Specification	Results	Reference
Vapour pressure	96.0% Muscalure	6.4×10^{-2} Pa (20°C) 0.119 ± 0.003 Pa (25°C)	**Doc. III-A 3; Study A 3.2**

5.2.3 Distribution modelling

The applicant provided a justification for non-submission of data for a test on adsorption/desorption (cf. Doc III-A 7.1.3) based on limited exposure due to the intended use. Based on the exposure assessment, this justification is acceptable. Furthermore, the experimental determination of the adsorption of Muscalure might be difficult due its low water solubility (cf. Doc. IV-A 3.5 and Doc III-A 3). The applicant submitted a model estimation (PCKCOWIN v1.66) of the EPI SUITE program (Doc IV-A 7.1.1). Also the estimation method provided in the TGD, Part III, p. 26 (EC, 2003) for hydrophobics yield the same result as listed in table 21a.

Table 21c Adsorption onto / desorption from soils

Guideline / Test method	Adsorbed a.s. [%]	K_a [1]	KaOC [2]	Reference
PCKOCWIN v 1.66	-	-	Log 6.7	Doc. IV-A 7.1.1, Doc. III-A 7.1.3
TGD, Part III	-	-	Log 6.7	Doc. III-A 7.1.3

[1] K_a = Adsorption coefficient
[2] K_{aOC} = Adsorption coefficient based on organic carbon content

The calculations made with the Level III Fugacity Model of the US-EPA EPIWIN v3.12 (Doc. IV-A 7.1.1) package indicate that 68.2% of the substance will be adsorbed to the sediment, 28% will adsorb to soil and only 3.75% will stay in the water.

5.3 Aquatic Bioaccumulation

5.3.1 Aquatic bioaccumulation

5.3.1.1 Bioaccumulation estimation

Based on log Kow of >8.2 (cf. Doc III-A3, Doc. IV-A 3.9/01), there is an indication of bioaccumulation potential. The applicant provided a justification for non-submission of a bioconcentration study based on limited exposure of the representative biocidal product Denka Flylure. Direct exposure of natural surface waters can be neglected. According to model calculation suggested in the TGD, 2003 the log BCF fish is 4.3 (cf. table 4.1.3-1, Doc. III-A 7.4.2). However it should be noted that this mathematical relationship has a higher degree of uncertainty because of the hydrophobic properties of Muscalure. Based on calculations with the EPI SUITE software BCFBAFWIN v3.00, the log BCF fish is 2.9 (log Kow input value: 8.2). Thus the QSAR models yield different results that suggest low to high bioconcentration potential. In addition, the log Kow was not exactly determined, the experimentally derived value is >8.2. Thus the BCF estimations were based on the value of 8.2, acknowledging that the actual value might be higher. On the other hand it is known that the reliability of measured high log Kow (above 8) is limited.

Table 22: Summary of relevant information on aquatic bioaccumulation

Basis for estimation	**log K_{OW} (measured)**	**Estimated BCF for fish (freshwater)**	**Reference**
Calculation according to the TGD on Risk Assessment, Part II (EC, 2003)	8.2	The log BCF-value can be calculated using the log KOW value (>8.2) Log BCFfish = -0.20 x logKow2 + 2.75 x log Kow – 4.72 Log BCFfish = 4.3	**Doc. III-A 7.4.2**
Calculation according to BCFBAFwin v3.00	8.2	Log BCFfish = 2.9	

Besides the low aqueous solubility (<7 x 10^{-3} mg/L at 20°C, cf. chapter 1), several factors are not taken into consideration, when the BCF is estimated only on the basis of log Kow, e.g. active transport phenomena, uptake and depuration kinetics as well as metabolism in organisms. Based on negligible exposure Muscalure is not expected accumulate to effective concentrations in biota.

5.3.1.2 Measured bioaccumulation data

No data available

5.3.2 Summary and discussion of aquatic bioaccumulation

See chapter 5.3.1.1

5.4 Aquatic toxicity

Tables 23: Summary of relevant information on aquatic toxicity

See chapters 5.4.1, 5.4.2, 5.4.3, 5.4.4.

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

The acute toxicity of Muscalure (purity >98%) was investigated on rainbow trout in a semi-static study for 96 hours (**Doc. IV-A 7.4.1.1 and Doc. III-A 7.4.1.1**). The LC_{50} values could not be calculated because no mortality up to the highest tested concentration of 100 mg/L was observed. For the results see table 23a. Only one concentration was tested, because the preliminary range finding test indicated that no effects were to be expected at that concentration. The solubility of the test substance was poor so the measured concentration of Muscalure could not accurately be established. Measured concentrations varied between 140 to 160 mg/L except on 0h were Muscalure concentration was 7 mg/L. The test concentration was far above the water solubility of Muscalure of $<7 \times 10^{-6}$ g/L (20°C). The actual water solubility of Muscalure in the test system was not determined. An oil-like layer was observed on the surface of the test solutions.

According to the Guidance Document on Aquatic Ecotoxicology[4] and the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures[5] the geometric mean measured concentration for the relevant test period should be used to express toxicity if the measured concentrations are <80% or >120% of nominal ones during the test.

In conclusion Muscalure is not acutely toxic to the rainbow trout within its water solubility; however the submitted study suffers several shortcomings e.g. the determination of the actual exposure concentration was not possible and the non dissolved material present can also disturb the test system.

[4] http://ec.europa.eu/food/plant/protection/evaluation/guidance/wrkdoc10_en.pdf

[5] http://www.oecd.org/document/30/0,3343,en_2649_34377_1916638_1_1_1_1,00.html

Table 23a: Acute toxicity to fish

Guideline / Test method	Species	Endpoint / Type of test	Exposure		Results			Remarks	Reference
			design	duration	LC_0	LC_{50}	LC_{100}		
EPA OPP 72-1	*Oncorhyn-chus mykiss* (rainbow trout)	Mortality; limit test	Semi-static	96h	100 mg/L (n) 71 mg/L (mean, m)	>100 mg/L (n)	>100 mg/L (n)	15 mL/L t-butyl alcohol as a vehicle.	**Doc. IV-A 7.4.1.1. Doc. III-A 7.4.1.1**

n …… nominal, m ……measured

5.4.1.2 Long-term toxicity to fish

No data available.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

Acute toxicity of Muscalure to daphnids (*Daphnia magna*) was investigated in a static study (**Doc. IV-A 7.4.1.2, Doc. III-A 7.4.1.2**). The highest tested nominal concentration causing no effects according to immobilisation after 48 hours was 10 mg/L. At this concentration all daphnids were mobile, but already 9 out of 40 animals were trapped in a thin transparent fleece. Effects found at 100 mg/L were attributed to a physical effect (all animals were trapped in a transparent fleece, 11 out of 20 were immobile; microscopically assessed). For the results see table 23b. Nominal test concentrations exceeded by far the water solubility of Muscalure. Even the mean measured concentrations still exceeded the water solubility by three orders of magnitude. No visible oily layer could be observed during the test. In addition due to the poor solubility of the test compound and the low measured concentrations, the obtained result has limitations.

Since 0.25 mg/L was the highest tested concentrations without physical effects on mobility, the EC_{50} value was determined with >0.25 mg/L.

At 0.83 mg/L the observed effects on mobility were attributed to physical burden. Therefore it is considered, that an EC_{50} based on toxicological effects would be higher and in any case exceed 1mg/L.

Table 23b: Acute toxicity to invertebrates

Guideline / Test method	Species	Endpoint / Type of test	Exposure		Results in mg Muscalure/L			Remarks	Reference
			design	duration	EC_0	EC_{50}	EC_{100}		
EPA OPP 72-2 OECD 202	*Daphnia magna*	immobilisation / acute	Static	48h	0.25 mg/l (mean, m)	>0.25 mg/l (mean, m)	>0.25 mg/l (mean, m)	Vehicle t-butyl alcohol	**Doc. IV-A 7.4.1.2 Doc. III-A 7.4.1.2**

m ……measured

5.4.2.2 Long-term toxicity to aquatic invertebrates

No data available.

5.4.3 Algae and aquatic plants

The applicant submitted a justification for non-submission of data (Doc. III-A 7.4.1.3) based on the low solubility/high Kow of the test compound. Therefore it is likely that any undissolved substance will cause the algal cells to aggregate. In addition since exposure estimates do not indicate concern because the intended usage is limited indoors in electrocution or glue traps or small glue strips the waiver concerning growth inhibition on algae is acceptable.

5.4.4 Other aquatic organisms (including sediment)

No data available.

5.5 Comparison with criteria for environmental hazards (sections 7.1 – 7.4)

CLP:

Aquatic Acute 1:

Acute aquatic toxicity: $L(E)C_{50}$ values are only available for fish (>100 mg/L, nominal, corresponding to >71 mg/L, mean measured) and daphnia (>10 mg/L, nominal, corresponding to >0.25 mg/L mean measured); in both cases the $L(E)C_{50}$ values are > water solubility of $7x10^{-3}$ mg/L. The EC_{50} value for daphnids was chosen with >0.25 mg/L, since this was the highest concentration tested, without physical effects on mobility. But also at 0.83 mg/L mean measured (=100 mg/L, nominal) the observed effects on mobility were attributed to physical burden. Therefore it is considered, that an EC_{50} based on toxicological effects would be higher and in any case exceed 1mg/L.

➔ **No classification**

Aquatic Chronic Categories:

Classification according to chronic toxicity data:

There are no chronic data available for Cis-tricos-9-ene and it is considered to be rapidly biodegradable (weight of evidence decision, see chapter 7.1 Degradation).

➔ **No classification**

Classification according to acute toxicity data:

No toxic effects were recorded up to the highest concentrations tested (100 mg/L, nominal, corresponding to 71 (fish) and 0.83 mg/L (crustacean), mean measured) or the water solubility (see chapters 5.4.1 and 5.4.2). Furthermore Cis-tricos-9-ene is considered to be rapidly biodegradable (weight of evidence decision, see chapter 7.1 Degradation), although it has a log P_{ow} >8.2 and BCF estimations range from 794.3 to 19952.

➔ **No classification**

DSD:

R50/53:

No toxic effects were recorded up to the highest concentrations tested (100 mg/L, nominal, corresponding to 71 (fish) and 0.83 mg/L (crustacean), mean measured)) or the water solubility. Furthermore Cis-tricos-9-ene is considered to be rapidly biodegradable (weight of evidence

decision, see chapter 7.1 Degradation), although it has a log P_{ow} >8.2 and BCF estimations range from 794.3 to 19952.

➔ **No classification**

5.6 Conclusions on classification and labelling for environmental hazards (sections 7.1 – 7.4)

Cis-tricos-9-ene has not to be classified for its environmental hazards.

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

The dossier submitter (DS) proposed no classification for cis-tricos-9-ene (muscalure) regarding its environmental hazard.

1. *Degradation.*

The CLH report did not contain experimental data following the application of the Guidance on Data Requirements for active substances in biocidal products under Directive 98/8/EC (ECB, 2000, 2008). Only QSAR estimations were provided.

The technical note on data requirements is available at http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/guidance-documents

a. Biodegradation.

A QSAR estimation on ready biodegradability is provided. The predictions from the models BIOWIN1, 2, 3, 5 and 6 indicate that muscalure; cis-tricos-9-ene is readily biodegradable. Several higher alkanes were used to derive this QSAR estimation. According to Fuchs et al. (2006), the aerobic microbial degradation mechanism for alkanes can also apply to alkenes. In addition, all probability cut-off points as suggested by ECHA (2008)6 regarding ready biodegradability of the utilised QSAR model were met.

b. Hydrolysis and photolysis in water.

Abiotic degradation due to hydrolysis and photolysis in water was not investigated.

HYDROWIN model v1.67 is not applicable to this kind of chemical and therefore no rate constant could be estimated. The Henry´s law constant (>2.95 x 103 Pa x m3/mol) indicates that if cis-tricos-9-ene reaches the water surface it is partitioned to the atmosphere at a rapid rate.

6 ECHA, 2008: Guidance on information requirements and chemical safety Assessment, R.7 b: Endpoint Specific Guidance.

c. Phototransformation in air.

Muscalure; cis-tricos-9-ene is susceptible to photochemical degradation in the gas phase by OH-radicals and ozone, with half-life of 4.7 h and 2.1 h, respectively. Based on these results, accumulation or long-range transport of muscalure; cis-tricos-9-ene in air is not expected.

2. Aquatic Bioaccumulation.

Experimental BCF data was not available and therefore, two BCF values were estimated in the dossier using the log Kow > 8.2 (Competent Authority Report, CAR; Doc. III-A3, Doc. IV-A 3.9/01) (CAR, 2009).

First, the BCFfish was calculated according to the equation provided in the Technical Guidance Document (TGD) on Risk assessment and a value of log BCF = 4.3 was obtained which indicated a high potential for bioaccumulation. However it should be noted that this mathematical relationship has a high degree of uncertainty because of the hydrophobic properties of Muscalure.

Second, based on calculations with the EPI SUITE software BCFBAFWIN v3.00, a log BCFfish of 2.9 was obtained, which is lower than the calculated BCF from the TGD equation.

3. Aquatic toxicity.

Two acute-tests on fish and Daphnia were reported in the CLH report.

The acute toxicity of muscalure; cis-tricos-9-ene was investigated on rainbow trout in a semi-static study for 96 h. The LC_{50} values could not be calculated because no mortality up to the highest tested concentration of 100 mg/L had been observed. The test concentrations were far in excess of the water solubility (7µg/L). This test shows some deficiencies such as the actual exposure concentration could not accurately be established due to the poor solubility of the test substance. In addition, the un-dissolved material present may have disturbed the test system.

The acute toxicity of muscalure; cis-tricos-9-ene to daphnia was investigated in a static study with measured concentrations of muscalure; cis-tricos-9-ene, which were far below nominal values at the end of the study. Test concentrations exceeded the water solubility of muscalure. The LC_{50} was established at 0.25 mg/L (mean measured concentration), effects found at higher values, 0.83 mg/L (mean measured concentration), were attributed to a physical effect (the animals were trapped in a transparent fleece).

A test on microalgae was not supplied following the application of the Guidance on Data Requirements for active substances in biocidal products under Directive 98/8/EC (ECB, 2000, 2008)..

Comments received during public consultation

Two comments on the environmental section were submitted by France. The first comment concerned biodegradation and the fact that the assessment for this endpoint should be based on the intrinsic properties of the substance and not upon the intended

use, as has been presented by the dossier submitter. In the revised CLH report, the dossier submitter deleted argumentation about the intended indoor use in the biodegradation section, but this argumentation is still present within the CLH report.

The second comment referred to the aquatic toxicity of this substance that should be considered higher than the threshold value of 1 mg/L, if the result of the daphnia test was expressed as a value of EC_{50}>0.25 mg/L. An argumentation why the aquatic toxicity of daphnia should be considered higher was added to the revised CLH report, as follows: "…At 0.83 mg/L the observed effects on mobility were attributed to physical burden. Therefore it is considered that an EC_{50} based on toxicological effects would be higher and in any case exceed 1mg/L".

Assessment and comparison with the classification criteria

According to the dossier submitter, the assessment of cis-tricos-9-ene has been carried out under consideration of the Guidance for waiving data requirements for pheromones for inclusion in Annex I/IA of Directive 98/8/EC. However, this Guidance emphasised that "…as data required for classification and labelling cannot be generated solely to satisfy this purpose, this evaluation considers only the data that would be required to satisfy biocidal data requirements and does not consider the classification and labelling requirements…". Thus, for classification purposes, intrinsic properties of the substance should be taken into consideration, and therefore, the degradation in the environment, bioaccumulation and the aquatic toxicity should be clearly established and described.

Biodegradation:

QSARs estimations have been used to study biodegradation, and according to these results it is reasonable to assume that muscalure; cis-tricos-9-ene will be rapidly degraded to CO2 and water in environmental compartments.

This information is supported by OECD Screening Information Data Set (OECD SIDS, 2004) reported in Doc. IIA of the CAR prepared for Muscalure (CAR, 2009).

In this work C20-C24 branched and linear alkenes (>70% branched) were tested in an OECD 301B test. The internal olefins attained a total of 92% degradation after 28 days and met the 10-day window validity criterion=. The toxicity control attained 100% degradation after 28% days confirming that the test material was not toxic to sewage treatment microorganisms used in the study. All validity criteria required were achieved; therefore C20-24 alkenes, branched and linear can be considered to be readily biodegradable under OCDE 301B.

Cis-tricos-9-ene is structurally quite similar to these internal olefins, it is a C23 alkene, and therefore the results from this test can be used to confirm the QSAR estimations.

It is reasonable to assume that cis-tricos-9-ene is rapidly/readily degradable.

Bioaccumulation:

experimental BCF data was not available and therefore, two BCF values were estimated in the dossier using the log Kow > 8.2 (CAR; Doc. III-A3, Doc. IV-A 3.9/01). Both BCFfish values estimated are above the cut-off values reported in CLP (section 4.1.2.8.1) but are not reliable due to the hydrophobic properties of Muscalure.

Aquatic toxicity:

the CLH report only contains information about short-term toxicity of cis-tricos-9-ene in fish and Daphnia, there is no information regarding toxicity in microalgae.

The LC_{50} value for the acute toxicity to fish could not be calculated because no mortality up to the nominal highest tested concentration of 100 mg/L was observed. This concentration was far above the water solubility of muscalure; cis-tricos-9-ene (< 7 x 10-6 g/L 20°C).

The acute toxicity test in Daphnia shows that the highest tested nominal concentration causing no effects after 48 hours was 10 mg/L (equal to 0.25 mg/L mean measured concentration). However, effects appear at tested concentration of 100 mg/L (n) (equal to 0.82 mg/L), these effects were attributed to a physical effect (the animals were trapped in a transparent fleece, microscopically assessed), therefore it is possible to establish a LC_{50} of >0.25 mg/L (mean measured concentrations).

According to the Guidance on the Application of Regulation (EC) No 1272/2008 relating to poorly soluble substances:

a. Where the acute toxicity is recorded at levels in excess of water solubility, the L(E)C50 for classification purposes may be considered to be equal to or below the measured water solubility. In such circumstances it is likely that Chronic Category 1 and/or Acute Category 1 should be applied. In making this decision, due attention should be paid to the possibility that the excess undissolved substances may have given rise to physical effects on the test organism. Where this is considered the likely cause of the effects observed, the test should be considered as invalid for classification purposes.

b. Where no Acute toxicity is recorded at levels in excess of water solubility, the $L(E)C_{50}$ for classification purposes may be considered to be greater than the measured water solubility. In such circumstances, consideration should be given to whether the Chronic Category 4 should apply. In making a decision that the substance shows no acute toxicity, due account should be taken of the techniques used to achieve the maximum dissolved concentrations. Where these are not considered as adequate, the test should be considered as invalid for classification purposes;

The acute toxicity test in fish shows some deficiencies. The actual exposure concentration was not accurately established due to the poor solubility of muscalure and the undissolved material. However, the study was considered reliable (klimish score 2) (CAR,2009). The conclusion of the study is that the LC_{50} for fish is greater than the water solubility. From this it appears that cis-tricos-9-ene does not meet the criteria for Aquatic Acute 1 and, considering the fact that cis-tricos-9-ene is considered to be rapidly degradable (from QSAR), the safety net classification criteria (chronic 4) is not met.

With the Daphnia toxicity test, the acute toxicity is also recorded at levels in excess of the water solubility, however, according to the dossier submitter, this effect was attributed to physical effects, and therefore, according to Guidance on the application of Regulation (EC) No. 1272/2008, therefore, the test should be considered invalid for classification purposes.

According to OECD SIDS (2004), the higher molecular weight olefins, those greater than C10, whose water solubility is low, are not expected to cause acute aquatic toxicity. Testing with water accommodated fractions of C20-24 internal branched and linear olefins (similar to muscalure) showed no aquatic toxicity in acute aquatic tests with fish, invertebrates and algae (see table 3 - additional key elements). The end-points for the three trophic levels are greater than the water solubility, which is in agreement with the available toxicity data to fish for cis-tricos-9-ene.

Taking into account this information, RAC agreed with the DS's proposal not to classify muscalure; cis-triscos-9-ene for environmental hazard.

CLP classification:

Acute hazard: Not classified.

Chronic hazard: Not classified. No toxic effects were recorded up to the water solubility. Furthermore, muscalure; cis-tricos-9-ene is considered to be rapidly biodegradable

DSD classification:

R50: Not classified.

Not classified as R53 assuming rapid degradation according to QSAR estimations.

Additional key elements

In order support the classification of cis-tricos-9-ene considering the few available data, information of substances with a structure similar to cis-tricos-9-ene has been included in the ODD. These data regarding biodegradation and aquatic acute toxicity have been obtained from the literature.

According to the work for the OECD HPV programme, OECD SIDS, 2004 and US EPA Chemical program C20-C24 branched and linear alkenes (>70% branched), which are structurally similar to cis-tricos-9-ene*, resulted in 92% degradation in 28 days fulfilling the validity criteria for OECD 301B test. Furthermore results of BIOWIN modelling of Olefins estimate that substances with structures similar to* cis-tricos-9-ene *are readily biodegradable, see tables below:*

Table 1. Biodegradation Olefins.

Olefins chemical substance	Internal olefins	Method	Biodegradation at 28 Days (%)
CAS Nº 182636-03-9 and 182636-05-1; C20-24	*(Eicosene, tetracosene) IO*	*301B CO2*	*92*

alkenes, branched and linear			

Table 2. Results of BIOWIN modelling for Olefins

Chemical	***CAS No.***	***Carbon number***	***Linear biodeg probability***	***Non-linear biodeg probability***	***Ultimate biodeg***	***Primary biodeg***	***MITI linear biodeg probability***	***MITI non-linear biodeg probabi ty***
1-tetracosene	*10192-32-2*	*24*	*0.70 fast*	*0.52*	*2.8 weeks*	*3.6 days-weeks*	*0.77 readily degradable*	*0.87 readily degrada e*
4-tetracosene		*24*	*0.80 fast*	*0.87*	*3.1 weeks*	*3.9 days*	*0.71 readily degradable*	*0.82 readily degrada e*
1-triacontene	*18435-53-5*	*30*	*0.66 fast*	*0.25*	*2.6 weeks-months*	*3.5 days-weeks*	*0.81 readily degradable*	*0.89 readily degrada e*
7-triacontene		*30*	*0.76 fast*	*0.67*	*2.9 weeks*	*3.8 days*	*0.76 readily degradable*	*0.84 readily degrada e*
1-tetracontene		*40*	*0.59 fast*	*0.04*	*2.3 weeks-months*	*3.3 days-weeks*	*0.89 readily degradable*	*0.91 readily degrada e*
6-tetracontene		*40*	*0.70 fast*	*0.22*	*2.6 weeks-months*	*3.6 days-weeks*	*0.84 readily degradable*	*0.87 readily degrada e*
Octadecene	*27070-58-2*	*18*	*0.74 fast*	*0.78 fast*	*2.9 weeks*	*3.8 days*	*0.72 readily degradable*	*0.86 readily degrada e*
1-octadecene	*112-88-9*	*18*	*0.74 fast*	*0.78 fast*	*2.9 weeks*	*3.8 days*	*0.72 readily degradable*	*0.86 readily degrada e*

The table below summarises the aquatic acute toxicity for C20-C24 branched and linear alkenes which are structurally similar to cis-tricos-9-ene*. The results show that the toxicity values for the three trophic levels are greater than the water solubility.*

Table 3. Aquatic acute toxicity of C20-C24 branched and linear alkenes (internal olefins) in fish, invertebrates and algae.

Internal olefins: C20-24			
Species	**Duration**	**Endpoints (mg/L)**	**Comments**
Algae			
Selenastrum capricornutum	72-hr EC50 72-hr EL0	>water solubility 1000 (nominal loading rates)	C20-24 internal linear and branched blend. Growth; static test; WAF; concentrations utilized in testing greater than solubility; no toxicity seen at 1000 mg/L.
Invertebrates			
Daphnia Magna	48-hr EC50 48-hr EL0	>water solubility 1000 (nominal loading rates)	C20-24 alkenes, linear and branched blend (internal olefins). Immobility; static test; WAF; concentrations utilized in testing greater than solubility; no toxicity seen at 1000 mg/L.
Vertebrates			
Rainbow trout *(Oncorhynchus mykiss)*	96-hr LC50 96-hr LL0	>water solubility 1000 (nominal loading rates)	C20-24 alkenes, linear and branched blend (internal olefins). Mortality; semi static test; WAF; concentrations utilized in testing greater than solubility; no toxicity seen at 1000 mg/L.

-

RAC evaluation of hazards to the ozone layer

Summary of the Dossier submitter's proposal

No information available

Comments received during public consultation

No comments received

Additional key elements

-

Assessment and comparison with the classification criteria

This endpoint was not assessed by the RAC, as the CLH report does not contain data about this endpoint and no comments were submitted during public consultation.

Supplemental information - In depth analyses by RAC

-

6 OTHER INFORMATION

Not available.

7 REFERENCES

Section point/ reference number from the risk assessment report on Cis-tricos-9-ene (Biodides)	**Year**	**Title** **Testing Facility** **Owner / Source (where different from owner)** **Report No** **GLP or GEP status (where relevant)** **Published or not**	**Data protection claimed** **yes/no**	**Owner**
A 2.8 (= A 4.1/01) Confidential	1999	Muscalure Technical, five batch analysis. TNO Nutrition and Food Research Institute. Report no. V 98.1116. GLP Unpublished	Y	Denka Int.
A 2.10/01	2004	Decrease of muscalure in Flybait at room temperatures in course of time. Denka report. No GLP Unpublished	Y	Denka Int.
A 2.10/02	2006	Flylure granulate production process Denka report. No GLP Unpublished	Y	Denka Int.
A 2.10/03	2007	Document in response to request from Austria; ENVIRON, project no. DI-MDO-20070050 No GLP Unpublished	Y	Denka Int.
A 3.1.1/ 01 A 3.1.2/ 02	2006	Determination of the melting and boiling temperature of muscalure by differential scanning calorimetry. NOTOX B.V. Project 450438. GLP Unpublished	Y	Denka Int.
A 3.1.1/ 01 A 3.1.2/ 02	2006	Determination of the melting and boiling temperature of muscalure technical by differential scanning calorimetry. NOTOX B.V. Project 450585. GLP Unpublished	Y	Denka Int.
A 3.1.3	2006	Determination of the density (liquid) of muscalure. NOTOX B.V. Project 450449. GLP Unpublished	Y	Denka Int.
A 3.2	2006	Determination of the vapour pressure of muscalure by the static method. Project 450451. NOTOX B.V. Project 450451. GLP Unpublished	Y	Denka Int.

Section point/ reference number from the risk assessment report on Cis-tricos-9-ene (Biodides)	**Year**	**Title** **Testing Facility** **Owner / Source (where different from owner)** **Report No** **GLP or GEP status (where relevant)** **Published or not**	**Data protection claimed** **yes/no**	**Owner**
A 3.2.1	2006	Calculation of Henry's law constant of muscalure. NOTOX B.V. Project 450462. GLP Unpublished	Y	Denka Int.
A 3.3/01	2006	Determination of appearance of muscalure. NOTOX B.V. Project 450473. GLP Unpublished	Y	Denka Int.
A 3.3/02	2006	Determination of appearance of muscalure technical.. NOTOX B.V. Project 450574 GLP Unpublished	Y	Denka Int.
A 3.3/03	2006	Sporadic colouration of technical muscalure Denka report. No GLP Unpublished	Y	Denka Int.
A 3.4/01	2006	Determination of the UV-VIS absorption spectra of muscalure. NOTOX B.V. Project 450506. GLP Unpublished	Y	Denka Int.
A 3.4/02	2006	Determination of the IR absorption spectra of muscalure. NOTOX B.V. Project 450484. GLP Unpublished	Y	Denka Int.
A 3.4/03	2006	Determination of the 1H NMR spectrum of muscalure. NOTOX B.V. Project 450495. GLP Unpublished	Y	Denka Int.
A 3.4/04	2005	Determination of the mass spectrum of muscalure. NOTOX B.V. Project 450541. GLP Unpublished	Y	Denka Int.
A 3.5	2006	Determination of the water solubility of muscalure at 3 pH values. NOTOX B.V. Project 450517. GLP Unpublished	Y	Denka Int.

Section point/ reference number from the risk assessment report on Cis-tricos-9-ene (Biodides)	**Year**	**Title** **Testing Facility** **Owner / Source (where different from owner)** **Report No** **GLP or GEP status (where relevant)** **Published or not**	**Data protection claimed** **yes/no**	**Owner**
A 3.6	2006	Determination of the dissociation constant(s) of muscalure in water. NOTOX B.V. Project 450552. GLP Unpublished	Y	Denka Int.
A 3.7	2006	Solubility in organic solvents by room temperature of Muscalure Technical No GLP Unpublished	Y	Denka Int.
A 3.9	2006	Determination of the partition coefficient (n-octanol/water) of muscalure at 3 pH values. NOTOX B.V. Project 450528. GLP Unpublished	Y	Denka Int.
A 3.10	2006	The housefly pheromone muscalure as biocidal active substance. Statement on the thermal stability of cis-tricos-9-ene (muscalure), ENVIRON Nethetherlands B.V. Report no. Di-mbd-20060050 No GLP (Statement) Unpublished	Y	Denka Int.
A 3.11/01	2006	Statement on the pyrophoric properties of muscalure technical. NOTOX B.V. Project 450596. GLP Unpublished	Y	Denka Int.
A 3.11/02	2006	Determination of the auto-ignition temperature (liquid) of muscalure technical. NOTOX B.V. Project 450607. GLP Unpublished	Y	Denka Int.
A 3.12	2006	Determination of the flash-point of muscalure technical. NOTOX B.V. Project 450618. GLP Unpublished	Y	Denka Int.
A 3.14	2006	Determination of the viscosity of muscalure technical. NOTOX B.V. Project 450664. GLP Unpublished	Y	Denka Int.

Section point/ reference number from the risk assessment report on Cis-tricos-9-ene (Biodides)	**Year**	**Title** **Testing Facility** **Owner / Source (where different from owner)** **Report No** **GLP or GEP status (where relevant)** **Published or not**	**Data protection claimed** **yes/no**	**Owner**
A 3.15	2006	Statement on the explosive properties of muscalure technical. NOTOX B.V. Project 450629. GLP Unpublished	Y	Denka Int.
A 3.16	2006	Determination of the oxidizing properties of muscalure technical. NOTOX B.V. Project 450631. GLP Unpublished	Y	Denka Int.
A 3.17/01	2006	Determination of the corrosion characteristics of muscalure technical. NOTOX B.V. Project 450642. GLP Unpublished	Y	Denka Int.
A 3.17/02	2006	Details on packaging No GLP Unpublished	Y	Denka Int.
A 4.1/01 (= 2.8) Confidential	1999	Muscalure Techn., five batch analysis. TNO Nutrition and Food Research Institute. Report no. V 98.1116. GLP Unpublished	Y	Denka Int.
A 4.1/01	2011	5-Batch Analysis of Muscalure; Final Report; BioGenius, Study No. Mo4176 GLP Unpublished	Y	Denka Int.
A 4.1/02	2011	Validation of Method MV038: GC-Determination of (Z)-9-Tricosene and Corresponding Impurities in Z-9-Tricosene (Technical Material); BioGenius, Study No. Mo4066 GLP Unpublished	Y	Denka Int.
A 4.2c	2006	Development and validation of an analytical method for the analysis of Z-9-Tricosene (active ingredient in Muscalure) in double distilled water. NOTOX B.V., Project no. 450539 GLP Unpublished	Y	Denka Int.

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Section point/ reference number from the risk assessment report on Cis-tricos-9-ene (Biodides)	**Year**	**Title** **Testing Facility** **Owner / Source (where different from owner)** **Report No** **GLP or GEP status (where relevant)** **Published or not**	**Data protection claimed** **yes/no**	**Owner**
Translation of A 5.1.6	1981	Onderzoek naar de toepasbaarheid van feromonen bij de bestrijding van de huisvlieg (Musca domestica) onder praktijkomstandigheden. (Translation: Research into the applicability of pheromones in the control of houseflies (Musca domestica) in practice). TNO Maatschappelijke Technologie. Report no. CL 81/152. No GEP Unpublished	Y	Denka Int.
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Translation of A 5.1.7	1983	Onderzoek naar de toepasbaarheid van feromonen bij de bestrijding van de huisvlieg (Musca domestica) onder praktijkomstandigheden. (Translation: Research into the applicability of pheromones in the control of houseflies (Musca domestica) in practice). TNO Maatschappelijke Technologie. Report no. CL 82/207. No GEP Unpublished	Y	Denka Int.
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Translation of A 5.1.8	1982	Onderzoek naar de toepasbaarheid van feromonen bij de bestrijding van de huisvlieg (Musca domestica) onder praktijkomstandigheden. (Translation: Research into the applicability of pheromones in the control of houseflies (Musca domestica) in practice). TNO Maatschappelijke Technologie. Report no. CL 82/115. No GEP Unpublished	Y	Denka Int.

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A 5.1.9	1984 a	Onderzoek naar de bruikbaarheid van de combinatie elektrocutieval/UV licht/muscalure bij de bestrijding van de huisvlieg (Musca domestica) in pluimveebedrijven. (Translation: Research into the usefulness of the combination electric grid/UV light/muscalure in the control of houseflies (Musca domestica) in poultry farms). TNO Maatschappelijke Technologie. Report no. R 84/15. No GEP Unpublished	Y	Denka Int.
Translation of A 5.1.9	1984 a	Onderzoek naar de bruikbaarheid van de combinatie elektrocutieval/UV licht/muscalure bij de bestrijding van de huisvlieg (Musca domestica) in pluimveebedrijven. (Translation: Research into the usefulness of the combination electric grid/UV light/muscalure in the control of houseflies (Musca domestica) in poultry farms). TNO Maatschappelijke Technologie. Report no. R 84/15. No GEP Unpublished	Y	Denka Int.
A 5.1.10	1984 b	Een oriënterend onderzoek naar de bruikbaarheid van muscalure in aerosolvorm in combinatie met een elecrocutieval/UV-licht bij de bestrijding van de huisvlieg (Musca domestica). (Translation: A pilot research into the usefulness of muscalure as an aerosol in combination with an electric grid/UV light for the control of the house fly (Musca domestica)). TNO Maatschappelijke Technologie. Report no. R 84/177. No GEP Unpublished	Y	Denka Int.
Translation of A 5.1.10	1984 b	Een oriënterend onderzoek naar de bruikbaarheid van muscalure in aerosolvorm in combinatie met een elecrocutieval/UV-licht bij de bestrijding van de huisvlieg (Musca domestica). (Translation: A pilot research into the usefulness of muscalure as an aerosol in combination with an electric grid/UV light for the control of the house fly (Musca domestica)). TNO Maatschappelijke Technologie. Report no. R 84/177. No GEP Unpublished	Y	Denka Int.

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A 5.1.14	1993	Fly-bait trials. Spain. KenoGard No GEP Unpublished	Y	Denka Int.
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A 5.1.16	1990	Bekaempfung der adulten der Hausfliege im Kuhstall. Plüss-Staufer AG. Study no. IST 01 90. Unpublished	Y	Denka Int.
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A 5.1.19	1996	Field evaluation of triflumuron and methomyl for control of the housefly Musca domestica. Danish Pest Infestation Laboratory. Report no. 4-1996. No GLP Unpublished	Y	Denka Int.
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A 5.1.23	1992	Evaluation of methomyl bait plus Muscamone fly attractant against Musca domestica L. in a chicken farm in Malaysia. Jpn. J. Zool., vol. 43 (1992), 287-289. No GLP Published	N	
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A 5.1.27	2008	Room test to determine the attractiveness of different concentrations of Flylure (Z-9 tricosene) to male and female adult houseflies, Musca domestica. I2LResearch Ltd. Report no. 08/19 No GLP Unpublished	Y	Denka Int.
A 5.1.28	2008	Effects of mucalure on female houseflies and housefly parasitoids. ENVIRON Netherlands BV No GLP Unpublished	Y	Denka Int.
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A 5.1.33	1974	Evaluation of (Z)-9-tricosene for attractancy for Musca domestica in the field. The Florida Entomologist 57 (1974) 136-140. No GLP Published	N	
A 5.1.34	1975	Effect of muscalure on house fly traps of different color and location in poultry houses. Journal of the Georgia Entomological Society 10 (1975) 165-168. No GLP Published	N	
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A 6.1.4e	1990 b	Acute eye irritation/ corrosion study with muscalure in the rabbit. RCC NOTOX B.V. Project ID 038587. GLP Unpublished	Y	Denka Int.
A 6.1.5	1991	Contact hypersensitivity to MUSCALURE in the Albino Guinea Pig (Maximization-Test). RCC NOTOX B.V. Project ID 051637. GLP Unpublished	Y	Denka Int.

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A 6.6.1	2006	Evaluation of the mutagenic activity of muscalure technical in the Salmonella typhimurium reverse mutation assay and the Escherichia coli reverse mutation assay (with independent repeat) NOTOX B.V. Project no. 456457 GLP Unpublished	Y	Denka Int.
A 6.6.2	2008	Chromosomal aberration test with Muscalure in cultured Chinese Hamster Ovary (CHO) cells. TNO Quality of Life. Project V7902/02 GLP Unpublished	Y	Denka Int.
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A 7.5.3.1.1	1990 a	Acute oral toxicity study in bobwhite quail with muscalure. Limit. RCC NOTOX B.V. Project ID 038598. GLP Unpublished	Y	Denka Int.
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8 ANNEXES

Confidential Annex.